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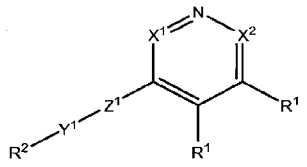
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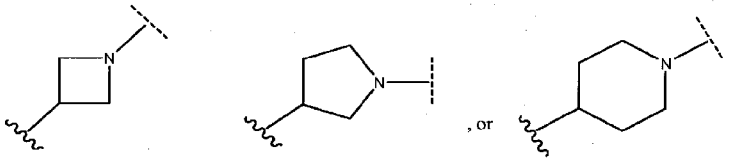
[Continued on next page]

(54) Title: PYRIDAZINE AND PYRIDINE DERIVATIVES AS NAMPT INHIBITORS



Formula (IC);

Z1 is



(57) Abstract: Disclosed are compounds of formula (IC), or a therapeutically acceptable salt thereof which inhibit the activity of NAMPT, compositions containing the compounds and methods of treating diseases during which NAMPT is expressed.

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PYRIDAZINE AND PYRIDINE DERIVATIVES AS NAMPT INHIBITORS

This application claims priority to United States Provisional Application Serial No. 61/645692, filed May 11, 2012, United States Provisional Application Serial No. 61/719013, filed October 26, 2012, and United States Provisional Application Serial No. 61/779756, filed March 13, 2013, which are incorporated by reference in their entirety.

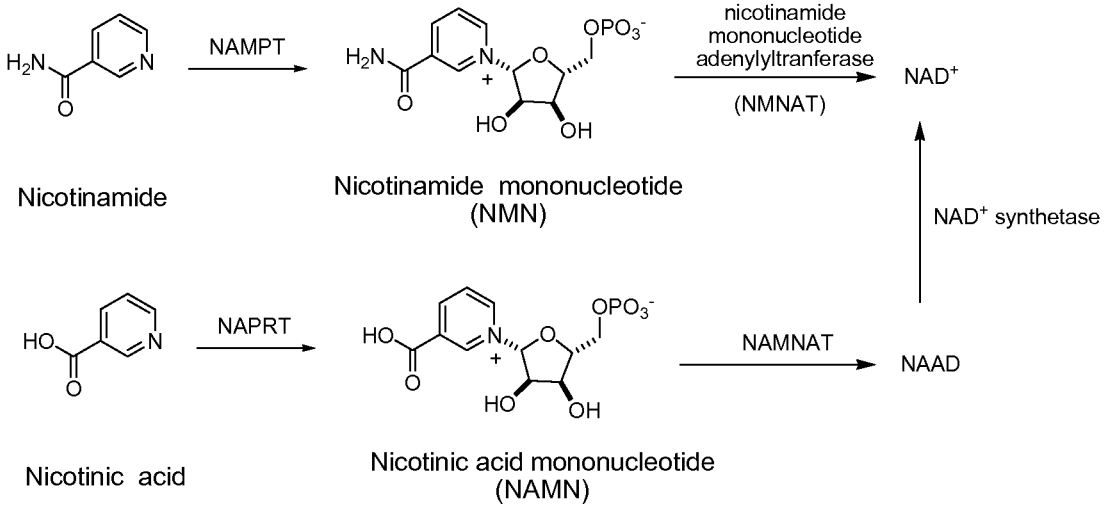
FIELD OF THE INVENTION

This invention pertains to compounds which inhibit the activity of NAMPT, compositions containing the compounds, and methods of treating diseases during which NAMPT is expressed.

BACKGROUND OF THE INVENTION

NAD+ (nicotinamide adenine dinucleotide) is a coenzyme that plays a critical role in many physiologically essential processes (Ziegkel, M. *Eur. J. Biochem.* **267**,1550-1564, 2000). NAD is necessary for several signaling pathways including among others poly ADP-ribosylation in DNA repair, mono-ADP-ribosylation in both the immune system and G-protein-coupled signaling, and NAD is also required by sirtuins for their deacetylase activity (Garten, A. et al *Trends in Endocrinology and Metabolism*, **20**, 130-138, 2008).

NAMPT (also known as pre-B-cell-colony-enhancing factor (PBEF) and visfatin) is an enzyme that catalyzes the phosphoribosylation of nicotinamide and is the rate-limiting enzyme in one of two pathways that salvage NAD.



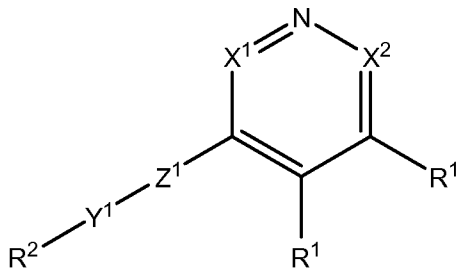
Increasing evidence suggests that NAMPT inhibitors have potential as anticancer agents. Cancer cells have a higher basal turnover of NAD and also display higher energy requirements compared with normal cells. Additionally, increased NAMPT expression has been reported in colorectal cancer (Van Beijnum, J.R. et al *Int. J. Cancer* **101**, 118-127, 2002)

and NAMPT is involved in angiogenesis (Kim, S.R. et al. *Biochem. Biophys. Res. Commun.* **357**, 150-156, 2007). Small-molecule inhibitors of NAMPT have been shown to cause depletion of intracellular NAD+ levels and ultimately induce tumor cell death (Hansen, CM et al. *Anticancer Res.* **20**, 42111-4220, 2000) as well as inhibit tumor growth in xenograft models (Olese, U.H. et al. *Mol Cancer Ther.* **9**, 1609-1617, 2010).

NAMPT inhibitors also have potential as therapeutic agents in inflammatory and metabolic disorders (Galli, M. et al *Cancer Res.* **70**, 8-11, 2010). For example, NAMPT is the predominant enzyme in T and B lymphocytes. Selective inhibition of NAMPT leads to NAD+ depletion in lymphocytes blocking the expansion that accompanies autoimmune disease progression whereas cell types expressing the other NAD+ generating pathways might be spared. A small molecule NAMPT inhibitor (FK866) has been shown to selectively block proliferation and induce apoptosis of activated T cells and was efficacious in animal models of arthritis (collagen –induced arthritis) (Busso, N.et al. *Plos One* **3**, e2267, 2008). FK866 ameliorated the manifestations of experimental autoimmune encephalomyelitis (EAE), a model of T-cell mediated autoimmune disorders. (Bruzzone, Set al. *Plos One* **4**, e7897, 2009). NaMPT activity increases NF-kB transcriptional activity in human vascular endothelial cell, resulting in MMP-2 and MMP-9 activation, suggesting a role for NAMPT inhibitors in the prevention of inflammatory mediated complications of obesity and type 2 diabetes (Adya, R. et. Al. *Diabetes Care*, **31**, 758-760, 2008).

SUMMARY OF THE INVENTION

One embodiment of this invention, therefore, pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (IC)



Formula (IC);

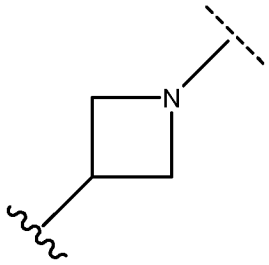
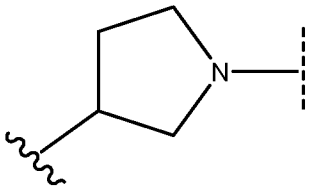
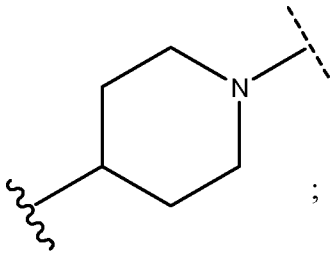
X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

Z^1 is

wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl;

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^3, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, and heterocyclyl; wherein each R^3 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, $C(O)NHOH$, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, C(O)H,

C(O)OH, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^3 aryl, cycloalkyl, cycloalkenyl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^6)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, C(O)NHOH, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^5, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^5 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), C(O)OH, N_3, CN, NH_2, F, Cl, Br and I;

R^6, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^6 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^8, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^9, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, R^5, R^6, R^7, R^8, and R^9 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

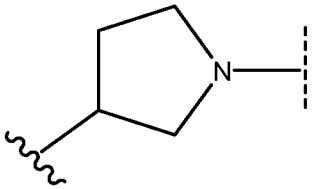
R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

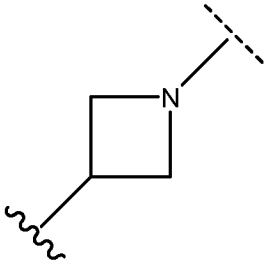
R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

with the proviso that

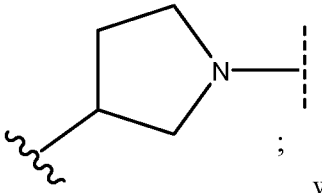
when X^1 is CR^1 and X^2 is CR^1; R^1 is hydrogen; Y^1 is NHC(O); Z^1 is



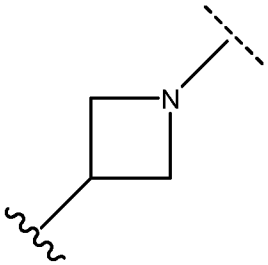
; and R^2 is pyrrolyl; the R^2 pyrrolyl is not substituted with two alkyl groups. In another embodiment of Formula (IC), Z^1 is



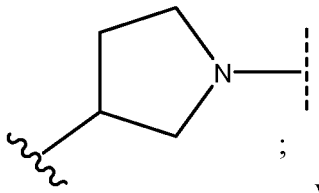
; wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (IC), Z^1 is



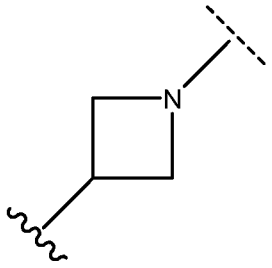
; wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (IC), Z^1 is



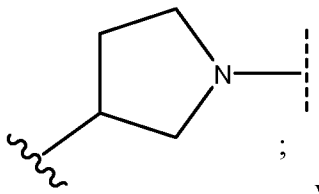
; wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl; and Y^1 is C(O)NH. In another embodiment of Formula (IC), Z^1 is



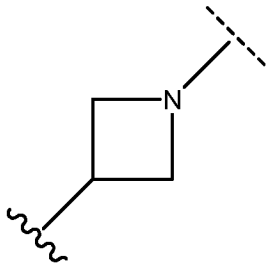
; wherein indicates the point of attachment to Y^1 and indicates the point of attachment to the nitrogen containing heteroaryl; and Y^1 is C(O)NH. In another embodiment of Formula (IC), Z^1 is



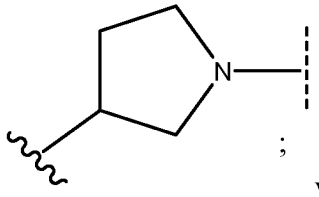
; wherein indicates the point of attachment to Y^1 and indicates the point of attachment to the nitrogen containing heteroaryl; Y^1 is C(O)NH; and X^1 is N and X^2 is CR^1. In another embodiment of Formula (IC), Z^1 is



; wherein indicates the point of attachment to Y^1 and indicates the point of attachment to the nitrogen containing heteroaryl; Y^1 is C(O)NH; X^1 is N and X^2 is CR^1. In another embodiment of Formula (IC), Z^1 is

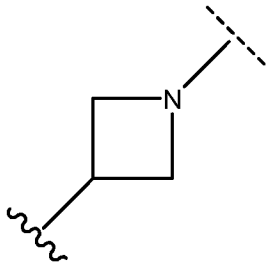


; wherein indicates the point of attachment to Y^1 and indicates the point of attachment to the nitrogen containing heteroaryl; Y^1 is C(O)NH; X^1 is N and X^2 is CR^1; wherein R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4. In another embodiment of Formula (IC), Z^1 is

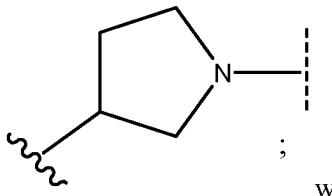


; wherein indicates the point of attachment to Y^1 and indicates the point of attachment to the nitrogen containing heteroaryl; Y^1 is C(O)NH; X^1 is N and X^2 is CR^1; wherein R^2 is phenyl; wherein each R^2 phenyl is substituted with one

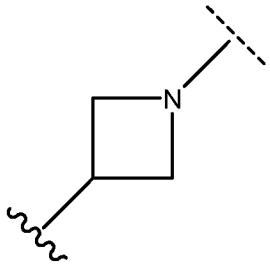
substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4. In another embodiment of Formula (IC), Z^1 is



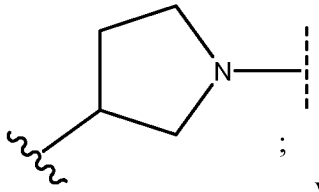
; wherein indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl; Y^1 is C(O)NH; X^1 is N and X^2 is CR^1; wherein R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4; and R^1, at each occurrence, is hydrogen. In another embodiment of Formula (IC), Z^1 is



; wherein  indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl; Y^1 is C(O)NH; X^1 is N and X^2 is CR^1; wherein R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4; and R^1, at each occurrence, is hydrogen. In another embodiment of Formula (IC), Z^1 is



; wherein indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl; Y^1 is C(O)NH; X^1 is N and X^2 is CR^1; wherein R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4; R^1, at each occurrence, is hydrogen; and R^4, at each occurrence, is heterocyclyl. In another embodiment of Formula (IC), Z^1 is



; wherein  indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl; Y^1 is C(O)NH; X^1 is N

and X^2 is CR^1; wherein R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4; and R^1, at each occurrence, is hydrogen; and R^4, at each occurrence, is heterocyclyl.

Still another embodiment pertains to compounds, which are

1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(2-cyanopyridin-3-yl)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-[2-(trifluoromethyl)pyridin-3-yl]azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(4-methylpyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(4-fluoropyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-[4-(trifluoromethyl)pyridin-3-yl]azetidine-3-carboxamide;

tert-butyl 4-[4-({[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate;

tert-butyl 4-[4-({[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate;

1-(pyridin-3-yl)-N-(4-{1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-[4-({1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-[4-({1-[(2R)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[1-(pyridin-3-yl)azetidin-3-yl]-4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}benzamide;

N-(4-{1-[(2S)-2-methylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)-N-[1-(pyridin-3-yl)azetidin-3-yl]benzamide;

4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}-N-[1-(pyridin-3-yl)azetidin-3-yl]benzamide;

1-(pyridin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-(4-{[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbamoyl}phenoxy)piperidine-1-carboxylate;

tert-butyl 4-(4-{[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbamoyl}phenoxy)piperidine-1-carboxylate;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-[4-({1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-{4-[(1-pentanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylpentanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-ethoxypropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-butanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(ethoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(N-acetyl-L-leucyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(morpholin-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(furan-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methoxypyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylmethyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpentyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-ethylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-cyclopropylethyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylmethyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylmethyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylmethyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpentyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methoxypyridin-3-yl)azetidine-3-carboxamide;

1-(4-cyanopyridin-3-yl)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-pentanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(morpholin-4-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(pyrrolidin-1-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(5-oxo-D-prolyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperazin-1-yl)acetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(5-oxo-L-prolyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(morpholin-4-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(piperidin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide;

N-(4-{1-[(2S)-2-methylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(pyridazin-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-[4-(1-pentanoylpiperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(morpholin-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(pyrrolidin-1-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(5-oxo-D-prolyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperazin-1-yl)acetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(5-oxo-L-prolyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[3-(morpholin-4-yl)propanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[3-(piperidin-1-yl)propanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]azetidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-{4-[(1-benzoylazetidin-3-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-hydroxy-2-methylpropanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-pentanoylazetidin-3-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclobutylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(3,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]furan-2-carboxamide;

(3S)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

tert-butyl 4-(4-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}phenyl)piperidine-1-carboxylate;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-pentanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-hexanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-heptanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(but-3-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(pent-4-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(methylsulfanyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-nitropropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(pent-4-ynoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{1-[(3,5-dimethylphenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(5-methylpyrazin-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[(pyrimidin-2-ylsulfanyl)acetyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-(4-{1-[(1-acetylpiperidin-4-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(diphenylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(5-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluoro-4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-tert-butylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-fluoro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-chloro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylphenoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{1-[(3-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2R)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[N-(furan-2-ylcarbonyl)glycyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(benzyloxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-1-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(N-benzoylglycyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[4-(thiophen-2-yl)butanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclobutylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-{N-[(4-methylphenyl)sulfonyl]glycyl}piperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,3-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-2-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-phenylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,6-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(phenylsulfonyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2,5-dimethylfuran-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-oxopropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(1,3-thiazol-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2S)-2-methylbutanoyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydro-2H-pyran-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethoxy)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(thiophen-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3,5-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[3-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2,4-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(5-methylthiophen-2-yl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[3-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(pyridin-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methyl-2-phenylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(methoxyacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(thiophen-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[3-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[4-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[4-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(3,3,3-trifluoropropanoyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[difluoro(phenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2S)-2-methylbutanoyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydro-2H-pyran-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethoxy)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(thiophen-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3,5-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[3-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2,4-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(5-methylthiophen-2-yl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[3-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(pyridin-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methyl-2-phenylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(methoxyacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(thiophen-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[3-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[4-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[4-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(3,3,3-trifluoropropanoyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[difluoro(phenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-(4-{1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[difluoro(phenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-tert-butylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]sulfonyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,5-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-dimethylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-dichlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(phenylacetyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylalanyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

tert-butyl 4-(2-methyl-1-oxo-1-{4-[4-({[1-(pyridin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidin-1-yl}propan-2-yl)piperazine-1-carboxylate;

N-(4-{1-[2-methyl-2-(piperazin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[(3R)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3R)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3S)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3R)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)piperidine-4-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}piperidine-4-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2S)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2R)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-methylphenoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2,6-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-1-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[4-(thiophen-2-yl)butanoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-2-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[3-(phenylsulfonyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(N-benzoylglycyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-5-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-fluoropyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-fluoro-6-methylpyridin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-heptanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-hexanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3,5-dimethylphenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[2-chloro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(5-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(diphenylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(pent-4-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[2-fluoro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-tert-butylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(pent-4-ynoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-acetylpiperidin-4-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(but-3-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluoro-4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-4-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-methylpyridin-3-yl)azetidine-3-carboxamide;

2-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-1,3-thiazole-5-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(2-methylpyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]furan-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]furan-2-carboxamide;

N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-4-[1-(2-methylpropanoyl)piperidin-4-yl]benzamide;

N-(4-{1-[2-(piperazin-1-yl)ethyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

4-[1-(2-methylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]benzamide;

N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(3-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(4-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

(3S)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

5-[1-(2-methylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-(1-benzoylpiperidin-4-yl)-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-{1-[(2R)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}thiophene-2-carboxamide;

5-{1-[(1-methylpiperidin-4-yl)acetyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide;

(3S)-N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(propan-2-yl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylmethyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-2-ylmethyl)-1H-pyrazol-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-tert-butyl-1H-pyrazol-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2-methylbenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(4,4,4-trifluorobutanoyl)pyrrolidin-3-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(5-propyl-1,2,4-oxadiazol-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylazetidin-3-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-difluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-difluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[(1-benzoylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,3,4-oxadiazol-2-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-imidazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,2,4-oxadiazol-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-cyclopropyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-(5-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}thiophen-2-yl)piperidine-1-carboxylate;

tert-butyl 4-fluoro-4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidine-1-carboxylate;

5-(1-benzoylpiperidin-4-yl)-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylbenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(3-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(4-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[3-cyclopropyl-1-(2-hydroxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

1-(6-fluoropyridazin-3-yl)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[(1-benzoylpiperidin-4-yl)oxy]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[8-(2-methylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[8-(4,4,4-trifluorobutanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}azetidine-3-carboxamide;

N-[4-(8-benzoyl-8-azabicyclo[3.2.1]oct-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2-fluorobenzoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2,2-dimethylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{8-[(1-methylcyclopropyl)carbonyl]-8-azabicyclo[3.2.1]oct-3-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methoxyethyl)-3-(2-methylpropyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-[1-(pyridazin-3-yl)azetidin-3-yl]-5-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-fluoropiperidine-1-carboxylate;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-hydroxypiperidine-1-carboxylate;

N-[1-(pyridazin-3-yl)azetidin-3-yl]-5-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(cyclopropylcarbonyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[4-fluoro-1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(2-fluoro-4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoyl-4-fluoropiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)-4-fluoropiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butyl-3-tert-butyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(tetrahydro-2H-pyran-4-ylmethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(6-chloropyridazin-3-yl)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-3-fluorophenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(6-methylpyridazin-3-yl)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-ethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-{[4-methyl-1-(oxetan-3-yl)piperidin-4-yl]methyl}-1H-pyrazol-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]furan-2-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-aminopyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylic acid;

ethyl 1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate;

ethyl 1-phenyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate;

N-{6-[1-(2-fluorobenzoyl)piperidin-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

1-(6-methylpyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{6-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]pyridin-3-yl}azetidine-3-carboxamide;

N-{6-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{6-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)-1H-pyrazol-1-yl]piperidine-1-carboxylate;

N-(6-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}pyridin-3-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(1H-pyrazol-4-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(methylsulfanyl)acetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(1H-pyrazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(pent-4-ynoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(ethoxyacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-{4-[(1-hexanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(but-3-enoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(1,2-oxazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-butanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclobutylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-pentanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbenzoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{1-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-1H-pyrazol-4-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{1-[1-(2-fluorobenzoyl)piperidin-4-yl]-1H-pyrazol-4-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(phenylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2,2-dimethylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(3-methoxy-2,2-dimethylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-cyclopropylethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[2-(2-ethylpiperidin-1-yl)ethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(cyclobutylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2S)-butan-2-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(butylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2,2-dimethyltetrahydro-2H-pyran-4-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(1S)-1-cyclopropylethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({2-[methyl(phenyl)amino]ethyl}carbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1,1'-bi(cyclopropyl)-1-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(thiophen-3-ylcarbamoyl)phenyl]azetidine-3-carboxamide;

N-(4-{[(1R)-1-cyclopropylethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylpiperidin-4-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2R)-butan-2-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-azabicyclo[2.2.2]oct-3-ylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(tetrahydrofuran-3-ylmethyl)carbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(oxetan-3-ylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-methylcyclopropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclobutylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylcyclopropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-methoxy-2-methylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(cyclopropylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(2R)-tetrahydrofuran-2-ylmethyl]carbamoyl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3,3,3-trifluoropropyl)carbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(1-methylpiperidin-3-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3-methyloxetan-3-yl)methyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(2S)-tetrahydrofuran-2-ylmethyl]carbamoyl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(tetrahydro-2H-pyran-4-ylmethyl)carbamoyl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(tetrahydro-2H-pyran-4-ylcarbamoyl)phenyl]azetidine-3-carboxamide;

N-(4-{[(1-methylpiperidin-3-yl)methyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclopropylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclopentylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(benzylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(3-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(propylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(4-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylcyclobutyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(prop-2-en-1-ylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(cyclopropylacetyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(bicyclo[2.2.1]hept-2-ylacetyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3S)-tetrahydrofuran-3-ylcarbamoyl]phenyl}azetidine-3-carboxamide;

N-[4-({4-[2-(dimethylamino)ethyl]phenyl}carbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3R)-tetrahydrofuran-3-ylcarbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(2-methoxyethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-amino-2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2,2-dimethyl-3-(piperazin-1-yl)propyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-methyl-2-(piperazin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide; and pharmaceutically acceptable salts thereof.

Still another embodiment pertains to compounds of Formula (1A), selected from the group consisting of

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(methylsulfanyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide; and pharmaceutically acceptable salts thereof.

Another embodiment pertains to a composition for treating inflammatory and tissue repair disorders; particularly rheumatoid arthritis, inflammatory bowel disease, asthma and COPD (chronic obstructive pulmonary disease), osteoarthritis, osteoporosis and fibrotic diseases; dermatosis, including psoriasis, atopic dermatitis and ultra-violet induced skin damage; autoimmune diseases including systemic upus erythematosis, multiple sclerosis, psoriatic arthritis, ankylosing spondylitis, tissue and organ rejection, Alzheimer's disease, stroke, athersclerosis, restenosis, diabetes, glomerulonephritis, cancer, particularly wherein the cancer is selected from breast, prostate, lung, colon, cervix, ovary, skin, CNS, bladder, pancreas, leukemia, lymphoma or Hodgkin's disease, cachexia, inflammation associated with infection and certain viral infections, including Acquired Immune Deficiency Syndrome (AIDS), adult respiratory distress syndrome, and ataxia telengiectasia, said composition comprising an excipient and a therapeutically effective amount of a compound of Formula (IC), or pharmaceutically acceptable salts thereof.

Another embodiment pertains to a method of treating inflammatory and tissue repair disorders; particularly rheumatoid arthritis, inflammatory bowel disease, asthma and COPD (chronic obstructive pulmonary disease), osteoarthritis, osteoporosis and fibrotic diseases; dermatosis, including psoriasis, atopic dermatitis and ultra-violet induced skin damage; autoimmune diseases including systemic lupus erythematosis, multiple sclerosis, psoriatic arthritis, ankylosing spondylitis, tissue and organ rejection, Alzheimer's disease, stroke, athersclerosis, restenosis, diabetes, glomerulonephritis, cancer, particularly wherein the cancer is selected from breast, prostate, lung, colon, cervix, ovary, skin, CNS, bladder, pancreas, leukemia, lymphoma or Hodgkin's disease, cachexia, inflammation associated with infection and certain viral infections, including Acquired Immune Deficiency Syndrome (AIDS), adult respiratory distress syndrome, and ataxia telengiectasia in a patient, said method comprising administering to the patient a therapeutically effective amount of a compound of Formula (IC), or pharmaceutically acceptable salts thereof.

Another embodiment pertains to a method of treating inflammatory and tissue repair disorders; particularly rheumatoid arthritis, inflammatory bowel disease, asthma and COPD (chronic obstructive pulmonary disease), osteoarthritis, osteoporosis and fibrotic diseases;

dermatosis, including psoriasis, atopic dermatitis and ultra-violet induced skin damage; autoimmune diseases including systemic lupus erythematosis, multiple sclerosis, psoriatic arthritis, ankylosing spondylitis, tissue and organ rejection, Alzheimer's disease, stroke, athersclerosis, restenosis, diabetes, glomerulonephritis, cancer, particularly wherein the cancer is selected from breast, prostate, lung, colon, cervix, ovary, skin, CNS, bladder, pancreas, leukemia, lymphoma or Hodgkin's disease, cachexia, inflammation associated with infection and certain viral infections, including Acquired Immune Deficiency Syndrome (AIDS), adult respiratory distress syndrome, and ataxia telengiectasia or spleen cancer in a patient, said method comprising administering to the patient therapeutically effective amount of the compound of Formula (IC), or pharmaceutically acceptable salts thereof; and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent.

DETAILED DESCRIPTION OF THE INVENTION

This detailed description is intended only to acquaint others skilled in the art with Applicants' invention, its principles, and its practical application so that others skilled in the art may adapt and apply the invention in its numerous forms, as they may be best suited to the requirements of a particular use. This description and its specific examples are intended for purposes of illustration only. This invention, therefore, is not limited to the embodiments described in this patent application, and may be variously modified.

Abbreviations and Definitions

Unless otherwise defined herein, scientific and technical terms used in connection with the present invention shall have the meanings that are commonly understood by those of ordinary skill in the art. The meaning and scope of the terms should be clear, however, in the event of any latent ambiguity, definitions provided herein take precedent over any dictionary or extrinsic definition. In this application, the use of "or" means "and/or" unless stated otherwise. Furthermore, the use of the term "including", as well as other forms, such as "includes" and "included", is not limiting. With reference to the use of the words "comprise" or "comprises" or "comprising" in this patent application (including the claims), Applicants note that unless the context requires otherwise, those words are used on the basis and clear understanding that they are to be interpreted inclusively, rather than exclusively, and that Applicants intend each of those words to be so interpreted in construing this patent application, including the claims below. For a variable that occurs more than one time in any substituent or in the compound of the invention or any other formulae herein, its definition on each occurrence is independent of its definition at every other occurrence. Combinations of substituents are permissible only if such combinations result in stable compounds. Stable compounds are compounds which can be isolated in a useful degree of purity from a reaction mixture.

It is meant to be understood that proper valences are maintained for all combinations herein, that monovalent moieties having more than one atom are attached through their left ends, and that divalent moieties are drawn from left to right.

As used in the specification and the appended claims, unless specified to the contrary, the following terms have the meaning indicated:

The term "alkyl" (alone or in combination with another term(s)) means a straight-or branched-chain saturated hydrocarbyl substituent typically containing from 1 to about 10 carbon atoms; or in another embodiment, from 1 to about 8 carbon atoms; in another embodiment, from 1 to about 6 carbon atoms; and in another embodiment, from 1 to about 4 carbon atoms. Examples of such substituents include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, pentyl, iso-amyl, and hexyl and the like.

The term "alkenyl" (alone or in combination with another term(s)) means a straight-or branched-chain hydrocarbyl substituent containing one or more double bonds and typically from 2 to about 10 carbon atoms; or in another embodiment, from 2 to about 8 carbon atoms; in another embodiment, from 2 to about 6 carbon atoms; and in another embodiment, from 2 to about 4 carbon atoms. Examples of such substituents include ethenyl (vinyl), 2-propenyl, 3-propenyl, 1,4-pentadienyl, 1,4-butadienyl, 1-butenyl, 2-butenyl, and 3-butenyl and the like.

The term "alkynyl" (alone or in combination with another term(s)) means a straight-or branched-chain hydrocarbyl substituent containing one or more triple bonds and typically from 2 to about 10 carbon atoms; or in another embodiment, from 2 to about 8 carbon atoms; in another embodiment, from 2 to about 6 carbon atoms; and in another embodiment, from 2 to about 4 carbon atoms. Examples of such substituents include ethynyl, 2-propynyl, 3-propynyl, 2-butynyl, and 3-butynyl and the like.

The term "carbocyclyl" (alone or in combination with another term(s)) means a saturated cyclic (*i.e.*, "cycloalkyl"), partially saturated cyclic (*i.e.*, "cycloalkenyl"), or completely unsaturated (*i.e.*, "aryl") hydrocarbyl substituent containing from 3 to 14 carbon ring atoms ("ring atoms" are the atoms bound together to form the ring or rings of a cyclic substituent). A carbocyclyl may be a single-ring (monocyclic) or polycyclic ring structure.

A carbocyclyl may be a single ring structure, which typically contains from 3 to 8 ring atoms, more typically from 3 to 6 ring atoms, and even more typically 5 to 6 ring atoms. Examples of such single-ring carbocyclyls include cyclopropyl (cyclopropanyl), cyclobutyl (cyclobutanyl), cyclopentyl (cyclopentanyl), cyclopentenyl, cyclopentadienyl, cyclohexyl (cyclohexanyl), cyclohexenyl, cyclohexadienyl, and phenyl. A carbocyclyl may alternatively be polycyclic (i.e., may contain more than one ring). Examples of polycyclic carbocyclyls include bridged, fused, and spirocyclic carbocyclyls. In a spirocyclic carbocyclyl, one atom is common to two different rings. An example of a spirocyclic carbocyclyl is spiropentanyl. In a bridged carbocyclyl, the rings share at least two common non-adjacent atoms. Examples of

bridged carbocyclyls include bicyclo[2.2.1]heptanyl, bicyclo[2.2.1]hept-2-enyl, and adamantanyl. In a fused-ring carbocyclyl system, two or more rings may be fused together, such that two rings share one common bond. Examples of two- or three-fused ring carbocyclyls include naphthalenyl, tetrahydronaphthalenyl (tetralinyl), indenyl, indanyl (dihydroindenyl), anthracenyl, phenanthrenyl, and decalinyl.

The term "cycloalkyl" (alone or in combination with another term(s)) means a saturated cyclic hydrocarbyl substituent containing from 3 to 14 carbon ring atoms. A cycloalkyl may be a single carbon ring, which typically contains from 3 to 8 carbon ring atoms and more typically from 3 to 6 ring atoms. Examples of single-ring cycloalkyls include cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. A cycloalkyl may alternatively be polycyclic or contain more than one ring. Examples of polycyclic cycloalkyls include bridged, fused, and spirocyclic carbocyclyls.

The term "aryl" (alone or in combination with another term(s)) means an aromatic carbocyclyl containing from 6 to 14 carbon ring atoms. An aryl may be monocyclic or polycyclic (i.e., may contain more than one ring). In the case of polycyclic aromatic rings, only one ring the polycyclic system is required to be unsaturated while the remaining ring(s) may be saturated, partially saturated or unsaturated. Examples of aryls include phenyl, naphthalenyl, indenyl, indanyl, and tetrahydronapthyl.

In some instances, the number of carbon atoms in a hydrocarbyl substituent (e.g., alkyl, alkenyl, alkynyl, or cycloalkyl) is indicated by the prefix "C_x-C_y-", wherein x is the minimum and y is the maximum number of carbon atoms in the substituent. Thus, for example, "C_1-C_6-alkyl" refers to an alkyl substituent containing from 1 to 6 carbon atoms. Illustrating further, C_3-C_8-cycloalkyl means a saturated hydrocarbyl ring containing from 3 to 8 carbon ring atoms.

The term "hydrogen" (alone or in combination with another term(s)) means a hydrogen radical, and may be depicted as -H.

The term "hydroxy" (alone or in combination with another term(s)) means -OH.

The term "carboxy" (alone or in combination with another term(s)) means -C(O)-OH.

The term "amino" (alone or in combination with another term(s)) means $-NH_2$.

The term "halogen" or "halo" (alone or in combination with another term(s)) means a fluorine radical (which may be depicted as -F), chlorine radical (which may be depicted as -Cl), bromine radical (which may be depicted as -Br), or iodine radical (which may be depicted as -I).

If a substituent is described as being "substituted", a non-hydrogen radical is in the place of hydrogen radical on a carbon or nitrogen of the substituent. Thus, for example, a substituted alkyl substituent is an alkyl substituent in which at least one non-hydrogen radical is in the place of a hydrogen radical on the alkyl substituent. To illustrate, monofluoroalkyl is

alkyl substituted with a fluoro radical, and difluoroalkyl is alkyl substituted with two fluoro radicals. It should be recognized that if there are more than one substitution on a substituent, each non-hydrogen radical may be identical or different (unless otherwise stated).

If a substituent is described as being "optionally substituted", the substituent may be either (1) not substituted or (2) substituted. If a substituent is described as being optionally substituted with up to a particular number of non-hydrogen radicals, that substituent may be either (1) not substituted; or (2) substituted by up to that particular number of non-hydrogen radicals or by up to the maximum number of substitutable positions on the substituent, whichever is less. Thus, for example, if a substituent is described as a heteroaryl optionally substituted with up to 3 non-hydrogen radicals, then any heteroaryl with less than 3 substitutable positions would be optionally substituted by up to only as many non-hydrogen radicals as the heteroaryl has substitutable positions. To illustrate, tetrazolyl (which has only one substitutable position) would be optionally substituted with up to one non-hydrogen radical. To illustrate further, if an amino nitrogen is described as being optionally substituted with up to 2 non-hydrogen radicals, then a primary amino nitrogen will be optionally substituted with up to 2 non-hydrogen radicals, whereas a secondary amino nitrogen will be optionally substituted with up to only 1 non-hydrogen radical. If a substituent is described as being optionally substituted with one or more non-hydrogen radicals, that substituent may be either (1) not substituted; or (2) substituted by up to the maximum number of substitutable positions on the substituent. Thus, for example, if a substituent is described as a heteroaryl optionally substituted with one or more non-hydrogen radicals, then any heteroaryl with 3 substitutable positions would be optionally substituted by one, two or three non-hydrogen radicals. To illustrate, tetrazolyl (which has only one substitutable position) would be optionally substituted with up to one non-hydrogen radical.

This patent application uses the terms "substituent" and "radical" interchangeably.

The prefix "halo" indicates that the substituent to which the prefix is attached is substituted with one or more independently selected halogen radicals. For example, haloalkyl means an alkyl substituent in which at least one hydrogen radical is replaced with a halogen radical. Examples of haloalkyls include chloromethyl, 1-bromoethyl, fluoromethyl, difluoromethyl, trifluoromethyl, and 1,1,1-trifluoroethyl. It should be recognized that if a substituent is substituted by more than one halogen radical, those halogen radicals may be identical or different (unless otherwise stated).

The prefix "perhalo" indicates that every hydrogen radical on the substituent to which the prefix is attached is replaced with independently selected halogen radicals, *i.e.*, each hydrogen radical on the substituent is replaced with a halogen radical. If all the halogen radicals are identical, the prefix typically will identify the halogen radical. Thus, for example, the term "perfluoro" means that every hydrogen radical on the substituent to which the prefix

is attached is substituted with a fluorine radical. To illustrate, the term "perfluoroalkyl" means an alkyl substituent wherein a fluorine radical is in the place of each hydrogen radical.

The term "carbonyl" (alone or in combination with another term(s)) means -C(O)-.

The term "aminocarbonyl" (alone or in combination with another term(s)) means -C(O)-NH_2.

The term "oxo" (alone or in combination with another term(s)) means (=O).

The term "oxy" (alone or in combination with another term(s)) means an ether substituent, and may be depicted as -O-.

The term "alkylhydroxy" (alone or in combination with another term(s)) means –alkyl-OH.

The term "alkylamino" (alone or in combination with another term(s)) means –alkyl-NH_2.

The term "alkyloxy" (alone or in combination with another term(s)) means an alkylether substituent, i.e., -O-alkyl. Examples of such a substituent include methoxy (-O-CH_3), ethoxy, n-propoxy, isopropoxy, n-butoxy, iso-butoxy, sec-butoxy, and tert-butoxy.

The term "alkylcarbonyl" (alone or in combination with another term(s)) means -C(O)-alkyl.

The term "aminoalkylcarbonyl" (alone or in combination with another term(s)) means -C(O)-alkyl-NH_2.

The term "alkyloxycarbonyl" (alone or in combination with another term(s)) means -C(O)-O-alkyl.

The term "carbocyclylcarbonyl" (alone or in combination with another term(s)) means -C(O)-carbocyclyl.

Similarly, the term "heterocyclylcarbonyl" (alone or in combination with another term(s)) means -C(O)-heterocyclyl.

The term "carbocyclylalkylcarbonyl" (alone or in combination with another term(s)) means -C(O)-alkyl-carbocyclyl.

Similarly, the term "heterocyclylalkylcarbonyl" (alone or in combination with another term(s)) means -C(O)-alkyl-heterocyclyl.

The term "carbocyclyloxycarbonyl" (alone or in combination with another term(s)) means -C(O)-O-carbocyclyl.

The term "carbocyclylalkyloxycarbonyl" (alone or in combination with another term(s)) means -C(O)-O-alkyl-carbocyclyl.

The term "thio" or "thia" (alone or in combination with another term(s)) means a thiaether substituent, *i.e.*, an ether substituent wherein a divalent sulfur atom is in the place of the ether oxygen atom. Such a substituent may be depicted as -S-. This, for example, "alkyl-thio-alkyl" means alkyl-S-alkyl (alkyl-sulfanyl-alkyl).

The term "thiol" or "sulfhydryl" (alone or in combination with another term(s)) means a sulfhydryl substituent, and may be depicted as -SH.

The term "(thiocarbonyl)" (alone or in combination with another term(s)) means a carbonyl wherein the oxygen atom has been replaced with a sulfur. Such a substituent may be depicted as -C(S)-.

The term "sulfonyl" (alone or in combination with another term(s)) means $-S(O)_2-$.

The term "aminosulfonyl" (alone or in combination with another term(s)) means $-S(O)_2-NH_2$.

The term "sulfinyl" or "sulfoxido" (alone or in combination with another term(s)) means -S(O)-.

The term "heterocyclyl" (alone or in combination with another term(s)) means a saturated (*i.e.*, "heterocycloalkyl"), partially saturated (*i.e.*, "heterocycloalkenyl"), or completely unsaturated (*i.e.*, "heteroaryl") ring structure containing a total of 3 to 14 ring atoms. At least one of the ring atoms is a heteroatom (*i.e.*, oxygen, nitrogen, or sulfur), with the remaining ring atoms being independently selected from the group consisting of carbon, oxygen, nitrogen, and sulfur. A heterocyclyl may be a single-ring (monocyclic) or polycyclic ring structure.

A heterocyclyl may be a single ring, which typically contains from 3 to 7 ring atoms, more typically from 3 to 6 ring atoms, and even more typically 5 to 6 ring atoms. Examples of single-ring heterocyclyls include 1,2,3,6-tetrahydropyridine, thiomorpholinyl, tetrahydropyranyl, furanyl, dihydrofuranyl, tetrahydrofuranyl, thiophenyl (thiofuranyl), dihydrothiophenyl, tetrahydrothiophenyl, pyrrolyl, pyrrolinyl, pyrrolidinyl, imidazolyl, imidazolinyl, imidazolidinyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, triazolyl, tetrazolyl, oxazolyl, oxazolidinyl, isoxazolidinyl, isoxazolyl, thiazolyl, isothiazolyl, thiazolinyl, isothiazolinyl, thiazolidinyl, isothiazolidinyl, thiodiazolyl, oxadiazolyl (including 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl (furazanyl), or 1,3,4-oxadiazolyl), oxatriazolyl (including 1,2,3,4-oxatriazolyl or 1,2,3,5-oxatriazolyl), dioxazolyl (including 1,2,3-dioxazolyl, 1,2,4-dioxazolyl, 1,3,2-dioxazolyl, or 1,3,4-dioxazolyl), oxathiazolyl, oxathiolyl, oxathiolanyl, pyranyl, dihydropyranyl, thiopyranyl, tetrahydrothiopyranyl, pyridinyl (azinyl), piperidinyl, diazinyl (including pyridazinyl (1,2-diazinyl), pyrimidinyl (1,3-diazinyl), or pyrazinyl (1,4-diazinyl)), piperazinyl, pyrrolidin-2-only, triazinyl (including 1,3,5-triazinyl, 1,2,4-triazinyl, and 1,2,3-triazinyl)), oxazinyl (including 1,2-oxazinyl, 1,3-oxazinyl, or 1,4-oxazinyl)), oxathiazinyl (including 1,2,3-oxathiazinyl, 1,2,4-oxathiazinyl, 1,2,5-oxathiazinyl, or 1,2,6-oxathiazinyl)), oxadiazinyl (including 1,2,3-oxadiazinyl, 1,2,4-oxadiazinyl, 1,4,2-oxadiazinyl, or 1,3,5-oxadiazinyl)), morpholinyl, azepinyl, oxepinyl, thiepinyl, and diazepinyl.

A heterocyclyl may alternatively be polycyclic (i.e., may contain more than one ring). Examples of polycyclic heterocyclyls include bridged, fused, and spirocyclic heterocyclyls. In a spirocyclic heterocyclyl, one atom is common to two different rings. In a bridged heterocyclyl, the rings share at least two common non-adjacent atoms. In a fused-ring heterocyclyl, two or more rings may be fused together, such that two rings share one common bond. Examples of fused-ring heterocyclyls include hexahydro-furo[3,4-c]pyrrole, hexahydro-furo[3,4-b]pyrrole, octahydro-pyrrolo[3,4-b]pyridine, octahydro-pyrrolo[3,4-c]pyridine, (3aR,6aR)-5-methyl-octahydro-pyrrolo[3,4-b]pyrrole, (3aR,6aR)-octahydro-pyrrolo[3,4-b]pyrrole, 6-methyl-2,6-diaza-bicyclo[3.2.0]heptane, (3aS,6aR)-2-methyl-octahydro-pyrrolo[3,4-c]pyrrole, decahydro-[1,5]naphthyridine, 2,3-dihydrobenzofuranyl, 2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indolyl, thieno[3,2-c]pyridinyl, furo[3,2-c]pyridinyl, phthalazin-1(2H)-onyl, isoquinolinyl, isoquinolin-1(2H)-onyl, 5,6,7,8-tetrahydrophthalazin-1(2H)-onyl, fluorophthalazin-1(2H)-onyl, (Z)-3H-benzo[d][1,2]diazepin-4(5H)-onyl, (trifluoromethyl)phthalazin-1(2H)-onyl, pyrrolo[1,2-d][1,2,4]triazin-1(2H)-onyl, 1,2,3,4-tetrahydroisoquinolinyl, 2,3-dihydrobenzo[b][1,4]dioxinyl, 5,6,7,8-tetrahydrophthalazin-1(2H)-onyl, 5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazinyl, 5,6,7,8-tetrahydroimidazo[1,5-a]pyrazinyl, thieno[3,2-c]pyridinyl, furo[3,2-c]pyridinyl, indolizinyl, pyranopyrrolyl, 4H-quinolizinyl, purinyl, naphthyridinyl, pyridopyridinyl (including pyrido[3,4-b]-pyridinyl, pyrido[3,2-b]-pyridinyl, or pyrido[4,3-b]-pyridinyl), and pteridinyl. Other examples of fused-ring heterocyclyls include benzo-fused heterocyclyls, such as benzimidazolyl, benzo[d][1,3]dioxolyl, indolyl, isoindolyl (isobenzazolyl, pseudoisoindolyl), indoleninyl (pseudoindolyl), isoindazolyl (benzpyrazolyl), benzazinyl (including quinolinyl (1-benzazinyl) or isoquinolinyl (2-benzazinyl)), phthalazinyl, quinoxalinyl, quinazolinyl, benzodiazinyl (including cinnolinyl (1,2-benzodiazinyl) or quinazolinyl (1,3-benzodiazinyl)), benzopyranyl (including chromanyl or isochromanyl), benzoxazinyl (including 1,3,2-benzoxazinyl, 1,4,2-benzoxazinyl, 2,3,1-benzoxazinyl, or 3,1,4-benzoxazinyl), and benzisoxazinyl (including 1,2-benzisoxazinyl or 1,4-benzisoxazinyl). Examples of spirocyclic heterocyclyls include 1,4-dioxa-8-azaspiro[4.5]decanyl.

The term "5-6 membered heteroaryl" (alone or in combination with another term(s)) means aromatic heterocyclyl containing a total of 5 to 6 ring atoms. At least one of the ring atoms is a heteroatom (*i.e.*, oxygen, nitrogen, or sulfur), with the remaining ring atoms being independently selected from the group consisting of carbon, oxygen, nitrogen, and sulfur.

The term "heterocycloalkyl" (alone or in combination with another term(s)) means a saturated heterocyclyl.

The term "heteroaryl" (alone or in combination with another term(s)) means an aromatic heterocyclyl containing from 5 to 14 ring atoms. A heteroaryl may be a single ring or 2 or 3 fused rings. Examples of heteroaryl substituents include 6-membered ring

substituents such as pyridyl, pyrazyl, pyrimidinyl, pyridazinyl, and 1,3,5-, 1,2,4- or 1,2,3-triazinyl; 5-membered ring substituents such as imidazyl, furanyl, thiophenyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, 1,2,3-, 1,2,4-, 1,2,5-, or 1,3,4-oxadiazolyl and isothiazolyl; 6/5-membered fused ring substituents such as benzothiofuranyl, benzisoxazolyl, benzoxazolyl, and purinyl; and 6/6-membered fused rings such as benzopyranyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and benzoxazinyl.

A prefix attached to a multi-component substituent only applies to the first component. To illustrate, the term "alkylcycloalkyl" contains two components: alkyl and cycloalkyl. Thus, the C_1-C_6- prefix on C_1-C_6-alkylcycloalkyl means that the alkyl component of the alkylcycloalkyl contains from 1 to 6 carbon atoms; the C_1-C_6-prefix does not describe the cycloalkyl component. To illustrate further, the prefix "halo" on haloalkyloxyalkyl indicates that only the alkyloxy component of the alkyloxyalkyl substituent is substituted with one or more halogen radicals. If halogen substitution may alternatively or additionally occur on the alkyl component, the substituent would instead be described as "halogen-substituted alkyloxyalkyl" rather than "haloalkyloxyalkyl." And finally, if the halogen substitution may only occur on the alkyl component, the substituent would instead be described as "alkyloxyhaloalkyl."

The terms "treat", "treating" and "treatment" refer to a method of alleviating or abrogating a disease and/or its attendant symptoms.

The terms "prevent", "preventing" and "prevention" refer to a method of preventing the onset of a disease and/or its attendant symptoms or barring a subject from acquiring a disease. As used herein, "prevent", "preventing" and "prevention" also include delaying the onset of a disease and/or its attendant symptoms and reducing a subject's risk of acquiring a disease.

The term "therapeutically effective amount" refers to that amount of the compound being administered sufficient to prevent development of or alleviate to some extent one or more of the symptoms of the condition or disorder being treated.

The term "modulate" refers to the ability of a compound to increase or decrease the function, or activity, of a kinase. "Modulation", as used herein in its various forms, is intended to encompass antagonism, agonism, partial antagonism and/or partial agonism of the activity associated with kinase. Kinase inhibitors are compounds that, e.g., bind to, partially or totally block stimulation, decrease, prevent, delay activation, inactivate, desensitize, or down regulate signal transduction. Kinase activators are compounds that, e.g., bind to, stimulate, increase, open, activate, facilitate, enhance activation, sensitize or up regulate signal transduction.

The term "composition" as used herein is intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which

results, directly or indirectly, from combination of the specified ingredients in the specified amounts. By "pharmaceutically acceptable" it is meant the carrier, diluent or excipient must be compatible with the other ingredients of the formulation and not deleterious to the recipient thereof.

The "subject" is defined herein to include animals such as mammals, including, but not limited to, primates (e.g., humans), cows, sheep, goats, horses, dogs, cats, rabbits, rats, mice and the like. In preferred embodiments, the subject is a human.

Isotope Enriched or Labeled Compounds

Compounds of the invention can exist in isotope-labeled or -enriched form containing one or more atoms having an atomic mass or mass number different from the atomic mass or mass number most abundantly found in nature. Isotopes can be radioactive or non-radioactive isotopes. Isotopes of atoms such as hydrogen, carbon, phosphorous, sulfur, fluorine, chlorine, and iodine include, but are not limited to, ^{2}H, ^{3}H, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{32}P, ^{35}S, ^{18}F, ^{36}Cl, and ^{125}I. Compounds that contain other isotopes of these and/or other atoms are within the scope of this invention.

In another embodiment, the isotope-labeled compounds contain deuterium (^{2}H), tritium (^{3}H) or ^{14}C isotopes. Isotope-labeled compounds of this invention can be prepared by the general methods well known to persons having ordinary skill in the art. Such isotope-labeled compounds can be conveniently prepared by carrying out the procedures disclosed in the Examples disclosed herein and Schemes by substituting a readily available isotope-labeled reagent for a non-labeled reagent. In some instances, compounds may be treated with isotope-labeled reagents to exchange a normal atom with its isotope, for example, hydrogen for deuterium can be exchanged by the action of a deuteric acid such as D_2SO_4/D_2O. In addition to the above, relevant procedures and intermediates are disclosed, for instance, in Lizondo, J et al., *Drugs Fut*, 21(11), 1116 (1996); Brickner, S J *et al., J Med Chem*, 39(3), 673 (1996); Mallesham, B et al., *Org Lett*, 5(7), 963 (2003); PCT publications WO1997010223, WO2005099353, WO1995007271, WO2006008754; US Patent Nos. 7538189; 7534814; 7531685; 7528131; 7521421; 7514068; 7511013; and US Patent Application Publication Nos. 20090137457; 20090131485; 20090131363; 20090118238; 20090111840; 20090105338; 20090105307; 20090105147; 20090093422; 20090088416; and 20090082471, the methods are hereby incorporated by reference.

The isotope-labeled compounds of the invention may be used as standards to determine the effectiveness in binding assays. Isotope containing compounds have been used in pharmaceutical research to investigate the in vivo metabolic fate of the compounds by evaluation of the mechanism of action and metabolic pathway of the nonisotope-labeled parent compound (Blake et al. *J. Pharm. Sci.* 64, 3, 367-391 (1975)). Such metabolic studies are important in the design of safe, effective therapeutic drugs, either because the *in vivo*

active compound administered to the patient or because the metabolites produced from the parent compound prove to be toxic or carcinogenic (Foster et al., Advances in Drug Research Vol. 14, pp. 2-36, Academic press, London, 1985; Kato et al., J. *Labelled Comp. Radiopharmaceut.*, 36(10):927-932 (1995); Kushner et al., *Can. J. Physiol. Pharmacol.*, 77, 79-88 (1999).

In addition, non-radio active isotope containing drugs, such as deuterated drugs called "heavy drugs," can be used for the treatment of diseases and conditions related to NAMPT activity. Increasing the amount of an isotope present in a compound above its natural abundance is called enrichment. Examples of the amount of enrichment include from about 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 16, 21, 25, 29, 33, 37, 42, 46, 50, 54, 58, 63, 67, 71, 75, 79, 84, 88, 92, 96, to about 100 mol %. Replacement of up to about 15% of normal atom with a heavy isotope has been effected and maintained for a period of days to weeks in mammals, including rodents and dogs, with minimal observed adverse effects (Czajka D M and Finkel A J, Ann. N.Y. Acad. Sci. 1960 84: 770; Thomson J F, Ann. New York Acad. Sci 1960 84: 736; Czakja D M et al., Am. J. Physiol. 1961 201: 357). Acute replacement of as high as 15%-23% in human fluids with deuterium was found not to cause toxicity (Blagojevic N et al. in "Dosimetry & Treatment Planning for Neutron Capture Therapy", Zamenhof R, Solares G and Harling O Eds. 1994. Advanced Medical Publishing, Madison Wis. pp.125-134; Diabetes Metab. 23: 251 (1997)).

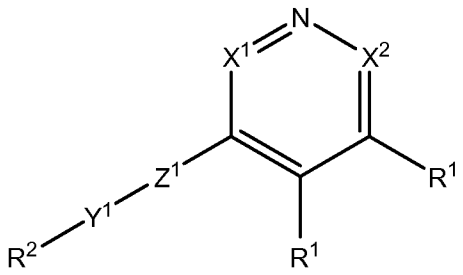
Stable isotope labeling of a drug can alter its physico-chemical properties such as pKa and lipid solubility. These effects and alterations can affect the pharmacodynamic response of the drug molecule if the isotopic substitution affects a region involved in a ligand-receptor interaction. While some of the physical properties of a stable isotope-labeled molecule are different from those of the unlabeled one, the chemical and biological properties are the same, with one important exception: because of the increased mass of the heavy isotope, any bond involving the heavy isotope and another atom will be stronger than the same bond between the light isotope and that atom. Accordingly, the incorporation of an isotope at a site of metabolism or enzymatic transformation will slow said reactions potentially altering the pharmacokinetic profile or efficacy relative to the non-isotopic compound.

Compounds

Suitable groups for X^1, X^2, Y^1, Z^1, R^1, and R^2 in compounds of all Formulas are independently selected. The described embodiments of the present invention may be combined. Such combination is contemplated and within the scope of the present invention. For example, it is contemplated that embodiments for any of X^1, X^2, Y^1, Z^1, R^1, and R^2 can be combined with embodiments defined for any other of X^1, X^2, Y^1, Z^1, R^1, and R^2.

Embodiments of Formula (I)

One embodiment of this invention, therefore, pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (I)



Formula (I);

wherein

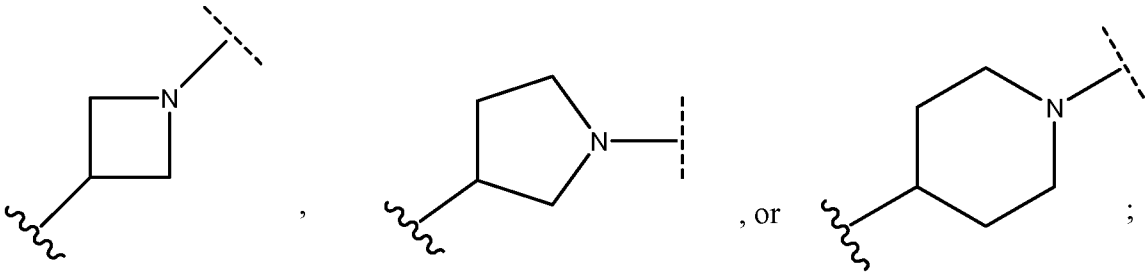
X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

Z^1 is



wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl;

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more

substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^3, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, and heterocyclyl; wherein each R^3 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, C(O)NHOH, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^3 aryl, cycloalkyl, cycloalkenyl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^6)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, C(O)NHOH, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^5, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^5 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently

selected from the group consisting of R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), C(O)OH, N_3, CN, NH_2, F, Cl, Br and I;

R^6, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^6 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^8, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^9, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, R^5, R^6, R^7, R^8, and R^9 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected

from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

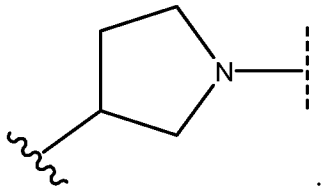
R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

with the proviso that

when X^1 is CR^1 and X^2 is CR^1; R^1 is hydrogen; Y^1 is NHC(O); Z^1 is



; and R^2 is pyrrolyl; the R^2 pyrrolyl is not substituted with two alkyl groups.

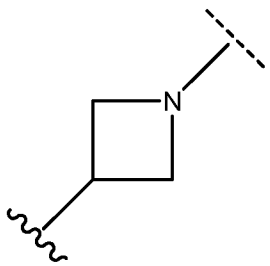
In one embodiment of Formula (I), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (I), X^1 is N and X^2 is CR^1. In another embodiment of Formula (I), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (I), X^1 is CR^1 and X^2 is CR^1.

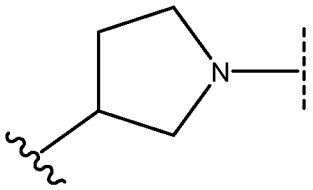
In one embodiment of Formula (I), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (I), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (I), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, and F. In another embodiment of Formula (I), R^1, at each occurrence, is hydrogen.

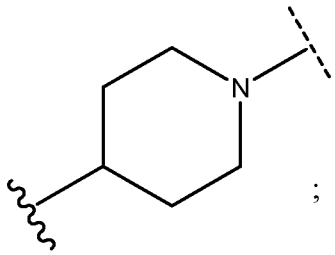
In one embodiment of Formula (I), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (I), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (I), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, and F. In another embodiment of Formula (I), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (I), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (I), Y^1 is C(O)NH. In another embodiment of Formula (I), Y^1 is NHC(O).

In one embodiment of Formula (I), Z^1 is

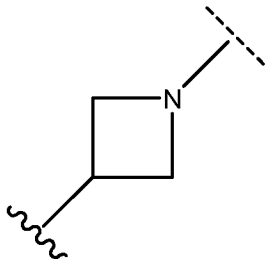


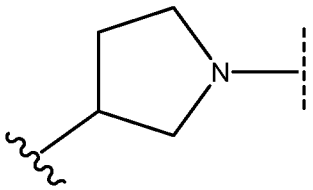
,


, or


;

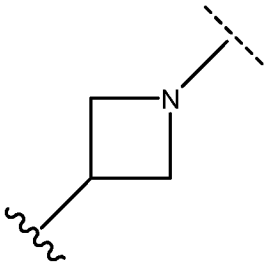
wherein ~~~ indicates the point of attachment to Y^1 and ⁄⁄⁄ indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (I), Z^1 is



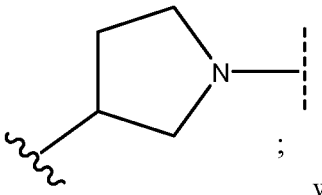
, or


;

wherein ~~~ indicates the point of attachment to Y^1 and ⁄⁄⁄ indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (I), Z^1 is



; wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (I), Z^1 is



; wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl.

In one embodiment of Formula (I), R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (I), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (I), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, and SO_2R^4. In another embodiment of Formula (I), R^2 is phenyl; wherein each R^2 phenyl is optionally

substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

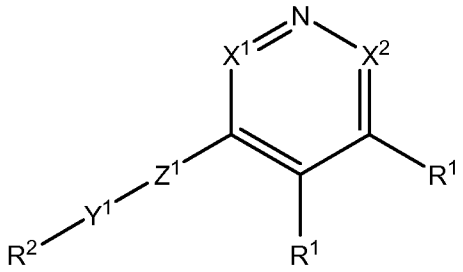
In another embodiment of Formula (I), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (I), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, and SO_2R^4. In another embodiment of Formula (I), R^2 is furanyl or thiophenyl; wherein each R^2 furanyl and thiophenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

In one embodiment of Formula (I), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (I), R^4, at each occurrence, is heterocyclyl.

In one embodiment of Formula (I), each R^4 heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$,

$C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with alkyl or alkoxy; and R^{12}, at each occurrence, is independently selected alkyl. In another embodiment of Formula (I), each R^4 heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, and heterocyclyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (I)



Formula (I);

wherein

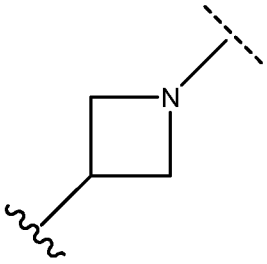
X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

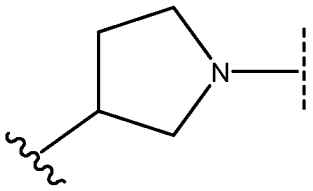
X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

Z^1 is



, or



;

wherein  indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl;

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, and F;

R^2 is aryl or 5-6 membered heteroaryl wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, SO_2R^4, and OR^4;

R^4, at each occurrence, is heterocyclyl;

wherein the cyclic moiety represented by R^4 is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, and $CO(O)R^{10}$;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

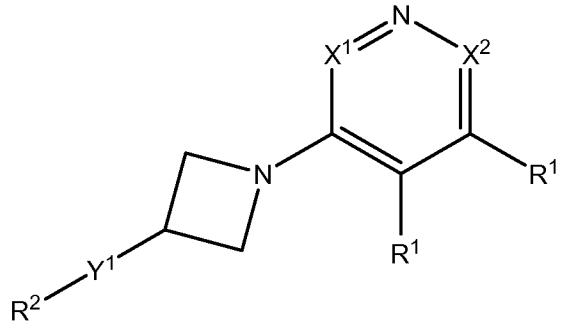
R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, and heterocyclyl.

Still another embodiment pertains to compounds having Formula (I), which includes Examples 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537,

538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, and pharmaceutically acceptable salts thereof.

Embodiments of Formula (II)

In another aspect, the present invention provides compounds of Formula (II)



(II);

and pharmaceutically acceptable salts thereof; wherein X^1, X^2, Y^1, R^1, and R^2 are as described herein for Formula (I).

One embodiment of this invention pertains to compounds of Formula (II) and pharmaceutically acceptable salts thereof;

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more

substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^3, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, and heterocyclyl; wherein each R^3 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, C(O)NHOH, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^3 aryl, cycloalkyl, cycloalkenyl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^6)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, C(O)NHOH, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^5, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^5 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently

selected from the group consisting of R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), C(O)OH, N_3, CN, NH_2, F, Cl, Br and I;

R^6, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^6 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^8, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^9, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, R^5, R^6, R^7, R^8, and R^9 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected

from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In one embodiment of Formula (II), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (II), X^1 is N and X^2 is CR^1. In another embodiment of Formula (II), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (II), X^1 is CR^1 and X^2 is CR^1.

In one embodiment of Formula (II), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (II), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (II), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, and F. In another embodiment of Formula (II), R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (II), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (II), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (II), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl,

haloalkyl, alkoxy, CN, and F. In another embodiment of Formula (II), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (II), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (II), Y^1 is C(O)NH. In another embodiment of Formula (II), Y^1 is NHC(O).

In one embodiment of Formula (II), R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (II), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (II), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, and SO_2R^4. In another embodiment of Formula (II), R^2 is phenyl; wherein each R^2 phenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

In another embodiment of Formula (II), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (II), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, and SO_2R^4. In another embodiment of Formula (II), R^2 is furanyl or thiophenyl; wherein each R^2 furanyl and thiophenyl is optionally substituted with

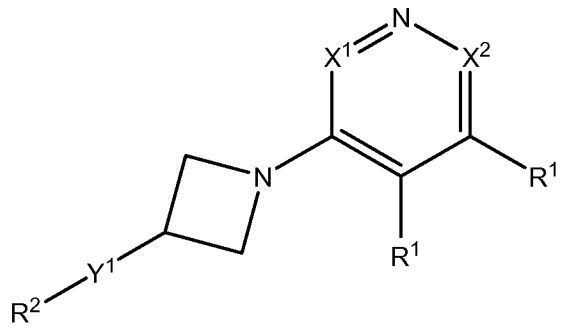
one or more substituents independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

In one embodiment of Formula (II), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (II), R^4, at each occurrence, is heterocyclyl.

In one embodiment of Formula (II), each R^4 heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$,

$C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with alkyl or alkoxy; and R^{12}, at each occurrence, is independently selected alkyl. In another embodiment of Formula (II), each R^4 heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, and heterocyclyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (II)



Formula (II);

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, and F;

R^2 is aryl or 5-6 membered heteroaryl wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, SO_2R^4, and OR^4;

R^4, at each occurrence, is heterocyclyl;

wherein the cyclic moiety represented by R^4 is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, and $CO(O)R^{10}$;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

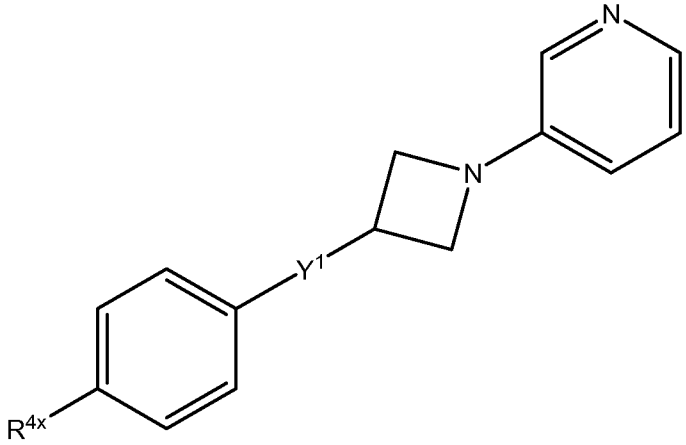
R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, and heterocyclyl.

Still another embodiment pertains to compounds having Formula (II), which includes Examples 1, 2, 3, 4, 5, 6, 7, 10, 20, 21, 22, 23, 24, 25, 26, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264,

265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 609, 610, 611, 612, 613, and pharmaceutically acceptable salts thereof.

Embodiments of Formula (III)

In another aspect, the present invention provides compounds of Formula (III)



(III);

and pharmaceutically acceptable salts thereof; wherein Y^1 is as described in Formula (I) herein and R^{4x} is as described herein for substituents on R^2 when R^2 is aryl in Formula (I).

One embodiment of this invention pertains to compounds of Formula (III) or pharmaceutically acceptable salts thereof;

wherein

Y^1 is C(O)NH, or NHC(O);

R^{4x} is independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4 and R^7 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11},

$SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In one embodiment of Formula (III), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (III), Y^1 is C(O)NH. In another embodiment of Formula (III), Y^1 is NHC(O).

In one embodiment of Formula (III), R^{4x} is selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (III), R^{4x} is selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (III), R^{4x} is selected from the group consisting of R^4, SO_2R^4,and OR^4.

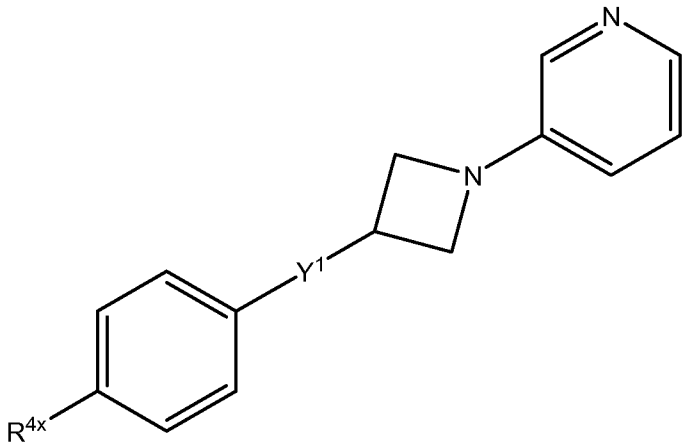
In one embodiment of Formula (III), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$,

$NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (III), R^4, at each occurrence, is heterocyclyl.

In one embodiment of Formula (III), each R^4 heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with alkyl or alkoxy; and R^{12}, at each occurrence, is independently selected alkyl. In another embodiment of Formula (III), each R^4 heterocyclyl is optionally substituted with one or more substituents independently selected from the group

consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, and heterocyclyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (III)



Formula (III);

wherein

Y^1 is C(O)NH, or NHC(O);

R^{4x} is independently selected from the group consisting of R^4, SO_2R^4, and OR^4;

R^4, at each occurrence, is heterocyclyl;

wherein the cyclic moiety represented by R^4 is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, and $CO(O)R^{10}$;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally

substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

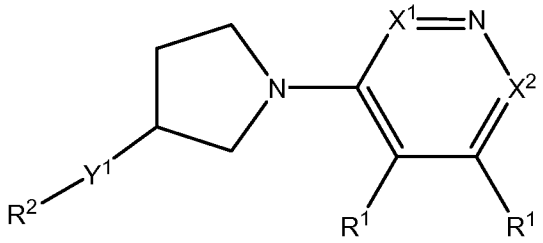
R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, and heterocyclyl.

Still another embodiment pertains to compounds having Formula (III), which includes Examples 1, 2, 3, 4, 5, 6, 7, 10, 20, 21, 22, 23, 24, 25, 26, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 602, 609, 610, and pharmaceutically acceptable salts thereof.

Embodiments of Formula (IV)

In another aspect, the present invention provides compounds of Formula (IV)



(IV);

and pharmaceutically acceptable salts thereof; wherein X^1, X^2, Y^1, R^1, and R^2 are as described herein for Formula (I).

One embodiment of this invention pertains to compounds of Formula (IV) and pharmaceutically acceptable salts thereof;

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^3, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, and heterocyclyl; wherein each R^3 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, C(O)NHOH, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^3 aryl, cycloalkyl, cycloalkenyl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^6)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, C(O)NHOH, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$,

SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^5, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^5 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), C(O)OH, N_3, CN, NH_2, F, Cl, Br and I;

R^6, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^6 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^8, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^9, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, R^5, R^6, R^7, R^8, and R^9 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$,

$NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In one embodiment of Formula (IV), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (IV), X^1 is N and X^2 is CR^1. In another embodiment of Formula (IV), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (IV), X^1 is CR^1 and X^2 is CR^1.

In one embodiment of Formula (IV), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IV), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IV), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, and F. In another embodiment of Formula (IV), R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (IV), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IV), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IV), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, and F. In another embodiment of Formula (IV), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (IV), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (IV), Y^1 is C(O)NH. In another embodiment of Formula (IV), Y^1 is NHC(O).

In one embodiment of Formula (IV), R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (IV),

R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (IV), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, and SO_2R^4. In another embodiment of Formula (IV), R^2 is phenyl; wherein each R^2 phenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

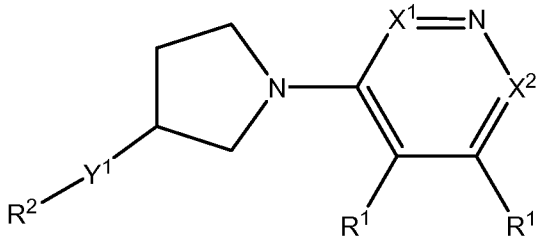
In another embodiment of Formula (IV), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (IV), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, and SO_2R^4. In another embodiment of Formula (IV), R^2 is furanyl or thiophenyl; wherein each R^2 furanyl and thiophenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

In one embodiment of Formula (IV), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IV), R^4, at each occurrence, is heterocyclyl.

In one embodiment of Formula (IV), each R^4 heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl

is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with alkyl or alkoxy; and R^{12}, at each occurrence, is independently selected alkyl. In another embodiment of Formula (IV), each R^4 heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, and heterocyclyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (IV)



Formula (IV);

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, and F;

R^2 is aryl or 5-6 membered heteroaryl wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, SO_2R^4, and OR^4;

R^4, at each occurrence, is heterocyclyl;

wherein the cyclic moiety represented by R^4 is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, and $CO(O)R^{10}$;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, and heterocyclyl;

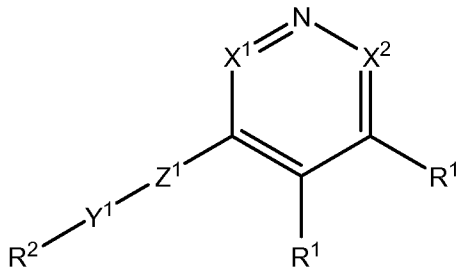
with the proviso that

when X^1 is CR^1 and X^2 is CR^1; R^1 is hydrogen; Y^1 is NHC(O); and R^2 is pyrrolyl; the R^2 pyrrolyl is not substituted with two alkyl groups.

Still another embodiment pertains to compounds having Formula (IV), which includes Examples 8, 9, 11, 12, 13, 14, 15, 16, 17, 18, 19, 27, 28, 141, 142, 204, 310, 311, 312, 313, and pharmaceutically acceptable salts thereof.

Embodiments of Formula (IA)

One embodiment of this invention, therefore, pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (IA)



Formula (IA);

wherein

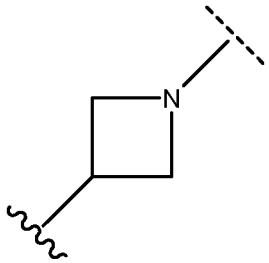
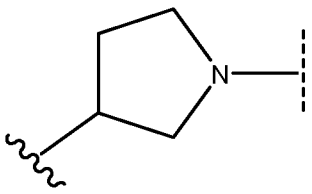
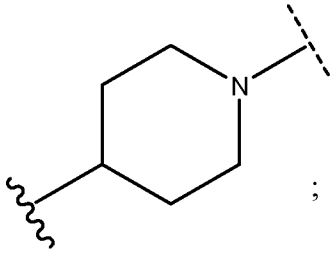
X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

Z^1 is


, 
, or 
;

wherein  indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl;

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^3, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, and heterocyclyl; wherein each R^3 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, $C(O)NHOH$, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^3 aryl, cycloalkyl, cycloalkenyl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^6)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, $C(O)NHOH$, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently

selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^5, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^5 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), C(O)OH, N_3, CN, NH_2, F, Cl, Br and I;

R^6, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^6 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^8, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^9, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, R^5, R^6, R^7, R^8, and R^9 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

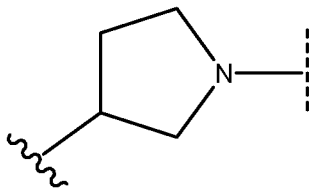
R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

with the proviso that

when X^1 is CR^1 and X^2 is CR^1; R^1 is hydrogen; Y^1 is NHC(O); Z^1 is



; and R^2 is pyrrolyl; the R^2 pyrrolyl is not substituted with two alkyl groups.

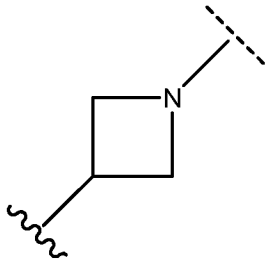
In one embodiment of Formula (IA), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (IA), X^1 is N and X^2 is CR^1. In another embodiment of Formula (IA), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (IA), X^1 is CR^1 and X^2 is CR^1.

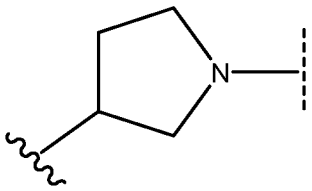
In one embodiment of Formula (IA), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IA), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IA), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IA), R^1, at each occurrence, is hydrogen.

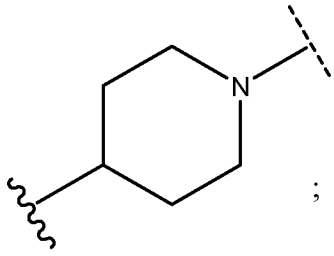
In one embodiment of Formula (IA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (IA), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (IA), Y^1 is C(O)NH. In another embodiment of Formula (IA), Y^1 is NHC(O).

In one embodiment of Formula (IA), Z^1 is

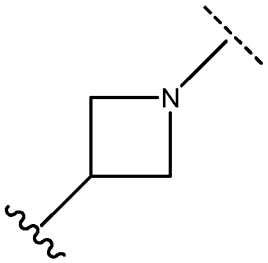
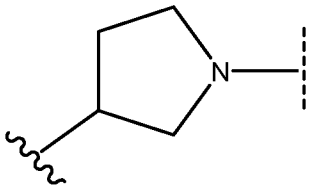


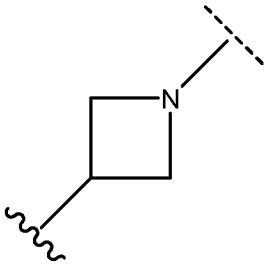
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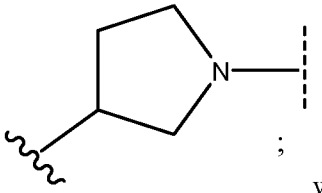
, or


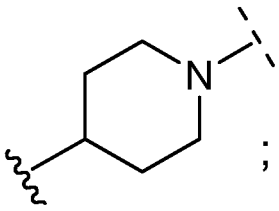
;

wherein  indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (IA), Z^1 is


, or 
; wherein  indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (IA), Z^1 is


; wherein  indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (IA), Z^1 is


; wherein  indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (IA), Z^1 is


; wherein  indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl.

In one embodiment of Formula (IA), R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2,

SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (IA), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (IA), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F. In another embodiment of Formula (IA), R^2 is phenyl; wherein each R^2 phenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F. In another embodiment of Formula (IA), R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

In another embodiment of Formula (IA), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (IA), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F. In another embodiment of Formula (IA), R^2 is furanyl or thiophenyl; wherein each R^2 furanyl and thiophenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F.

In one embodiment of Formula (IA), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH,

$CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IA), R^4, at each occurrence, is alkyl or heterocyclyl.

In one embodiment of Formula (IA), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IA), each R^4 alkyl is optionally substituted with one R^7.

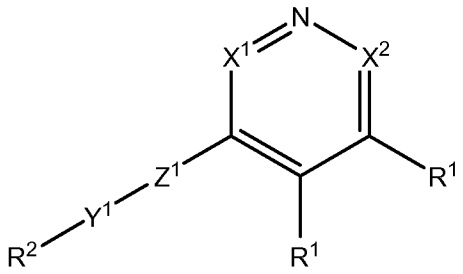
In one embodiment of Formula (IA), R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl. In another embodiment of Formula (IA), R^7, at each occurrence, is heterocyclyl.

In one embodiment of Formula (IA), each R^4 and R^7 heterocyclyl is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$,

$NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In another embodiment of Formula (IA), each R^4 and R^7 heterocyclyl is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, OH, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl and haloalkyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (IA)



Formula (IA);

wherein

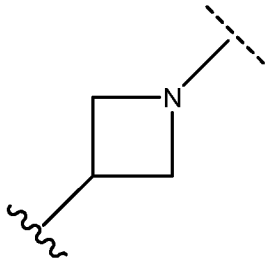
X^1 is N and X^2 is CR^1; or

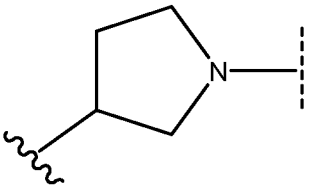
X^1 is CR^1 and X^2 is N; or

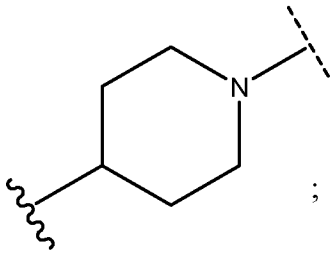
X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

Z^1 is



,


, or


;

wherein  indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl;

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, Cl, and F;

R^2 is aryl or 5-6 membered heteroaryl wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, SO_2R^4, OR^4, and F;

R^4, at each occurrence, is alkyl or heterocyclyl; wherein each R^4 alkyl is optionally substituted with R^7;

R^7, at each occurrence, is independently heterocyclyl;

wherein the cyclic moieties represented by R^4 and R^7 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, $CO(O)R^{10}$, OH and F;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or

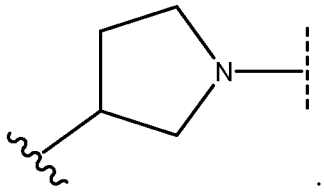
more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, and heterocyclyl;

with the proviso that

when X^1 is CR^1 and X^2 is CR^1; R^1 is hydrogen; Y^1 is NHC(O); Z^1 is



; and R^2 is pyrrolyl; the R^2 pyrrolyl is not substituted with two alkyl groups.

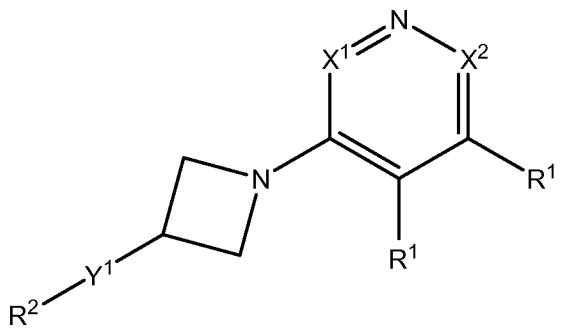
Still another embodiment pertains to compounds having Formula (IA), which includes Examples 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440,

441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, and pharmaceutically acceptable salts thereof.

Still another embodiment pertains to compounds of Formula (1A), selected from the group consisting of Examples 147, 310, 313, 316, 317, 320, 332, 333, 334, 402, 433, 440, 658, 681, 691, 706, 707, 723, 736, 795, and pharmaceutically acceptable salts thereof.

Embodiments of Formula (IIA)

In another aspect, the present invention provides compounds of Formula (IIA)



(IIA);

and pharmaceutically acceptable salts thereof; wherein X^1, X^2, Y^1, R^1, and R^2 are as described herein for Formula (IA).

One embodiment of this invention pertains to compounds of Formula (IIA) and pharmaceutically acceptable salts thereof;

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^3, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, and heterocyclyl; wherein each R^3 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, C(O)NHOH, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, C(O)H,

$C(O)OH$, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^3 aryl, cycloalkyl, cycloalkenyl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^6)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, C(O)NHOH, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^5, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^5 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), C(O)OH, N_3, CN, NH_2, F, Cl, Br and I;

R^6, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^6 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^8, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^9, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, R^5, R^6, R^7, R^8, and R^9 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

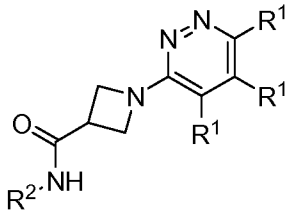
R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In one embodiment of Formula (IIA), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (IIA), X^1 is N and X^2 is CR^1. In another embodiment of Formula (IIA), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (IIA), X^1 is CR^1 and X^2 is CR^1.

In one embodiment of Formula (IIA), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (IIA), Y^1 is C(O)NH. In another embodiment of Formula (IIA), Y^1 is NHC(O).

In one embodiment of Formula (IIA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IIA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IIA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In another aspect, the present invention provides compounds of Formula (IIB),



Formula (IIB)

and pharmaceutically acceptable salts thereof; wherein R^1 and R^2 are as described herein for Formula (IA).

In one embodiment of Formula (IIA) and (IIB), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIA) and (IIB), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IIA) and (IIB), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IIA) and (IIB), R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (IIA) and (IIB), R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered

heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (IIA) and (IIB), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (IIA) and (IIB), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F. In another embodiment of Formula (IIA) and (IIB), R^2 is phenyl; wherein each R^2 phenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F. In another embodiment of Formula (IIA) and (IIB), R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

In another embodiment of Formula (IIA) and (IIB), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (IIA) and (IIB), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F. In another embodiment of Formula (IIA) and (IIB), R^2 is furanyl or thiophenyl; wherein each R^2 furanyl and thiophenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F.

In one embodiment of Formula (IIA) and (IIB), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIA) and (IIB), R^4, at each occurrence, is alkyl or heterocyclyl.

In one embodiment of Formula (IIA) and (IIB), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (I), each R^4 alkyl is optionally substituted with one R^7.

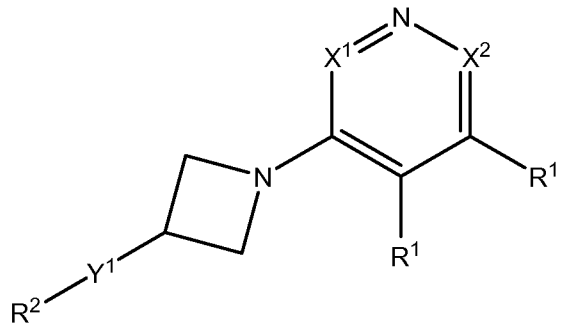
In one embodiment of Formula (IIA) and (IIB), R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl. In another embodiment of Formula (IIA) and (IIB), R^7, at each occurrence, is heterocyclyl.

In one embodiment of Formula (IIA) and (IIB), each R^4 and R^7 heterocyclyl is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$,

CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In another embodiment of Formula (IIA) and (IIB), each R^4 and R^7 heterocyclyl is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, OH, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl and haloalkyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (IIA)



Formula (IIA);

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, Cl, and F;

R^2 is aryl or 5-6 membered heteroaryl wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, SO_2R^4, OR^4, and F;

R^4, at each occurrence, is alkyl or heterocyclyl; wherein each R^4 alkyl is optionally substituted with R^7;

R^7, at each occurrence, is independently heterocyclyl;

wherein the cyclic moieties represented by R^4 and R^7 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, $CO(O)R^{10}$, OH and F;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

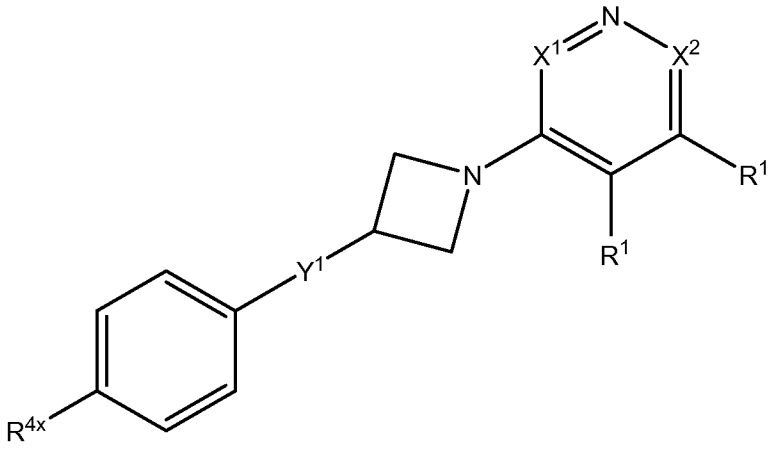
R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, and heterocyclyl.

Still another embodiment pertains to compounds having Formula (IIA), which includes Examples 1, 2, 3, 4, 5, 6, 7, 10, 20, 21, 22, 23, 24, 25, 26, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 609, 610, 611, 612, 613, 614, 615, 616, 617, 665, 666, 667, 668, 737, 738, 739, 740, 741, 748, 750, 751, 753, 784, 803, 804, 805, 806, 807, 809, 817, 818, 819, 820, 821, 822, 823, 828, 829, 830, 831, 832, 833, 834, 835, 840, 841, 842, 843, 844, 845, 846, 851, 852, 853, 854, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, and pharmaceutically acceptable salts thereof.

Embodiments of Formula (IIIA)

In another aspect, the present invention provides compounds of Formula (IIIA)



(IIIA);

and pharmaceutically acceptable salts thereof; wherein X^1, X^2, R^1, and Y^1 are as described in Formula (IA) herein and R^{4x} is as described herein for substituents on R^2 when R^2 is aryl in Formula (IA).

One embodiment of this invention pertains to compounds of Formula (IIIA) or pharmaceutically acceptable salts thereof;

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^{4X} is independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$,

$OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4 and R^7, are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl,

alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

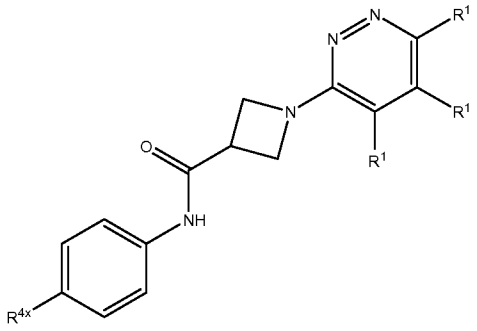
R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In one embodiment of Formula (IIIA), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (IIIA), X^1 is N and X^2 is CR^1. In another embodiment of Formula (IIIA), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (IIIA), X^1 is CR^1 and X^2 is CR^1.

In one embodiment of Formula (IIIA), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (IIIA), Y^1 is C(O)NH. In another embodiment of Formula (IIIA), Y^1 is NHC(O).

In one embodiment of Formula (IIIA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIIA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IIIA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IIIA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In another aspect, the present invention provides compounds of Formula (IIIB),



Formula (IIIB)

and pharmaceutically acceptable salts thereof; wherein R^1 is described herein for Formula (IA) and R^{4x} is as described herein for substituents on R^2 when R^2 is aryl in Formula (IA).

In one embodiment of Formula (IIIA) and (IIIB), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl,

haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIIA) and (IIIB), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IIIA) and (IIIB), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IIIA) and (IIIB), R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (IIIA) and (IIIB), R^{4X} is independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (IIIA) and (IIIB), R^{4X} is independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (IIIA) and (IIIB), R^{4X} is independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F.

In one embodiment of Formula (IIIA) and (IIIB), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIIA) and (IIIB), R^4, at each occurrence, is alkyl or heterocyclyl.

In one embodiment of Formula (IIIA) and (IIIB), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIIA) and (IIIB), each R^4 alkyl is optionally substituted with one R^7.

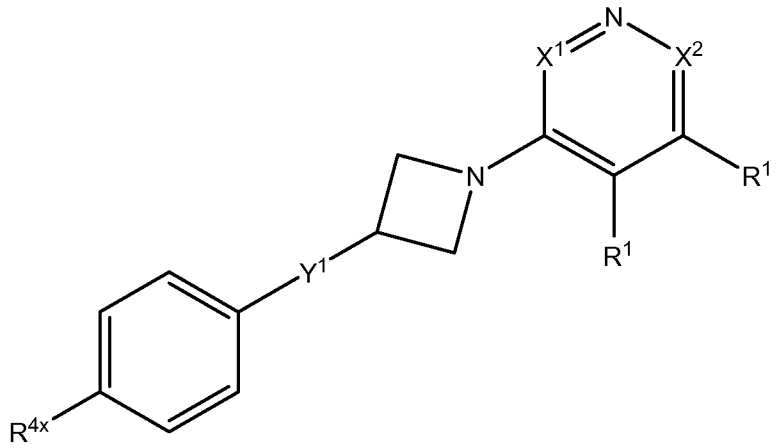
In one embodiment of Formula (IIIA) and (IIIB), R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl. In another embodiment of Formula (IIIA) and (IIIB), R^7, at each occurrence, is heterocyclyl.

In one embodiment of Formula (IIIA) and (IIIB), each R^4 and R^7 heterocyclyl is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and R^{13}, at each occurrence, is independently

selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In another embodiment of Formula (IIIA) and (IIIB), each R^4 and R^7 heterocyclyl is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, OH, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl and haloalkyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (IIIA)



(IIIA);

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, Cl, and F;

R^{4X} is independently selected from the group consisting of R^4, SO_2R^4, OR^4, and F;

R^4, at each occurrence, is alkyl or heterocyclyl; wherein each R^4 alkyl is optionally substituted with R^7;

R^7, at each occurrence, is independently heterocyclyl;

wherein the cyclic moieties represented by R^4 and R^7 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, $CO(O)R^{10}$, OH and F;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

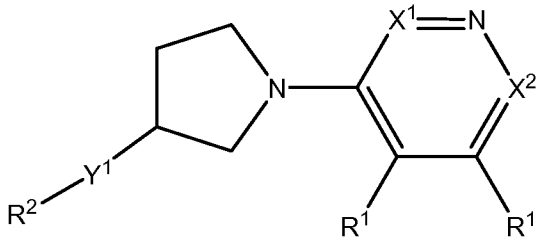
R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, and heterocyclyl.

Still another embodiment pertains to compounds having Formula (IIIA), which includes Examples 1, 2, 3, 4, 5, 6, 7, 10, 20, 22, 25, 26, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264,

265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 609, 610, 611, 612, 613, 614, 615, 616, 617, 665, 666, 667, 668, 737, 738, 739, 740, 741, 748, 750, 751, 753, 784, 803, 804, 805, 806, 807, 809, 817, 818, 819, 820, 821, 822, 823, 840, 841, 842, 843, 844, 845, 846, 851, 852, 853, 854, 857, 863, 864, 865, 866, 867, and pharmaceutically acceptable salts thereof.

Embodiments of Formula (IVA)

In another aspect, the present invention provides compounds of Formula (IVA)



(IVA);

and pharmaceutically acceptable salts thereof; wherein each X^1, X^2, Y^1, R^1, and R^2 are as described herein for Formula (I).

One embodiment of this invention pertains to compounds of Formula (IVA) and pharmaceutically acceptable salts thereof;

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^3, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, and heterocyclyl; wherein each R^3 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, C(O)NHOH, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^3 aryl, cycloalkyl, cycloalkenyl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^6)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, C(O)NHOH, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$,

SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^5, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^5 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), C(O)OH, N_3, CN, NH_2, F, Cl, Br and I;

R^6, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^6 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^8, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^9, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, R^5, R^6, R^7, R^8, and R^9 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$,

$NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

with the proviso that

when X^1 is CR^1 and X^2 is CR^1; R^1 is hydrogen; Y^1 is NHC(O); and R^2 is pyrrolyl; the R^2 pyrrolyl is not substituted with two alkyl groups.

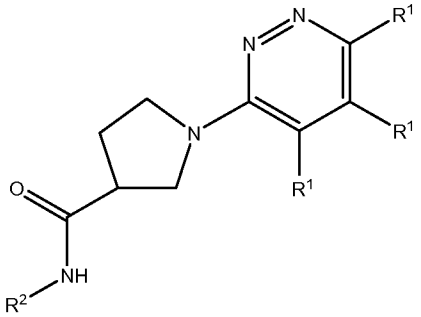
In one embodiment of Formula (IVA), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (IVA), X^1 is N and X^2 is

CR^1. In another embodiment of Formula (IVA), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (IVA), X^1 is CR^1 and X^2 is CR^1.

In one embodiment of Formula (IVA), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (IVA), Y^1 is C(O)NH. In another embodiment of Formula (IVA), Y^1 is NHC(O).

In one embodiment of Formula (IVA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IVA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IVA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IVA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In another aspect, the present invention provides compounds of Formula (IVB),



Formula (IVB)

and pharmaceutically acceptable salts thereof; wherein R^1 and R^2 are as described herein for Formula (IA).

In one embodiment of Formula (IVA) and (IVB), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IVA) and (IVB), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IVA) and (IVB), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IVA) and (IVB), R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (IVA) and (IVB), R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3,

$S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (IVA) and (IVB), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (IVA) and (IVB), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F. In another embodiment of Formula (IVA) and (IVB), R^2 is phenyl; wherein each R^2 phenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F. In another embodiment of Formula (IVA) and (IVB), R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

In another embodiment of Formula (IVA) and (IVB), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (IVA) and (IVB), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F. In another embodiment of Formula (IVA) and (IVB), R^2 is furanyl or thiophenyl; wherein each R^2 furanyl and thiophenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F.

In one embodiment of Formula (IVA) and (IVB), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$,

$NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IVA) and (IVB), R^4, at each occurrence, is alkyl or heterocyclyl.

In one embodiment of Formula (IVA) and (IVB), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IVA) and (IVB), each R^4 alkyl is optionally substituted with one R^7.

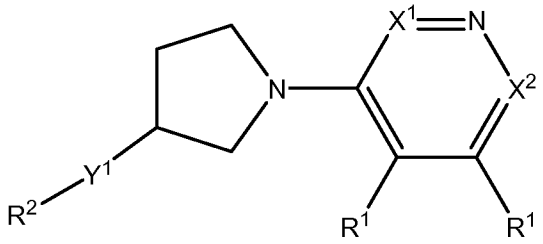
In one embodiment of Formula (IVA) and (IVB), R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl. In another embodiment of Formula (IVA) and (IVB), R^7, at each occurrence, is heterocyclyl.

In one embodiment of Formula (IVA) and (IVB), each R^4 and R^7 heterocyclyl is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents

independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In another embodiment of Formula (IVA) and (IVB), each R^4 and R^7 heterocyclyl is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, OH, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl and haloalkyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (IVA)



Formula (IVA);

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, Cl, and F;

R^2 is aryl or 5-6 membered heteroaryl wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, SO_2R^4, OR^4, and F;

R^4, at each occurrence, is alkyl or heterocyclyl; wherein each R^4 alkyl is optionally substituted with R^7;

R^7, at each occurrence, is independently heterocyclyl;

wherein the cyclic moieties represented by R^4 and R^7 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, $CO(O)R^{10}$, OH and F;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, and heterocyclyl;

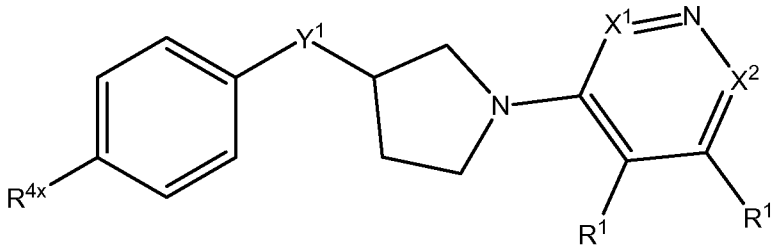
with the proviso that

when X^1 is CR^1 and X^2 is CR^1; R^1 is hydrogen; Y^1 is NHC(O); and R^2 is pyrrolyl; the R^2 pyrrolyl is not substituted with two alkyl groups.

Still another embodiment pertains to compounds having Formula (IVA), which includes Examples 8, 9, 11, 12, 13, 14, 15, 16, 17, 18, 19, 27, 28, 141, 142, 204, 310, 311, 312, 313, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, and pharmaceutically acceptable salts thereof.

Embodiments of Formula (VA)

In another aspect, the present invention provides compounds of Formula (VA)



(VA);

and pharmaceutically acceptable salts thereof; wherein X^1, X^2, R^1, and Y^1 are as described in Formula (IA) herein and R^{4x} is as described herein for substituents on R^2 when R^2 is aryl in Formula (IA).

One embodiment of this invention pertains to compounds of Formula (VA) or pharmaceutically acceptable salts thereof;

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^{4X} is independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, and R^7, are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl,

alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

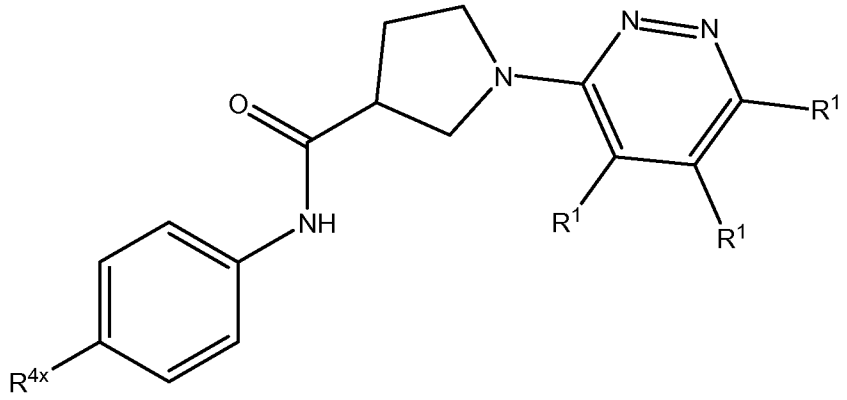
In one embodiment of Formula (VA), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (VA), X^1 is N and X^2 is CR^1. In another embodiment of Formula (VA), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (VA), X^1 is CR^1 and X^2 is CR^1.

In one embodiment of Formula (VA), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (VA), Y^1 is C(O)NH. In another embodiment of Formula (VA), Y^1 is NHC(O).

In one embodiment of Formula (VA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (VA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is

independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (VA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (VA), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In another aspect, the present invention provides compounds of Formula (VB),



Formula (VB)

and pharmaceutically acceptable salts thereof; wherein R^1 is described herein for Formula (IA) and R^{4x} is as described herein for substituents on R^2 when R^2 is aryl in Formula (IA).

In one embodiment of Formula (VA) and (VB), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (VA) and (VB), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (VA) and (VB), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (VA) and (VB), R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (VA) and (VB), R^{4X} is independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (VA) and (VB), R^{4X} is independently selected from the group consisting of R^4, OR^4, SO_2R^4, F, Cl, and I. In another embodiment of Formula (VA) and (VB), R^{4X} is independently selected from the group consisting of R^4, OR^4, SO_2R^4, and F.

In one embodiment of Formula (VA) and (VB), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (VA) and (VB), R^4, at each occurrence, is alkyl or heterocyclyl.

In one embodiment of Formula (VA) and (VB), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (I), each R^4 alkyl is optionally substituted with one R^7.

In one embodiment of Formula (VA) and (VB), R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl. In another embodiment of Formula (VA) and (VB), R^7, at each occurrence, is heterocyclyl.

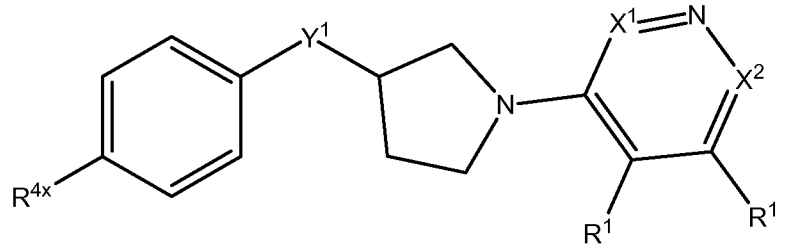
In one embodiment of Formula (VA) and (VB), each R^4 and R^7 heterocyclyl is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$,

$NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In another embodiment of Formula (VA) and (VB), each R^4 and R^7 heterocyclyl is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, OH, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the

group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl and haloalkyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (VA)



(VA);

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, Cl, and F;

R^{4X} is independently selected from the group consisting of R^4, SO_2R^4, OR^4, and F;

R^4, at each occurrence, is alkyl or heterocyclyl; wherein each R^4 alkyl is optionally substituted with R^7;

R^7, at each occurrence, is independently heterocyclyl;

wherein the cyclic moieties represented by R^4 and R^7 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, $CO(O)R^{10}$, OH and F;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

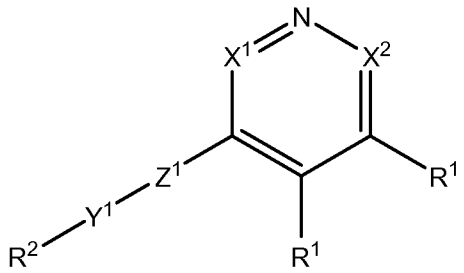
R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, and heterocyclyl.

Still another embodiment pertains to compounds having Formula (VA), which includes Examples 8, 9, 11, 12, 13, 14, 15, 16, 17, 18, 19, 27, 28, 141, 142, 204, 310, 311, 312, 313, 614, 615, 616, 617, 625, 626, 627, 628, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 743, 744, 745, 748, 749, 750, 751, 752, 753, 756, 757, 759, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, and pharmaceutically acceptable salts thereof.

Embodiments of Formula (IC)

One embodiment of this invention, therefore, pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (IC)



Formula (IC);

wherein

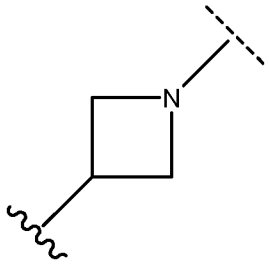
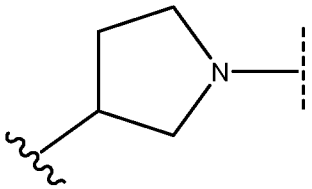
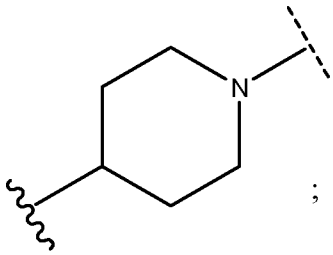
X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

Z^1 is

wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl;

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^3, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, and heterocyclyl; wherein each R^3 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, C(O)NHOH, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, C(O)H,

$C(O)OH$, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^3 aryl, cycloalkyl, cycloalkenyl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^6)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, C(O)NHOH, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^5, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^5 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), C(O)OH, N_3, CN, NH_2, F, Cl, Br and I;

R^6, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^6 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^8, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^9, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, R^5, R^6, R^7, R^8, and R^9 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

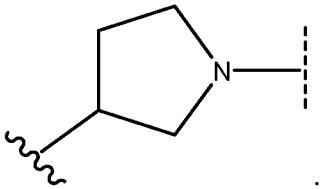
R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

with the proviso that

when X^1 is CR^1 and X^2 is CR^1; R^1 is hydrogen; Y^1 is NHC(O); Z^1 is



; and R^2 is pyrrolyl; the R^2 pyrrolyl is not substituted with two alkyl groups.

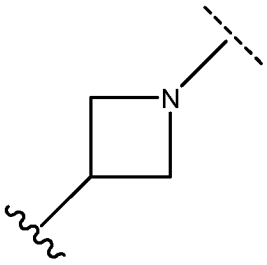
In one embodiment of Formula (IC), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (IC), X^1 is N and X^2 is CR^1. In another embodiment of Formula (IC), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (IC), X^1 is CR^1 and X^2 is CR^1.

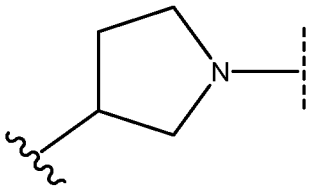
In one embodiment of Formula (IC), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IC), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IC), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IC), R^1, at each occurrence, is hydrogen.

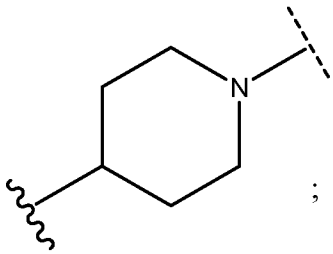
In one embodiment of Formula (IC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (IC), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (IC), Y^1 is C(O)NH. In another embodiment of Formula (IC), Y^1 is NHC(O).

In one embodiment of Formula (IC), Z^1 is

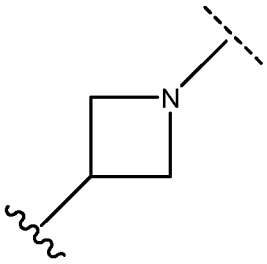


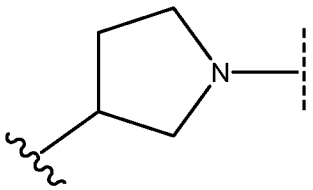
, 

, or 

;

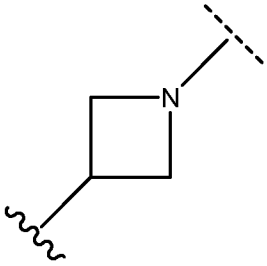
wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (IC), Z^1 is



, or 

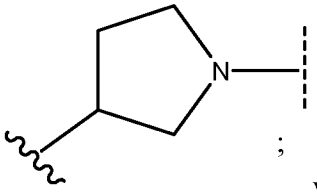
;

wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (IC), Z^1 is



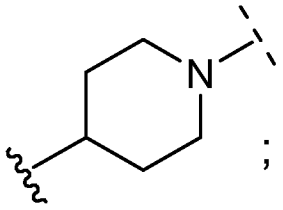
;

wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (IC), Z^1 is



;

wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl. In another embodiment of Formula (IC), Z^1 is



wherein ~~~ indicates the point of attachment to Y^1 and ----- indicates the point of attachment to the nitrogen containing heteroaryl.

In one embodiment of Formula (IC), R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (IC), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, F, Cl, and I. In another embodiment of Formula (IC), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F. In another embodiment of Formula (IC), R^2 is phenyl; wherein each R^2 phenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F. In another embodiment of Formula (IC), R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

In another embodiment of Formula (IC), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, F, Cl, and I. In another embodiment of Formula (IC), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently

selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F. In another embodiment of Formula (IC), R^2 is pyridinyl, furanyl, thiophenyl, pyrazole, or thiazolyl; wherein each R^2 pyridinyl, furanyl, thiophenyl, pyrazole, and thiazolyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F.

In one embodiment of Formula (IC), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IC), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl.

In one embodiment of Formula (IC), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IC), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, $N(R^7)_2$, F, Cl, Br and I.

In one embodiment of Formula (IC), R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl. In another embodiment of Formula (IC), R^7, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl.

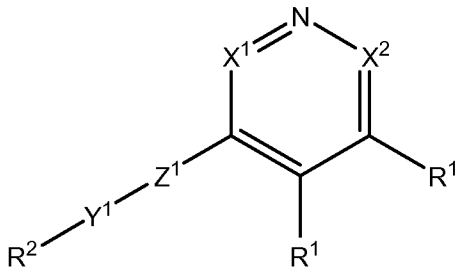
In one embodiment of Formula (IC), each R^4 and R^7 cyclic moiety is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$,

$C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In another embodiment of Formula (IC), each R^4 and R^7 cyclic moiety is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, CO(O)H, OH, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12},

$C(O)R^{12}$, NH_2, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (IC)



Formula (IC);

wherein

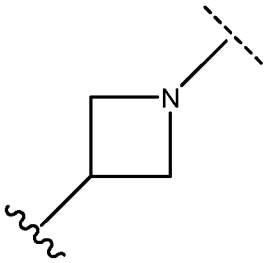
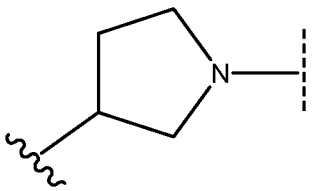
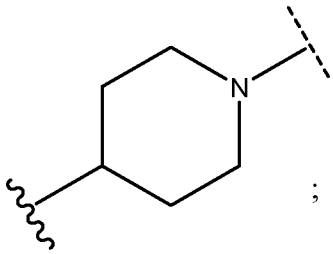
X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

Z^1 is


,

, or

;

wherein ~~~ indicates the point of attachment to Y^1 and ------ indicates the point of attachment to the nitrogen containing heteroaryl;

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, Cl, and F;

R^2 is aryl or 5-6 membered heteroaryl wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, SO_2R^4, OR^4, $C(O)NHR^4$, and F;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, $N(R^7)_2$, and F;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl;

wherein the cyclic moieties represented by R^4 and R^7 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, $CO(O)R^{10}$, C(O)OH, OH and F;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, NH_2, OH, CN, CF_3, OCF_3, F, and Cl;

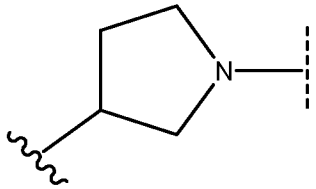
R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, cycloalkyl, and heterocyclyl;

with the proviso that

when X^1 is CR^1 and X^2 is CR^1; R^1 is hydrogen; Y^1 is NHC(O); Z^1 is



; and R^2 is pyrrolyl; the R^2 pyrrolyl is not substituted with two alkyl groups.

Still another embodiment pertains to compounds having Formula (IC), which include

1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(2-cyanopyridin-3-yl)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-[2-(trifluoromethyl)pyridin-3-yl]azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(4-methylpyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(4-fluoropyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-[4-(trifluoromethyl)pyridin-3-yl]azetidine-3-carboxamide;

tert-butyl 4-[4-({[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate;

tert-butyl 4-[4-({[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate;

1-(pyridin-3-yl)-N-(4-{1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-[4-({1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-[4-({1-[(2R)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[1-(pyridin-3-yl)azetidin-3-yl]-4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}benzamide;

N-(4-{1-[(2S)-2-methylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)-N-[1-(pyridin-3-yl)azetidin-3-yl]benzamide;

4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}-N-[1-(pyridin-3-yl)azetidin-3-yl]benzamide;

1-(pyridin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-(4-{[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbamoyl}phenoxy)piperidine-1-carboxylate;

tert-butyl 4-(4-{[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbamoyl}phenoxy)piperidine-1-carboxylate;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-[4-({1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-{4-[(1-pentanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylpentanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-ethoxypropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-butanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(ethoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(N-acetyl-L-leucyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(morpholin-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(furan-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methoxypyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylmethyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpentyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-ethylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-cyclopropylethyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylmethyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylmethyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylmethyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpentyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methoxypyridin-3-yl)azetidine-3-carboxamide;

1-(4-cyanopyridin-3-yl)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-pentanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(morpholin-4-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(pyrrolidin-1-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(5-oxo-D-prolyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperazin-1-yl)acetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(5-oxo-L-prolyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(morpholin-4-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(piperidin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide;

N-(4-{1-[(2S)-2-methylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(pyridazin-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-[4-(1-pentanoylpiperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(morpholin-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(pyrrolidin-1-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(5-oxo-D-prolyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperazin-1-yl)acetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(5-oxo-L-prolyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[3-(morpholin-4-yl)propanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[3-(piperidin-1-yl)propanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]azetidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-{4-[(1-benzoylazetidin-3-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-hydroxy-2-methylpropanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-pentanoylazetidin-3-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclobutylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(3,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]furan-2-carboxamide;

(3S)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

tert-butyl 4-(4-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}phenyl)piperidine-1-carboxylate;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-pentanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-hexanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-heptanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(but-3-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(pent-4-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(methylsulfanyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-nitropropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(pent-4-ynoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{1-[(3,5-dimethylphenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(5-methylpyrazin-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[(pyrimidin-2-ylsulfanyl)acetyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-(4-{1-[(1-acetylpiperidin-4-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(diphenylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(5-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluoro-4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-tert-butylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-fluoro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-chloro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylphenoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{1-[(3-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2R)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[N-(furan-2-ylcarbonyl)glycyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(benzyloxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-1-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(N-benzoylglycyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[4-(thiophen-2-yl)butanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclobutylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-{N-[(4-methylphenyl)sulfonyl]glycyl}piperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,3-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-2-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-phenylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,6-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(phenylsulfonyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2,5-dimethylfuran-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-oxopropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(1,3-thiazol-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2S)-2-methylbutanoyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydro-2H-pyran-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethoxy)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(thiophen-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3,5-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[3-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2,4-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(5-methylthiophen-2-yl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[3-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(pyridin-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methyl-2-phenylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(methoxyacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(thiophen-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[3-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[4-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[4-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(3,3,3-trifluoropropanoyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[difluoro(phenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2S)-2-methylbutanoyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydro-2H-pyran-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethoxy)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(thiophen-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3,5-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[3-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2,4-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(5-methylthiophen-2-yl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[3-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(pyridin-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methyl-2-phenylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(methoxyacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(thiophen-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[3-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[4-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[4-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(3,3,3-trifluoropropanoyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[difluoro(phenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-(4-{1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[difluoro(phenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-tert-butylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]sulfonyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,5-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-dimethylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-dichlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(phenylacetyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylalanyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

tert-butyl 4-(2-methyl-1-oxo-1-{4-[4-({[1-(pyridin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidin-1-yl}propan-2-yl)piperazine-1-carboxylate;

N-(4-{1-[2-methyl-2-(piperazin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[(3R)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3R)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3S)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3R)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)piperidine-4-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}piperidine-4-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2S)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2R)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-methylphenoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2,6-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-1-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[4-(thiophen-2-yl)butanoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-2-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[3-(phenylsulfonyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(N-benzoylglycyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-5-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-fluoropyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-fluoro-6-methylpyridin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-heptanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-hexanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3,5-dimethylphenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[2-chloro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(5-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(diphenylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(pent-4-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[2-fluoro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-tert-butylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(pent-4-ynoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-acetylpiperidin-4-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(but-3-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluoro-4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-4-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-methylpyridin-3-yl)azetidine-3-carboxamide;

2-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-1,3-thiazole-5-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(2-methylpyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]furan-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]furan-2-carboxamide;

N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-4-[1-(2-methylpropanoyl)piperidin-4-yl]benzamide;

N-(4-{1-[2-(piperazin-1-yl)ethyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

4-[1-(2-methylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]benzamide;

N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(3-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(4-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

(3S)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

5-[1-(2-methylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-(1-benzoylpiperidin-4-yl)-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-{1-[(2R)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}thiophene-2-carboxamide;

5-{1-[(1-methylpiperidin-4-yl)acetyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide;

(3S)-N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(propan-2-yl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylmethyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-2-ylmethyl)-1H-pyrazol-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-tert-butyl-1H-pyrazol-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2-methylbenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(4,4,4-trifluorobutanoyl)pyrrolidin-3-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(5-propyl-1,2,4-oxadiazol-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylazetidin-3-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-difluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-difluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[(1-benzoylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,3,4-oxadiazol-2-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-imidazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,2,4-oxadiazol-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-cyclopropyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-(5-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}thiophen-2-yl)piperidine-1-carboxylate;

tert-butyl 4-fluoro-4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidine-1-carboxylate;

5-(1-benzoylpiperidin-4-yl)-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylbenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(3-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(4-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[3-cyclopropyl-1-(2-hydroxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

1-(6-fluoropyridazin-3-yl)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[(1-benzoylpiperidin-4-yl)oxy]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[8-(2-methylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[8-(4,4,4-trifluorobutanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}azetidine-3-carboxamide;

N-[4-(8-benzoyl-8-azabicyclo[3.2.1]oct-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2-fluorobenzoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2,2-dimethylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{8-[(1-methylcyclopropyl)carbonyl]-8-azabicyclo[3.2.1]oct-3-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methoxyethyl)-3-(2-methylpropyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-[1-(pyridazin-3-yl)azetidin-3-yl]-5-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-fluoropiperidine-1-carboxylate;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-hydroxypiperidine-1-carboxylate;

N-[1-(pyridazin-3-yl)azetidin-3-yl]-5-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(cyclopropylcarbonyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[4-fluoro-1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(2-fluoro-4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoyl-4-fluoropiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)-4-fluoropiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butyl-3-tert-butyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(tetrahydro-2H-pyran-4-ylmethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(6-chloropyridazin-3-yl)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-3-fluorophenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(6-methylpyridazin-3-yl)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-ethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-{[4-methyl-1-(oxetan-3-yl)piperidin-4-yl]methyl}-1H-pyrazol-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]furan-2-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-aminopyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylic acid;

ethyl 1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate;

ethyl 1-phenyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate;

N-{6-[1-(2-fluorobenzoyl)piperidin-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

1-(6-methylpyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{6-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]pyridin-3-yl}azetidine-3-carboxamide;

N-{6-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{6-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)-1H-pyrazol-1-yl]piperidine-1-carboxylate;

N-(6-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}pyridin-3-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(1H-pyrazol-4-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(methylsulfanyl)acetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(1H-pyrazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(pent-4-ynoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(ethoxyacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-{4-[(1-hexanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(but-3-enoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(1,2-oxazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-butanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclobutylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-pentanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbenzoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{1-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-1H-pyrazol-4-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{1-[1-(2-fluorobenzoyl)piperidin-4-yl]-1H-pyrazol-4-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(phenylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2,2-dimethylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(3-methoxy-2,2-dimethylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-cyclopropylethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[2-(2-ethylpiperidin-1-yl)ethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(cyclobutylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2S)-butan-2-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(butylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2,2-dimethyltetrahydro-2H-pyran-4-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(1S)-1-cyclopropylethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({2-[methyl(phenyl)amino]ethyl}carbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1,1'-bi(cyclopropyl)-1-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(thiophen-3-ylcarbamoyl)phenyl]azetidine-3-carboxamide;

N-(4-{[(1R)-1-cyclopropylethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylpiperidin-4-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2R)-butan-2-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-azabicyclo[2.2.2]oct-3-ylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(tetrahydrofuran-3-ylmethyl)carbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(oxetan-3-ylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-methylcyclopropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclobutylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylcyclopropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-methoxy-2-methylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(cyclopropylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(2R)-tetrahydrofuran-2-ylmethyl]carbamoyl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3,3,3-trifluoropropyl)carbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(1-methylpiperidin-3-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3-methyloxetan-3-yl)methyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(2S)-tetrahydrofuran-2-ylmethyl]carbamoyl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(tetrahydro-2H-pyran-4-ylmethyl)carbamoyl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(tetrahydro-2H-pyran-4-ylcarbamoyl)phenyl]azetidine-3-carboxamide;

N-(4-{[(1-methylpiperidin-3-yl)methyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclopropylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclopentylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(benzylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(3-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(propylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(4-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylcyclobutyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(prop-2-en-1-ylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(cyclopropylacetyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(bicyclo[2.2.1]hept-2-ylacetyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3S)-tetrahydrofuran-3-ylcarbamoyl]phenyl}azetidine-3-carboxamide;

N-[4-({4-[2-(dimethylamino)ethyl]phenyl}carbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3R)-tetrahydrofuran-3-ylcarbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(2-methoxyethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-amino-2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2,2-dimethyl-3-(piperazin-1-yl)propyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-methyl-2-(piperazin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide; and pharmaceutically acceptable salts thereof.

Still another embodiment pertains to compounds of Formula (1A), selected from the group consisting of

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(methylsulfanyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

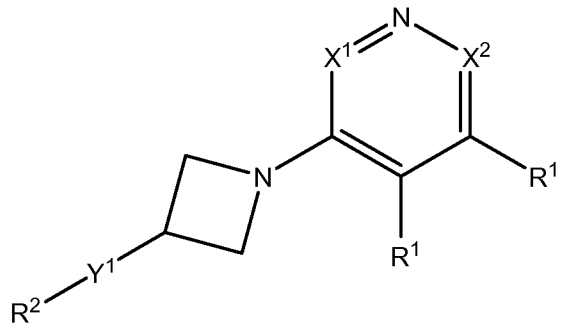
(3S)-N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide; and pharmaceutically acceptable salts thereof.

Embodiments of Formula (IIC)

In another aspect, the present invention provides compounds of Formula (IIC)



(IIC);

and pharmaceutically acceptable salts thereof; wherein X^1, X^2, Y^1, R^1, and R^2 are as described herein for Formula (IC).

One embodiment of this invention pertains to compounds of Formula (IIC) and pharmaceutically acceptable salts thereof;

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^3, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, and heterocyclyl; wherein each R^3 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, C(O)NHOH, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^3 aryl, cycloalkyl, cycloalkenyl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^6)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, C(O)NHOH, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^5, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^5 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), C(O)OH, N_3, CN, NH_2, F, Cl, Br and I;

R^6, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^6 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently

selected from the group consisting of R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), $C(O)OH$, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^8, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^9, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, R^5, R^6, R^7, R^8, and R^9 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

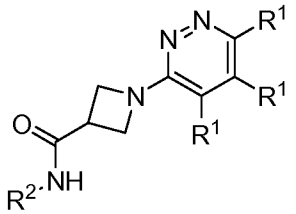
R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In one embodiment of Formula (IIC), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (IIC), X^1 is N and X^2 is CR^1. In another embodiment of Formula (IIC), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (IIC), X^1 is CR^1 and X^2 is CR^1.

In one embodiment of Formula (IIC), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (IIC), Y^1 is C(O)NH. In another embodiment of Formula (IIC), Y^1 is NHC(O).

In one embodiment of Formula (IIC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IIC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IIC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In another aspect, the present invention provides compounds of Formula (IID),



Formula (IID)

and pharmaceutically acceptable salts thereof; wherein R^1 and R^2 are as described herein for Formula (IC).

In one embodiment of Formula (IIC) and (IID), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl,

haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIC) and (IID), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IIC) and (IID), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IIC) and (IID), R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (IIC) and (IID), R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (IIC) and (IID), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, F, Cl, and I. In another embodiment of Formula (IIC) and (IID), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F. In another embodiment of Formula (IIC) and (IID), R^2 is phenyl; wherein each R^2 phenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F. In another embodiment of Formula (IIC) and (IID), R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

In another embodiment of Formula (IIC) and (IID), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, F, Cl, and I. In another embodiment of Formula (IIC) and (IID), R^2 is 5-6 membered

heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F. In another embodiment of Formula (IIC) and (IID), R^2 is pyridinyl, furanyl, thiophenyl, pyrazole, or thiazolyl; wherein each R^2 pyridinyl, furanyl, thiophenyl, pyrazole, and thiazolyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F.

In one embodiment of Formula (IIC) and (IID), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIC) and (IID), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl.

In one embodiment of Formula (IIC) and (IID), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIC) and (IID), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, $N(R^7)_2$, F, Cl, Br and I.

In one embodiment of Formula (IIC) and (IID), R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl. In another embodiment of Formula (IIC) and (IID), R^7, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl.

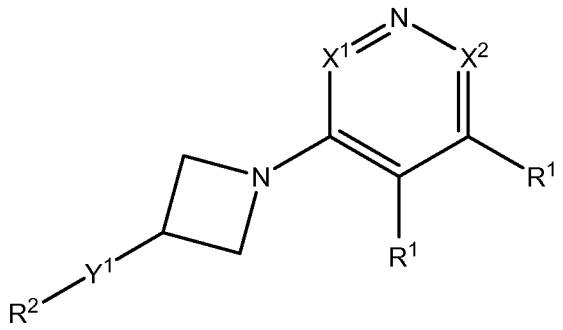
In one embodiment of Formula (IIC) and (IID), each R^4 and R^7 cyclic moiety is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$,

$NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In another embodiment of Formula (IIC) and (IID), each R^4 and R^7 cyclic moiety is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, CO(O)H, OH, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from

the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, NH_2, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (IIC)



Formula (IIC);

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, Cl, and F;

R^2 is aryl or 5-6 membered heteroaryl wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, SO_2R^4, OR^4, $C(O)NHR^4$, and F;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, $N(R^7)_2$, and F;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl;

wherein the cyclic moieties represented by R^4 and R^7 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, $CO(O)R^{10}$, C(O)OH, OH and F;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, NH_2, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, cycloalkyl, and heterocyclyl.

Still another embodiment pertains to compounds having Formula (IIC), which includes

1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(2-cyanopyridin-3-yl)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-[2-(trifluoromethyl)pyridin-3-yl]azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(4-methylpyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(4-fluoropyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-[4-(trifluoromethyl)pyridin-3-yl]azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[1-(pyridin-3-yl)azetidin-3-yl]-4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}benzamide;

N-(4-{1-[(2S)-2-methylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)-N-[1-(pyridin-3-yl)azetidin-3-yl]benzamide;

4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}-N-[1-(pyridin-3-yl)azetidin-3-yl]benzamide;

1-(pyridin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-[4-({1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-{4-[(1-pentanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylpentanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-ethoxypropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-butanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(ethoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(N-acetyl-L-leucyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(morpholin-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(furan-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methoxypyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylmethyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpentyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-ethylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-cyclopropylethyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylmethyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylmethyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylmethyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpentyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methoxypyridin-3-yl)azetidine-3-carboxamide;

1-(4-cyanopyridin-3-yl)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-pentanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(morpholin-4-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(pyrrolidin-1-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(5-oxo-D-prolyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperazin-1-yl)acetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(5-oxo-L-prolyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(morpholin-4-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(piperidin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-methylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(pyridazin-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-[4-(1-pentanoylpiperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(morpholin-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(pyrrolidin-1-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(5-oxo-D-prolyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperazin-1-yl)acetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(5-oxo-L-prolyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[3-(morpholin-4-yl)propanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[3-(piperidin-1-yl)propanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]azetidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-{4-[(1-benzoylazetidin-3-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-hydroxy-2-methylpropanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-pentanoylazetidin-3-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclobutylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(3,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]furan-2-carboxamide;

tert-butyl 4-(4-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}phenyl)piperidine-1-carboxylate;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-pentanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-hexanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-heptanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(but-3-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(pent-4-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(methylsulfanyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-nitropropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(pent-4-ynoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{1-[(3,5-dimethylphenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(5-methylpyrazin-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[(pyrimidin-2-ylsulfanyl)acetyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-(4-{1-[(1-acetylpiperidin-4-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(diphenylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(5-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluoro-4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-tert-butylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-fluoro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-chloro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylphenoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{1-[(3-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2R)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[N-(furan-2-ylcarbonyl)glycyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(benzyloxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-1-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(N-benzoylglycyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[4-(thiophen-2-yl)butanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclobutylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-{N-[(4-methylphenyl)sulfonyl]glycyl}piperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,3-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-2-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-phenylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,6-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(phenylsulfonyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2,5-dimethylfuran-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-oxopropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(1,3-thiazol-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2S)-2-methylbutanoyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydro-2H-pyran-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethoxy)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(thiophen-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3,5-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[3-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2,4-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(5-methylthiophen-2-yl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[3-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(pyridin-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methyl-2-phenylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(methoxyacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(thiophen-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[3-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[4-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[4-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(3,3,3-trifluoropropanoyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[difluoro(phenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2S)-2-methylbutanoyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydro-2H-pyran-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethoxy)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(thiophen-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3,5-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[3-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2,4-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(5-methylthiophen-2-yl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[3-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(pyridin-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methyl-2-phenylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(methoxyacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(thiophen-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[3-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[4-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[4-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(3,3,3-trifluoropropanoyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[difluoro(phenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-(4-{1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[difluoro(phenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-tert-butylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]sulfonyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,5-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-dimethylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-dichlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(phenylacetyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylalanyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-(2-methyl-1-oxo-1-{4-[4-({[1-(pyridin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidin-1-yl}propan-2-yl)piperazine-1-carboxylate;

N-(4-{1-[2-methyl-2-(piperazin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-5-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-fluoropyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-fluoro-6-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-4-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-(piperazin-1-yl)ethyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(5-propyl-1,2,4-oxadiazol-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,3,4-oxadiazol-2-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-imidazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,2,4-oxadiazol-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-cyclopropyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-fluoro-4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidine-1-carboxylate;

N-{4-[3-cyclopropyl-1-(2-hydroxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

1-(6-fluoropyridazin-3-yl)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2-methylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[8-(4,4,4-trifluorobutanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}azetidine-3-carboxamide;

N-[4-(8-benzoyl-8-azabicyclo[3.2.1]oct-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2-fluorobenzoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2,2-dimethylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{8-[(1-methylcyclopropyl)carbonyl]-8-azabicyclo[3.2.1]oct-3-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methoxyethyl)-3-(2-methylpropyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-fluoropiperidine-1-carboxylate;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-hydroxypiperidine-1-carboxylate;

N-{4-[4-fluoro-1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(2-fluoro-4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoyl-4-fluoropiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)-4-fluoropiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butyl-3-tert-butyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(tetrahydro-2H-pyran-4-ylmethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(6-chloropyridazin-3-yl)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-3-fluorophenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(6-methylpyridazin-3-yl)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-ethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-{[4-methyl-1-(oxetan-3-yl)piperidin-4-yl]methyl}-1H-pyrazol-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-aminopyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylic acid;

ethyl 1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate;

ethyl 1-phenyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate;

N-{6-[1-(2-fluorobenzoyl)piperidin-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

1-(6-methylpyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{6-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]pyridin-3-yl}azetidine-3-carboxamide;

N-{6-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{6-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)-1H-pyrazol-1-yl]piperidine-1-carboxylate;

N-(6-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}pyridin-3-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(1H-pyrazol-4-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(methylsulfanyl)acetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(1H-pyrazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(pent-4-ynoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(ethoxyacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-{4-[(1-hexanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(but-3-enoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(1,2-oxazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-butanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclobutylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-pentanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbenzoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{1-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-1H-pyrazol-4-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{1-[1-(2-fluorobenzoyl)piperidin-4-yl]-1H-pyrazol-4-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(phenylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2,2-dimethylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(3-methoxy-2,2-dimethylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-cyclopropylethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[2-(2-ethylpiperidin-1-yl)ethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(cyclobutylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2S)-butan-2-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(butylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2,2-dimethyltetrahydro-2H-pyran-4-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(1S)-1-cyclopropylethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({2-[methyl(phenyl)amino]ethyl}carbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1,1'-bi(cyclopropyl)-1-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(thiophen-3-ylcarbamoyl)phenyl]azetidine-3-carboxamide;

N-(4-{[(1R)-1-cyclopropylethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylpiperidin-4-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2R)-butan-2-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-azabicyclo[2.2.2]oct-3-ylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(tetrahydrofuran-3-ylmethyl)carbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(oxetan-3-ylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-methylcyclopropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclobutylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylcyclopropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-methoxy-2-methylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(cyclopropylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(2R)-tetrahydrofuran-2-ylmethyl]carbamoyl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3,3,3-trifluoropropyl)carbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(1-methylpiperidin-3-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3-methyloxetan-3-yl)methyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(2S)-tetrahydrofuran-2-ylmethyl]carbamoyl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(tetrahydro-2H-pyran-4-ylmethyl)carbamoyl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(tetrahydro-2H-pyran-4-ylcarbamoyl)phenyl]azetidine-3-carboxamide;

N-(4-{[(1-methylpiperidin-3-yl)methyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclopropylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclopentylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(benzylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(3-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(propylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(4-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylcyclobutyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(prop-2-en-1-ylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3S)-tetrahydrofuran-3-ylcarbamoyl]phenyl}azetidine-3-carboxamide;

N-[4-({4-[2-(dimethylamino)ethyl]phenyl}carbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3R)-tetrahydrofuran-3-ylcarbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(2-methoxyethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

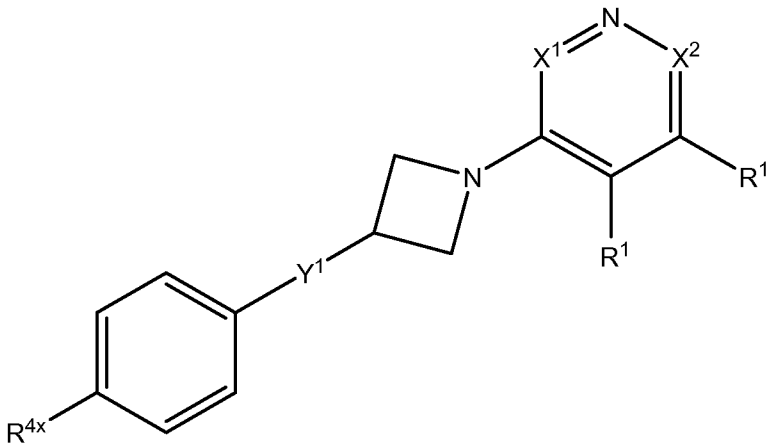
N-{4-[1-(3-amino-2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2,2-dimethyl-3-(piperazin-1-yl)propyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-methyl-2-(piperazin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide; and pharmaceutically acceptable salts thereof.

Embodiments of Formula (IIIC)

In another aspect, the present invention provides compounds of Formula (IIIC)



(IIIC);

and pharmaceutically acceptable salts thereof; wherein X^1, X^2, R^1, and Y^1 are as described in Formula (IC) herein and R^{4x} is as described herein for substituents on R^2 when R^2 is aryl in Formula (IC).

One embodiment of this invention pertains to compounds of Formula (IIIC) or pharmaceutically acceptable salts thereof;

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^{4X} is independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4 and R^7, are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$,

$NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

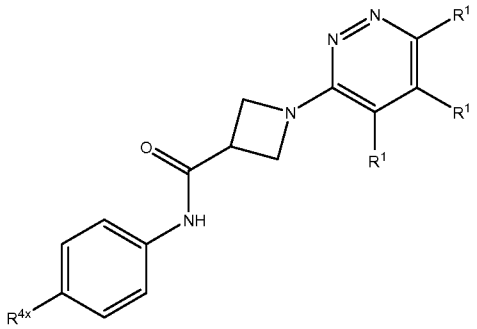
R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In one embodiment of Formula (IIIC), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (IIIC), X^1 is N and X^2 is CR^1. In another embodiment of Formula (IIIC), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (IIIC), X^1 is CR^1 and X^2 is CR^1.

In one embodiment of Formula (IIIC), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (IIIC), Y^1 is C(O)NH. In another embodiment of Formula (IIIC), Y^1 is NHC(O).

In one embodiment of Formula (IIIC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIIC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IIIC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IIIC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In another aspect, the present invention provides compounds of Formula (IIID),



Formula (IIID)

and pharmaceutically acceptable salts thereof; wherein R^1 is described herein for Formula (IC) and R^{4x} is as described herein for substituents on R^2 when R^2 is aryl in Formula (IC).

In one embodiment of Formula (IIIC) and (IIID), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIIC) and (IIID), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IIIC) and (IIID), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IIIC) and (IIID), R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (IIIC) and (IIID), R^{4X} is independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$,

CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (IIIC) and (IIID), R^{4X} is independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, F, Cl, and I. In another embodiment of Formula (IIIC) and (IIID), R^{4X} is independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F.

In one embodiment of Formula (IIIC) and (IIID), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIIC) and (IIID), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl.

In one embodiment of Formula (IIIC) and (IIID), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IIIC) and (IIID), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, $N(R^7)_2$, F, Cl, Br and I.

In one embodiment of Formula (IIIC) and (IIID), R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl. In another embodiment of Formula (IIIC) and (IIID), R^7, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl.

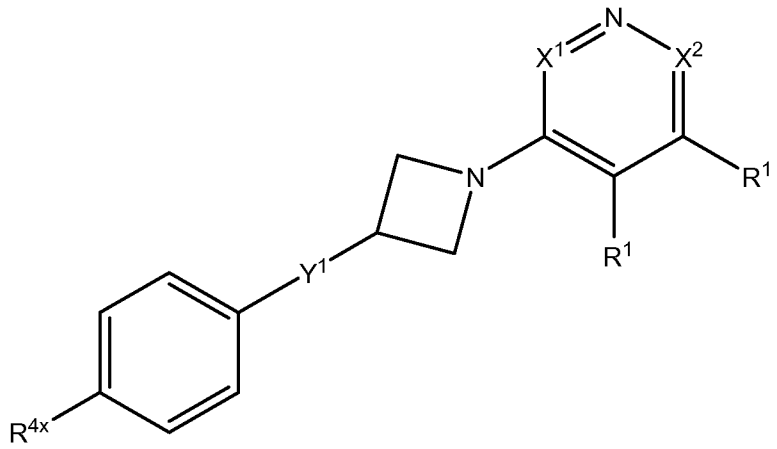
In one embodiment of Formula (IIIC) and (IIID), each R^4 and R^7 cyclic moiety is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$,

$C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In another embodiment of Formula (IIIC) and (IIID), each R^4 and R^7 cyclic moiety is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, $CO(O)H$, OH, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted

with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, NH_2, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (IIIC)



(IIIC);

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, Cl, and F;

R^{4X} is independently selected from the group consisting of R^4, SO_2R^4, OR^4, and F;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, $N(R^7)_2$, and F;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl;

wherein the cyclic moieties represented by R^4 and R^7 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, $CO(O)R^{10}$, C(O)OH, OH and F;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, NH_2, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, cycloalkyl, and heterocyclyl.

Still another embodiment pertains to compounds having Formula (IIIC), which include

1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(2-cyanopyridin-3-yl)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-[2-(trifluoromethyl)pyridin-3-yl]azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(4-methylpyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(4-fluoropyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-[4-(trifluoromethyl)pyridin-3-yl]azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-methylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-[4-({1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-{4-[(1-pentanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylpentanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-ethoxypropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-butanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(ethoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(N-acetyl-L-leucyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(morpholin-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(furan-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methoxypyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylmethyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpentyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-ethylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-cyclopropylethyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylmethyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylmethyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylmethyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpentyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methoxypyridin-3-yl)azetidine-3-carboxamide;

1-(4-cyanopyridin-3-yl)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-pentanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(morpholin-4-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(pyrrolidin-1-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(5-oxo-D-prolyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperazin-1-yl)acetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(5-oxo-L-prolyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(morpholin-4-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(piperidin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-methylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(pyridazin-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-[4-(1-pentanoylpiperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(morpholin-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(pyrrolidin-1-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(5-oxo-D-prolyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperazin-1-yl)acetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(5-oxo-L-prolyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[3-(morpholin-4-yl)propanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[3-(piperidin-1-yl)propanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]azetidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-{4-[(1-benzoylazetidin-3-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-hydroxy-2-methylpropanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-pentanoylazetidin-3-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclobutylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(3,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-pentanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-hexanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-heptanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(but-3-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(pent-4-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(methylsulfanyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-nitropropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(pent-4-ynoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{1-[(3,5-dimethylphenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(5-methylpyrazin-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[(pyrimidin-2-ylsulfanyl)acetyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-(4-{1-[(1-acetylpiperidin-4-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(diphenylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(5-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluoro-4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-tert-butylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-fluoro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-chloro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylphenoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{1-[(3-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2R)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[N-(furan-2-ylcarbonyl)glycyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(benzyloxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-1-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(N-benzoylglycyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[4-(thiophen-2-yl)butanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclobutylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-{N-[(4-methylphenyl)sulfonyl]glycyl}piperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,3-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-2-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-phenylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,6-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(phenylsulfonyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2,5-dimethylfuran-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-oxopropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(1,3-thiazol-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2S)-2-methylbutanoyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydro-2H-pyran-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethoxy)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(thiophen-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3,5-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[3-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2,4-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(5-methylthiophen-2-yl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[3-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(pyridin-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methyl-2-phenylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(methoxyacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(thiophen-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[3-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[4-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[4-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(3,3,3-trifluoropropanoyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[difluoro(phenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2S)-2-methylbutanoyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydro-2H-pyran-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethoxy)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(thiophen-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3,5-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[3-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2,4-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(5-methylthiophen-2-yl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[3-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(pyridin-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methyl-2-phenylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(methoxyacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(thiophen-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[3-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[4-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[4-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(3,3,3-trifluoropropanoyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[difluoro(phenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-(4-{1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[difluoro(phenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-tert-butylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]sulfonyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,5-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-dimethylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-dichlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(phenylacetyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylalanyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-(2-methyl-1-oxo-1-{4-[4-({[1-(pyridin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidin-1-yl}propan-2-yl)piperazine-1-carboxylate;

N-(4-{1-[2-methyl-2-(piperazin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-5-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-fluoropyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-fluoro-6-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-4-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-(piperazin-1-yl)ethyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(5-propyl-1,2,4-oxadiazol-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,3,4-oxadiazol-2-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-imidazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,2,4-oxadiazol-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-cyclopropyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-fluoro-4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidine-1-carboxylate;

N-{4-[3-cyclopropyl-1-(2-hydroxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

1-(6-fluoropyridazin-3-yl)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2-methylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[8-(4,4,4-trifluorobutanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}azetidine-3-carboxamide;

N-[4-(8-benzoyl-8-azabicyclo[3.2.1]oct-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2-fluorobenzoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2,2-dimethylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{8-[(1-methylcyclopropyl)carbonyl]-8-azabicyclo[3.2.1]oct-3-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methoxyethyl)-3-(2-methylpropyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-fluoropiperidine-1-carboxylate;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-hydroxypiperidine-1-carboxylate;

N-{4-[4-fluoro-1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoyl-4-fluoropiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)-4-fluoropiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butyl-3-tert-butyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(tetrahydro-2H-pyran-4-ylmethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(6-chloropyridazin-3-yl)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(6-methylpyridazin-3-yl)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-ethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-{[4-methyl-1-(oxetan-3-yl)piperidin-4-yl]methyl}-1H-pyrazol-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-aminopyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylic acid;

ethyl 1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate;

ethyl 1-phenyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

1-(6-methylpyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-{4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(1H-pyrazol-4-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(methylsulfanyl)acetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(1H-pyrazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(pent-4-ynoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(ethoxyacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-{4-[(1-hexanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(but-3-enoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(1,2-oxazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-butanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclobutylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-pentanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbenzoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(phenylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2,2-dimethylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(3-methoxy-2,2-dimethylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-cyclopropylethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[2-(2-ethylpiperidin-1-yl)ethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(cyclobutylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2S)-butan-2-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(butylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2,2-dimethyltetrahydro-2H-pyran-4-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(1S)-1-cyclopropylethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({2-[methyl(phenyl)amino]ethyl}carbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1,1'-bi(cyclopropyl)-1-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(thiophen-3-ylcarbamoyl)phenyl]azetidine-3-carboxamide;

N-(4-{[(1R)-1-cyclopropylethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylpiperidin-4-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2R)-butan-2-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-azabicyclo[2.2.2]oct-3-ylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(tetrahydrofuran-3-ylmethyl)carbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(oxetan-3-ylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-methylcyclopropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclobutylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylcyclopropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-methoxy-2-methylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(cyclopropylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(2R)-tetrahydrofuran-2-ylmethyl]carbamoyl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3,3,3-trifluoropropyl)carbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(1-methylpiperidin-3-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3-methyloxetan-3-yl)methyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(2S)-tetrahydrofuran-2-ylmethyl]carbamoyl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(tetrahydro-2H-pyran-4-ylmethyl)carbamoyl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(tetrahydro-2H-pyran-4-ylcarbamoyl)phenyl]azetidine-3-carboxamide;

N-(4-{[(1-methylpiperidin-3-yl)methyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclopropylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclopentylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(benzylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(3-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(propylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(4-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylcyclobutyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(prop-2-en-1-ylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3S)-tetrahydrofuran-3-ylcarbamoyl]phenyl}azetidine-3-carboxamide;

N-[4-({4-[2-(dimethylamino)ethyl]phenyl}carbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3R)-tetrahydrofuran-3-ylcarbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(2-methoxyethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

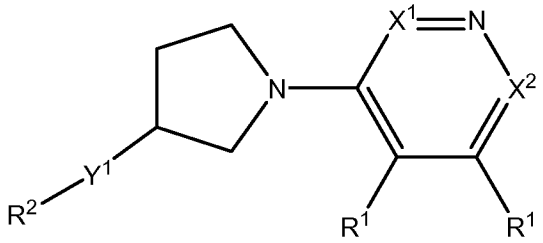
N-{4-[1-(3-amino-2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2,2-dimethyl-3-(piperazin-1-yl)propyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-methyl-2-(piperazin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide; and pharmaceutically acceptable salts thereof.

Embodiments of Formula (IVC)

In another aspect, the present invention provides compounds of Formula (IVC)



(IVC);

and pharmaceutically acceptable salts thereof; wherein each X^1, X^2, Y^1, R^1, and R^2 are as described herein for Formula (I).

One embodiment of this invention pertains to compounds of Formula (IVC) and pharmaceutically acceptable salts thereof;

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^3, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, and heterocyclyl; wherein each R^3 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, $C(O)NHOH$, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^3 aryl, cycloalkyl, cycloalkenyl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^6)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, $C(O)NHOH$, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently

selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^5, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^5 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), C(O)OH, N_3, CN, NH_2, F, Cl, Br and I;

R^6, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^6 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^8, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^9, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, R^5, R^6, R^7, R^8, and R^9 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

with the proviso that

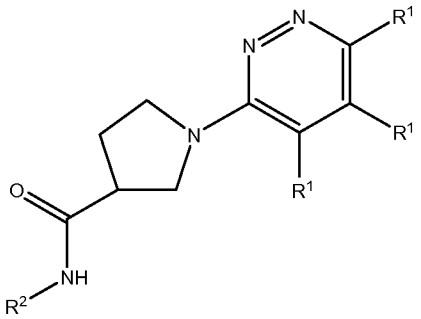
when X^1 is CR^1 and X^2 is CR^1; R^1 is hydrogen; Y^1 is NHC(O); and R^2 is pyrrolyl; the R^2 pyrrolyl is not substituted with two alkyl groups.

In one embodiment of Formula (IVC), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (IVC), X^1 is N and X^2 is CR^1. In another embodiment of Formula (IVC), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (IVC), X^1 is CR^1 and X^2 is CR^1.

In one embodiment of Formula (IVC), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (IVC), Y^1 is C(O)NH. In another embodiment of Formula (IVC), Y^1 is NHC(O).

In one embodiment of Formula (IVC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IVC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IVC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IVC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In another aspect, the present invention provides compounds of Formula (IVD),



Formula (IVD)

and pharmaceutically acceptable salts thereof; wherein R^1 and R^2 are as described herein for Formula (IC).

In one embodiment of Formula (IVC) and (IVD), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (IVC) and (IVD), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (IVC) and (IVD), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (IVC) and (IVD), R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (IVC) and (IVD), R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$,

$NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (IVC) and (IVD), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, F, Cl, and I. In another embodiment of Formula (IVC) and (IVD), R^2 is aryl; wherein each R^2 aryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F. In another embodiment of Formula (IVC) and (IVD), R^2 is phenyl; wherein each R^2 phenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F. In another embodiment of Formula (IVC) and (IVD), R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

In another embodiment of Formula (IVC) and (IVD), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, F, Cl, and I. In another embodiment of Formula (IVC) and (IVD), R^2 is 5-6 membered heteroaryl; wherein each R^2 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F. In another embodiment of Formula (IVC) and (IVD), R^2 is pyridinyl, furanyl, thiophenyl, pyrazole, or thiazolyl; wherein each R^2 pyridinyl, furanyl, thiophenyl, pyrazole, and thiazolyl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F.

In one embodiment of Formula (IVC) and (IVD), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$,

$NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IVC) and (IVD), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl.

In one embodiment of Formula (IVC) and (IVD), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (IVC) and (IVD), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, $N(R^7)_2$, F, Cl, Br and I.

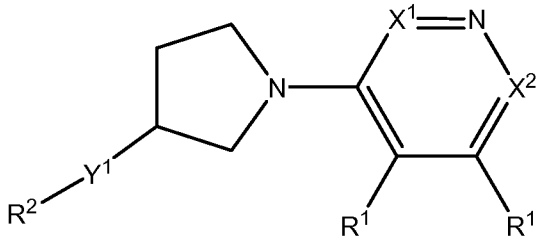
In one embodiment of Formula (IVC) and (IVD), R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl. In another embodiment of Formula (IVC) and (IVD), R^7, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl.

In one embodiment of Formula (IVC) and (IVD), each R^4 and R^7 cyclic moiety is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$,

SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In another embodiment of Formula (IVC) and (IVD), each R^4 and R^7 cyclic moiety is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, CO(O)H, OH, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, NH_2, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (IVC)



Formula (IVC);

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, Cl, and F;

R^2 is aryl or 5-6 membered heteroaryl wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, SO_2R^4, OR^4, $C(O)NHR^4$, and F;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, $N(R^7)_2$, and F;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl;

wherein the cyclic moieties represented by R^4 and R^7 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, $CO(O)R^{10}$, C(O)OH, OH and F;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, NH_2, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with

alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, cycloalkyl, and heterocyclyl;

with the proviso that

when X^1 is CR^1 and X^2 is CR^1; R^1 is hydrogen; Y^1 is NHC(O); and R^2 is pyrrolyl; the R^2 pyrrolyl is not substituted with two alkyl groups.

Still another embodiment pertains to compounds having Formula (IV), which include

tert-butyl 4-[4-({[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate;

tert-butyl 4-[4-({[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-[4-({1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-[4-({1-[(2R)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

tert-butyl 4-(4-{[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbamoyl}phenoxy)piperidine-1-carboxylate;

tert-butyl 4-(4-{[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbamoyl}phenoxy)piperidine-1-carboxylate;

(3S)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide; and pharmaceutically acceptable salts thereof.

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[(3R)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3R)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3S)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3R)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)piperidine-4-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidi4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}piperidine-4-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2S)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2R)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-methylphenoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2,6-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-1-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[4-(thiophen-2-yl)butanoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-2-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[3-(phenylsulfonyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(N-benzoylglycyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-5-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-fluoropyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-fluoro-6-methylpyridin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-heptanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-hexanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3,5-dimethylphenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[2-chloro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(5-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(diphenylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(pent-4-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[2-fluoro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-tert-butylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(pent-4-ynoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-acetylpiperidin-4-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(but-3-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluoro-4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-4-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-methylpyridin-3-yl)azetidine-3-carboxamide;

2-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-1,3-thiazole-5-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(2-methylpyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]furan-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]furan-2-carboxamide;

N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-4-[1-(2-methylpropanoyl)piperidin-4-yl]benzamide;

N-(4-{1-[2-(piperazin-1-yl)ethyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

4-[1-(2-methylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]benzamide;

N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(3-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(4-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

(3S)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

5-[1-(2-methylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-(1-benzoylpiperidin-4-yl)-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-{1-[(2R)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}thiophene-2-carboxamide;

5-{1-[(1-methylpiperidin-4-yl)acetyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide;

(3S)-N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(propan-2-yl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylmethyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-2-ylmethyl)-1H-pyrazol-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-tert-butyl-1H-pyrazol-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2-methylbenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(4,4,4-trifluorobutanoyl)pyrrolidin-3-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(5-propyl-1,2,4-oxadiazol-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylazetidin-3-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-difluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-difluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[(1-benzoylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,3,4-oxadiazol-2-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-imidazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,2,4-oxadiazol-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-cyclopropyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-(5-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}thiophen-2-yl)piperidine-1-carboxylate;

tert-butyl 4-fluoro-4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidine-1-carboxylate;

5-(1-benzoylpiperidin-4-yl)-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylbenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(3-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(4-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[3-cyclopropyl-1-(2-hydroxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

1-(6-fluoropyridazin-3-yl)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[(1-benzoylpiperidin-4-yl)oxy]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[8-(2-methylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[8-(4,4,4-trifluorobutanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}azetidine-3-carboxamide;

N-[4-(8-benzoyl-8-azabicyclo[3.2.1]oct-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2-fluorobenzoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2,2-dimethylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{8-[(1-methylcyclopropyl)carbonyl]-8-azabicyclo[3.2.1]oct-3-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methoxyethyl)-3-(2-methylpropyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-[1-(pyridazin-3-yl)azetidin-3-yl]-5-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-fluoropiperidine-1-carboxylate;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-hydroxypiperidine-1-carboxylate;

N-[1-(pyridazin-3-yl)azetidin-3-yl]-5-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(cyclopropylcarbonyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[4-fluoro-1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(2-fluoro-4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoyl-4-fluoropiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)-4-fluoropiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butyl-3-tert-butyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(tetrahydro-2H-pyran-4-ylmethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]furan-2-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

5-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

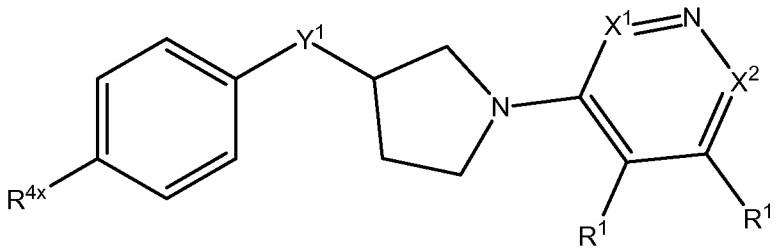
N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(cyclopropylacetyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(bicyclo[2.2.1]hept-2-ylacetyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide; and pharmaceutically acceptable salts thereof.

Embodiments of Formula (VC)

In another aspect, the present invention provides compounds of Formula (VC)



(VC);

and pharmaceutically acceptable salts thereof; wherein X^1, X^2, R^1, and Y^1 are as described in Formula (IC) herein and R^{4x} is as described herein for substituents on R^2 when R^2 is aryl in Formula (IC).

One embodiment of this invention pertains to compounds of Formula (VC) or pharmaceutically acceptable salts thereof;

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^{4X} is independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, and R^7, are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$,

$NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

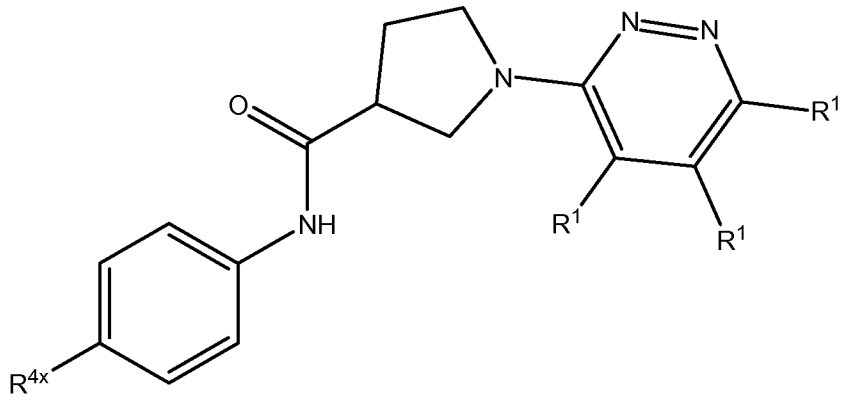
In one embodiment of Formula (VC), X^1 is N and X^2 is CR^1; or X^1 is CR^1 and X^2 is N; or X^1 is CR^1 and X^2 is CR^1. In another embodiment of Formula (VC), X^1 is N and X^2 is CR^1. In another embodiment of Formula (VC), X^1 is CR^1 and X^2 is N. In another embodiment of Formula (VC), X^1 is CR^1 and X^2 is CR^1.

In one embodiment of Formula (VC), Y^1 is C(O)NH, or NHC(O). In another embodiment of Formula (VC), Y^1 is C(O)NH. In another embodiment of Formula (VC), Y^1 is NHC(O).

In one embodiment of Formula (VC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (VC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (VC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl,

haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (VC), X^1 is CR^1 and X^2 is CR^1; and R^1, at each occurrence, is hydrogen.

In another aspect, the present invention provides compounds of Formula (VD),



Formula (VD)

and pharmaceutically acceptable salts thereof; wherein R^1 is described herein for Formula (IC) and R^{4x} is as described herein for substituents on R^2 when R^2 is aryl in Formula (IC).

In one embodiment of Formula (VC) and (VD), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I. In another embodiment of Formula (VC) and (VD), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, Cl, Br and I. In another embodiment of Formula (VC) and (VD), R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, F, and Cl. In another embodiment of Formula (VC) and (VD), R^1, at each occurrence, is hydrogen.

In one embodiment of Formula (VC) and (VD), R^{4X} is independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I. In another embodiment of Formula (VC) and (VD), R^{4X} is independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, F, Cl, and I. In another embodiment of Formula (VC) and (VD), R^{4X} is independently selected from the group consisting of R^4, OR^4, SO_2R^4, $C(O)NHR^4$, and F.

In one embodiment of Formula (VC) and (VD), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (VC) and (VD), R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl.

In one embodiment of Formula (VC) and (VD), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I. In another embodiment of Formula (VC) and (VD), each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, $N(R^7)_2$, F, Cl, Br and I.

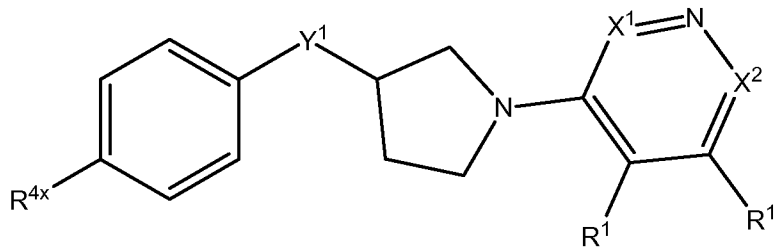
In one embodiment of Formula (VC) and (VD), R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl. In another embodiment of Formula (VC) and (VD), R^7, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl.

In one embodiment of Formula (VC) and (VD), each R^4 and R^7 cyclic moiety is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$,

$NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl.

In another embodiment of Formula (VC) and (VD), each R^4 and R^7 cyclic moiety is independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $C(O)C(O)R^{10}$, CO(O)H, OH, F, Cl, Br and I; R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl, alkenyl, and alkynyl, are optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, $C(O)R^{12}$, NH_2, OH, CN, CF_3, OCF_3, F, and Cl; R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, CF_3, F, and Cl; R^{12}, at each occurrence, is independently selected from the group consisting of alkyl and aryl; and R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

One embodiment of this invention pertains to compounds or pharmaceutically acceptable salts thereof, which are useful as inhibitors of NAMPT, the compounds having Formula (VC)



(VC);

wherein

X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, haloalkyl, alkoxy, CN, Cl, and F;

R^{4X} is independently selected from the group consisting of R^4, SO_2R^4, OR^4, and F;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^4 alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, $N(R^7)_2$, and F;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl;

wherein the cyclic moieties represented by R^4 and R^7 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, $C(O)R^{10}$, $C(O)C(O)R^{10}$, $CO(O)R^{10}$, C(O)OH, OH and F;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{10} alkyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, SO_2R^{11}, NH_2, $N(R^{11})_2$, $NHC(O)R^{11}$, $NHS(O)_2R^{11}$, OH, NO_2, and F; wherein each R^{10} aryl, heterocyclyl and cycloalkyl is optionally substituted with one or more R^{12}, OR^{12}, $C(O)R^{12}$, NH_2, OH, CN, CF_3, OCF_3, F, and Cl;

R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, aryl, heterocyclyl, and cycloalkyl; wherein each R^{11} alkyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, and heterocyclyl is optionally substituted with one or

more substituents independently selected from the group consisting of R^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, and Cl;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, and aryl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, cycloalkyl, and heterocyclyl.

Still another embodiment pertains to compounds having Formula (VC), which include

tert-butyl 4-[4-({[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate;

tert-butyl 4-[4-({[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-[4-({1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-[4-({1-[(2R)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

tert-butyl 4-(4-{[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbamoyl}phenoxy)piperidine-1-carboxylate;

tert-butyl 4-(4-{[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbamoyl}phenoxy)piperidine-1-carboxylate;

(3S)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide; and pharmaceutically acceptable salts thereof.

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)piperidine-4-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidi4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}piperidine-4-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2S)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2R)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-methylphenoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2,6-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-1-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[4-(thiophen-2-yl)butanoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-2-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[3-(phenylsulfonyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(N-benzoylglycyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-5-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-fluoropyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-fluoro-6-methylpyridin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-heptanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-hexanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3,5-dimethylphenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[2-chloro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(5-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(diphenylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(pent-4-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[2-fluoro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-tert-butylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(pent-4-ynoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-acetylpiperidin-4-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(but-3-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluoro-4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-4-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-methylpyridin-3-yl)azetidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(2-methylpyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-4-[1-(2-methylpropanoyl)piperidin-4-yl]benzamide;

N-(4-{1-[2-(piperazin-1-yl)ethyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

4-[1-(2-methylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]benzamide;

N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(propan-2-yl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylmethyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-2-ylmethyl)-1H-pyrazol-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-tert-butyl-1H-pyrazol-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2-methylbenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(4,4,4-trifluorobutanoyl)pyrrolidin-3-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(5-propyl-1,2,4-oxadiazol-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylazetidin-3-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-difluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-difluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[(1-benzoylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,3,4-oxadiazol-2-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-imidazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,2,4-oxadiazol-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-cyclopropyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-(5-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}thiophen-2-yl)piperidine-1-carboxylate;

tert-butyl 4-fluoro-4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidine-1-carboxylate;

5-(1-benzoylpiperidin-4-yl)-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylbenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(3-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(4-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[3-cyclopropyl-1-(2-hydroxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

1-(6-fluoropyridazin-3-yl)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[(1-benzoylpiperidin-4-yl)oxy]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[8-(2-methylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[8-(4,4,4-trifluorobutanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}azetidine-3-carboxamide;

N-[4-(8-benzoyl-8-azabicyclo[3.2.1]oct-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2-fluorobenzoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2,2-dimethylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{8-[(1-methylcyclopropyl)carbonyl]-8-azabicyclo[3.2.1]oct-3-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methoxyethyl)-3-(2-methylpropyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-[1-(pyridazin-3-yl)azetidin-3-yl]-5-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-fluoropiperidine-1-carboxylate;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-hydroxypiperidine-1-carboxylate;

N-[1-(pyridazin-3-yl)azetidin-3-yl]-5-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(cyclopropylcarbonyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[4-fluoro-1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(2-fluoro-4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoyl-4-fluoropiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)-4-fluoropiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butyl-3-tert-butyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(tetrahydro-2H-pyran-4-ylmethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide; and pharmaceutically acceptable salts thereof.

Pharmaceutical Compositions, Combination Therapies, Methods of Treatment, and Administration

Another embodiment comprises pharmaceutical compositions comprising a compound having Formula (I) and an excipient.

Still another embodiment comprises methods of treating cancer in a mammal comprising administering thereto a therapeutically acceptable amount of a compound having Formula (I).

Still another embodiment pertains to compositions for treating diseases during which NAMPT is expressed, said compositions comprising an excipient and a therapeutically effective amount of the compound having Formula (I).

Still another embodiment pertains to methods of treating disease in a patient during which NAMPT is expressed, said methods comprising administering to the patient a therapeutically effective amount of a compound having Formula (I).

Still another embodiment pertains to compositions for treating inflammatory and tissue repair disorders; particularly rheumatoid arthritis, inflammatory bowel disease, asthma

and COPD (chronic obstructive pulmonary disease), osteoarthritis, osteoporosis and fibrotic diseases; dermatosis, including psoriasis, atopic dermatitis and ultra-violet induced skin damage; autoimmune diseases including systemic lupus erythematosis, multiple sclerosis, psoriatic arthritis, ankylosing spondylitis, tissue and organ rejection, Alzheimer's disease, stroke, athersclerosis, restenosis, diabetes, glomerulonephritis, cancer, particularly wherein the cancer is selected from breast, prostate, lung, colon, cervix, ovary, skin, CNS, bladder, pancreas, leukemia, lymphoma or Hodgkin's disease, cachexia, inflammation associated with infection and certain viral infections, including Acquired Immune Deficiency Syndrome (AIDS), adult respiratory distress syndrome, and ataxia telengiectasia, said compositions comprising an excipient and a therapeutically effective amount of the compound having Formula (I).

Still another embodiment pertains to methods of treating inflammatory and tissue repair disorders; particularly rheumatoid arthritis, inflammatory bowel disease, asthma and COPD (chronic obstructive pulmonary disease), osteoarthritis, osteoporosis and fibrotic diseases; dermatosis, including psoriasis, atopic dermatitis and ultra-violet induced skin damage; autoimmune diseases including systemic lupus erythematosis, multiple sclerosis, psoriatic arthritis, ankylosing spondylitis, tissue and organ rejection, Alzheimer's disease, stroke, athersclerosis, restenosis, diabetes, glomerulonephritis, cancer, particularly wherein the cancer is selected from breast, prostate, lung, colon, cervix, ovary, skin, CNS, bladder, pancreas, leukemia, lymphoma or Hodgkin's disease, cachexia, inflammation associated with infection and certain viral infections, including Acquired Immune Deficiency Syndrome (AIDS), adult respiratory distress syndrome, and ataxia telengiectasia in a patient, said methods comprising administering to the patient a therapeutically effective amount of a compound having Formula (I).

Still another embodiment pertains to compositions for treating diseases during which NAMPT is expressed, said compositions comprising an excipient and a therapeutically effective amount of the compound having Formula (I) and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent.

Still another embodiment pertains to methods of treating disease in a patient during which NAMPT is expressed, said methods comprising administering to the patient a therapeutically effective amount of a compound having Formula (I) and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent.

Still another embodiment pertains to compositions for treating inflammatory and tissue repair disorders; particularly rheumatoid arthritis, inflammatory bowel disease, asthma and COPD (chronic obstructive pulmonary disease), osteoarthritis, osteoporosis and fibrotic diseases; dermatosis, including psoriasis, atopic dermatitis and ultra-violet induced skin

damage; autoimmune diseases including systemic lupus erythematosis, multiple sclerosis, psoriatic arthritis, ankylosing spondylitis, tissue and organ rejection, Alzheimer's disease, stroke, athersclerosis, restenosis, diabetes, glomerulonephritis, cancer, particularly wherein the cancer is selected from breast, prostate, lung, colon, cervix, ovary, skin, CNS, bladder, pancreas, leukemia, lymphoma or Hodgkin's disease, cachexia, inflammation associated with infection and certain viral infections, including Acquired Immune Deficiency Syndrome (AIDS), adult respiratory distress syndrome, and ataxia telengiectasia, said compositions comprising an excipient and a therapeutically effective amount of the compound having Formula (I) and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent.

Still another embodiment pertains to methods of treating inflammatory and tissue repair disorders; particularly rheumatoid arthritis, inflammatory bowel disease, asthma and COPD (chronic obstructive pulmonary disease), osteoarthritis, osteoporosis and fibrotic diseases; dermatosis, including psoriasis, atopic dermatitis and ultra-violet induced skin damage; autoimmune diseases including systemic lupus erythematosis, multiple sclerosis, psoriatic arthritis, ankylosing spondylitis, tissue and organ rejection, Alzheimer's disease, stroke, athersclerosis, restenosis, diabetes, glomerulonephritis, cancer, particularly wherein the cancer is selected from breast, prostate, lung, colon, cervix, ovary, skin, CNS, bladder, pancreas, leukemia, lymphoma or Hodgkin's disease, cachexia, inflammation associated with infection and certain viral infections, including Acquired Immune Deficiency Syndrome (AIDS), adult respiratory distress syndrome, and ataxia telengiectasia in a patient, said methods comprising administering to the patient a therapeutically effective amount of the compound having Formula (I) and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent.

Metabolites of compounds having Formula (I), produced by in vitro or in vivo metabolic processes, may also have utility for treating diseases associated with NAMPT.

Certain precursor compounds which may be metabolized in vitro or in vivo to form compounds having Formula (I) may also have utility for treating diseases associated with NAMPT.

Compounds having Formula (I) may exist as acid addition salts, basic addition salts or zwitterions. Salts of the compounds are prepared during isolation or following purification of the compounds. Acid addition salts of the compounds are those derived from the reaction of the compounds with an acid. For example, the acetate, adipate, alginate, bicarbonate, citrate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, camphorate, camphorsufonate, digluconate, formate, fumarate, glycerophosphate, glutamate, hemisulfate, heptanoate, hexanoate, hydrochloride, hydrobromide, hydroiodide, lactobionate, lactate, maleate, mesitylenesulfonate, methanesulfonate, naphthylenesulfonate, nicotinate, oxalate,

pamoate, pectinate, persulfate, phosphate, picrate, propionate, succinate, tartrate, thiocyanate, trichloroacetic, trifluoroacetic, para-toluenesulfonate, and undecanoate salts of the compounds are contemplated as being embraced by this invention. Basic addition salts of the compounds are those derived from the reaction of the compounds with the hydroxide, carbonate or bicarbonate of cations such as lithium, sodium, potassium, calcium, and magnesium.

The compounds having Formula (I) may be administered, for example, bucally, ophthalmically, orally, osmotically, parenterally (intramuscularly, intraperitoneally intrasternally, intravenously, subcutaneously), rectally, topically, transdermally or vaginally.

Therapeutically effective amounts of compounds having Formula (I) depend on the recipient of the treatment, the disorder being treated and the severity thereof, the composition containing the compound, the time of administration, the route of administration, the duration of treatment, the compound potency, its rate of clearance and whether or not another drug is co-administered. The amount of a compound of this invention having Formula (I) used to make a composition to be administered daily to a patient in a single dose or in divided doses is from about 0.03 to about 200 mg/kg body weight. Single dose compositions contain these amounts or a combination of submultiples thereof.

Compounds having Formula (I) may be administered with or without an excipient. Excipients include, for example, encapsulating materials or additives such as absorption accelerators, antioxidants, binders, buffers, coating agents, coloring agents, diluents, disintegrating agents, emulsifiers, extenders, fillers, flavoring agents, humectants, lubricants, perfumes, preservatives, propellants, releasing agents, sterilizing agents, sweeteners, solubilizers, wetting agents and mixtures thereof.

Excipients for preparation of compositions comprising a compound having Formula (I) to be administered orally in solid dosage form include, for example, agar, alginic acid, aluminum hydroxide, benzyl alcohol, benzyl benzoate, 1,3-butylene glycol, carbomers, castor oil, cellulose, cellulose acetate, cocoa butter, corn starch, corn oil, cottonseed oil, cross-povidone, diglycerides, ethanol, ethyl cellulose, ethyl laureate, ethyl oleate, fatty acid esters, gelatin, germ oil, glucose, glycerol, groundnut oil, hydroxypropylmethyl cellulose, isopropanol, isotonic saline, lactose, magnesium hydroxide, magnesium stearate, malt, mannitol, monoglycerides, olive oil, peanut oil, potassium phosphate salts, potato starch, povidone, propylene glycol, Ringer's solution, safflower oil, sesame oil, sodium carboxymethyl cellulose, sodium phosphate salts, sodium lauryl sulfate, sodium sorbitol, soybean oil, stearic acids, stearyl fumarate, sucrose, surfactants, talc, tragacanth, tetrahydrofurfuryl alcohol, triglycerides, water, and mixtures thereof. Excipients for preparation of compositions comprising a compound of this invention having Formula (I) to be administered ophthalmically or orally in liquid dosage forms include, for example,

1,3-butylene glycol, castor oil, corn oil, cottonseed oil, ethanol, fatty acid esters of sorbitan, germ oil, groundnut oil, glycerol, isopropanol, olive oil, polyethylene glycols, propylene glycol, sesame oil, water and mixtures thereof. Excipients for preparation of compositions comprising a compound of this invention having Formula (I) to be administered osmotically include, for example, chlorofluorohydrocarbons, ethanol, water and mixtures thereof. Excipients for preparation of compositions comprising a compound of this invention having Formula (I) to be administered parenterally include, for example, 1,3-butanediol, castor oil, corn oil, cottonseed oil, dextrose, germ oil, groundnut oil, liposomes, oleic acid, olive oil, peanut oil, Ringer's solution, safflower oil, sesame oil, soybean oil, U.S.P. or isotonic sodium chloride solution, water and mixtures thereof. Excipients for preparation of compositions comprising a compound of this invention having Formula (I) to be administered rectally or vaginally include, for example, cocoa butter, polyethylene glycol, wax and mixtures thereof.

Compounds having Formula (I) are expected to be useful when used with alkylating agents, angiogenesis inhibitors, antibodies, antimetabolites, antimitotics, antiproliferatives, antivirals, aurora kinase inhibitors, apoptosis promoters (for example, Bcl-xL, Bcl-w and Bfl-1) inhibitors, activators of death receptor pathway, Bcr-Abl kinase inhibitors, BiTE (Bi-Specific T cell Engager) antibodies, antibody drug conjugates, biologic response modifiers, cyclin-dependent kinase inhibitors, cell cycle inhibitors, cyclooxygenase-2 inhibitors, DVDs, leukemia viral oncogene homolog (ErbB2) receptor inhibitors, growth factor inhibitors, heat shock protein (HSP)-90 inhibitors, histone deacetylase (HDAC) inhibitors, hormonal therapies, immunologicals, inhibitors of inhibitors of apoptosis proteins (IAPs), intercalating antibiotics, kinase inhibitors, kinesin inhibitors, Jak2 inhibitors, mammalian target of rapamycin inhibitors, microRNA's, mitogen-activated extracellular signal-regulated kinase inhibitors, multivalent binding proteins, non-steroidal anti-inflammatory drugs (NSAIDs), poly ADP (adenosine diphosphate)-ribose polymerase (PARP) inhibitors, platinum chemotherapeutics, polo-like kinase (Plk) inhibitors, phosphoinositide-3 kinase (PI3K) inhibitors, proteosome inhibitors, purine analogs, pyrimidine analogs, receptor tyrosine kinase inhibitors, retinoids/deltoids plant alkaloids, small inhibitory ribonucleic acids (siRNAs), topoisomerase inhibitors, ubiquitin ligase inhibitors, and the like, and in combination with one or more of these agents .

BiTE antibodies are bi-specific antibodies that direct T-cells to attack cancer cells by simultaneously binding the two cells. The T-cell then attacks the target cancer cell. Examples of BiTE antibodies include adecatumumab (Micromet MT201), blinatumomab (Micromet MT103) and the like. Without being limited by theory, one of the mechanisms by which T-cells elicit apoptosis of the target cancer cell is by exocytosis of cytolytic granule components, which include perforin and granzyme B.

SiRNAs are molecules having endogenous RNA bases or chemically modified nucleotides. The modifications do not abolish cellular activity, but rather impart increased stability and/or increased cellular potency. Examples of chemical modifications include phosphorothioate groups, 2'-deoxynucleotide, 2'-OCH_3-containing ribonucleotides, 2'-F-ribonucleotides, 2'-methoxyethyl ribonucleotides, combinations thereof and the like. The siRNA can have varying lengths (e.g., 10-200 bps) and structures (e.g., hairpins, single/double strands, bulges, nicks/gaps, mismatches) and are processed in cells to provide active gene silencing. A double-stranded siRNA (dsRNA) can have the same number of nucleotides on each strand (blunt ends) or asymmetric ends (overhangs). The overhang of 1-2 nucleotides can be present on the sense and/or the antisense strand, as well as present on the 5'- and/ or the 3'-ends of a given strand.

Multivalent binding proteins are binding proteins comprising two or more antigen binding sites. Multivalent binding proteins are engineered to have the three or more antigen binding sites and are generally not naturally occurring antibodies. The term "multispecific binding protein" means a binding protein capable of binding two or more related or unrelated targets. Dual variable domain (DVD) binding proteins are tetravalent or multivalent binding proteins binding proteins comprising two or more antigen binding sites. Such DVDs may be monospecific (i.e., capable of binding one antigen) or multispecific (i.e., capable of binding two or more antigens). DVD binding proteins comprising two heavy chain DVD polypeptides and two light chain DVD polypeptides are referred to as DVD Ig's. Each half of a DVD Ig comprises a heavy chain DVD polypeptide, a light chain DVD polypeptide, and two antigen binding sites. Each binding site comprises a heavy chain variable domain and a light chain variable domain with a total of 6 CDRs involved in antigen binding per antigen binding site.

Alkylating agents include altretamine, AMD-473, AP-5280, apaziquone, bendamustine, brostallicin, busulfan, carboquone, carmustine (BCNU), chlorambucil, CLORETAZINE® (laromustine, VNP 40101M), cyclophosphamide, decarbazine, estramustine, fotemustine, glufosfamide, ifosfamide, KW-2170, lomustine (CCNU), mafosfamide, melphalan, mitobronitol, mitolactol, nimustine, nitrogen mustard N-oxide, ranimustine, temozolomide, thiotepa, TREANDA® (bendamustine), treosulfan, trofosfamide and the like.

Angiogenesis inhibitors include endothelial-specific receptor tyrosine kinase (Tie-2) inhibitors, epidermal growth factor receptor (EGFR) inhibitors, insulin growth factor-2 receptor (IGFR-2) inhibitors, matrix metalloproteinase-2 (MMP-2) inhibitors, matrix metalloproteinase-9 (MMP-9) inhibitors, platelet-derived growth factor receptor (PDGFR) inhibitors, thrombospondin analogs, vascular endothelial growth factor receptor tyrosine kinase (VEGFR) inhibitors and the like.

Antimetabolites include ALIMTA® (pemetrexed disodium, LY231514, MTA), 5-azacitidine, XELODA® (capecitabine), carmofur, LEUSTAT® (cladribine), clofarabine, cytarabine, cytarabine ocfosfate, cytosine arabinoside, decitabine, deferoxamine, doxifluridine, eflornithine, EICAR (5-ethynyl-1-β -D-ribofuranosylimidazole-4-carboxamide), enocitabine, ethnylcytidine, fludarabine, 5-fluorouracil alone or in combination with leucovorin, GEMZAR® (gemcitabine), hydroxyurea, ALKERAN®(melphalan), mercaptopurine, 6-mercaptopurine riboside, methotrexate, mycophenolic acid, nelarabine, nolatrexed, ocfosfate, pelitrexol, pentostatin, raltitrexed, Ribavirin, triapine, trimetrexate, S-1, tiazofurin, tegafur, TS-1, vidarabine, UFT and the like.

Antivirals include ritonavir, hydroxychloroquine and the like.

Aurora kinase inhibitors include ABT-348, AZD-1152, MLN-8054, VX-680, Aurora A-specific kinase inhibitors, Aurora B-specific kinase inhibitors and pan-Aurora kinase inhibitors and the like.

Bcl-2 protein inhibitors include AT-101 ((-)gossypol), GENASENSE® (G3139 or oblimersen (Bcl-2-targeting antisense oligonucleotide)), IPI-194, IPI-565, N-(4-(4-((4'-chloro(1,1'-biphenyl)-2-yl)methyl)piperazin-1-yl)benzoyl)-4-(((1R)-3-(dimethylamino)-1-((phenylsulfanyl)methyl)propyl)amino)-3-nitrobenzenesulfonamide) (ABT-737), N-(4-(4-((2-(4-chlorophenyl)-5,5-dimethyl-1-cyclohex-1-en-1-yl)methyl)piperazin-1-yl)benzoyl)-4-(((1R)-3-(morpholin-4-yl)-1-((phenylsulfanyl)methyl)propyl)amino)-3-((trifluoromethyl)sulfonyl)benzenesulfonamide (ABT-263), GX-070 (obatoclax) and the like.

Bcr-Abl kinase inhibitors include DASATINIB® (BMS-354825), GLEEVEC® (imatinib) and the like.

CDK inhibitors include AZD-5438, BMI-1040, BMS-032, BMS-387, CVT-2584, flavopyridol, GPC-286199, MCS-5A, PD0332991, PHA-690509, seliciclib (CYC-202, R-roscovitine), ZK-304709 and the like.

COX-2 inhibitors include ABT-963, ARCOXIA® (etoricoxib), BEXTRA® (valdecoxib), BMS347070, CELEBREX® (celecoxib), COX-189 (lumiracoxib), CT-3, DERAMAXX® (deracoxib), JTE-522, 4-methyl-2-(3,4-dimethylphenyl)-1-(4-sulfamoylphenyl-1H-pyrrole), MK-663 (etoricoxib), NS-398, parecoxib, RS-57067, SC-58125, SD-8381, SVT-2016, S-2474, T-614, VIOXX® (rofecoxib) and the like.

EGFR inhibitors include ABX-EGF, anti-EGFR immunoliposomes, EGF-vaccine, EMD-7200, ERBITUX® (cetuximab), HR3, IgA antibodies, IRESSA® (gefitinib), TARCEVA® (erlotinib or OSI-774), TP-38, EGFR fusion protein, TYKERB® (lapatinib) and the like.

ErbB2 receptor inhibitors include CP-724-714, CI-1033 (canertinib), HERCEPTIN® (trastuzumab), TYKERB® (lapatinib), OMNITARG® (2C4, petuzumab), TAK-165, GW-572016 (ionafarnib), GW-282974, EKB-569, PI-166, dHER2 (HER2 vaccine),

APC-8024 (HER-2 vaccine), anti-HER/2neu bispecific antibody, B7.her2IgG3, AS HER2 trifunctional bispecfic antibodies, mAB AR-209, mAB 2B-1 and the like.

Histone deacetylase inhibitors include depsipeptide, LAQ-824, MS-275, trapoxin, suberoylanilide hydroxamic acid (SAHA), TSA, valproic acid and the like.

HSP-90 inhibitors include 17-AAG-nab, 17-AAG, CNF-101, CNF-1010, CNF-2024, 17-DMAG, geldanamycin, IPI-504, KOS-953, MYCOGRAB® (human recombinant antibody to HSP-90), NCS-683664, PU24FCl, PU-3, radicicol, SNX-2112, STA-9090 VER49009 and the like.

Inhibitors of inhibitors of apoptosis proteins include HGS1029, GDC-0145, GDC-0152, LCL-161, LBW-242 and the like.

Antibody drug conjugates include anti-CD22-MC-MMAF, anti-CD22-MC-MMAE, anti-CD22-MCC-DM1, CR-011-vcMMAE, PSMA-ADC, MEDI-547, SGN-19Am SGN-35, SGN-75 and the like

Activators of death receptor pathway include TRAIL, antibodies or other agents that target TRAIL or death receptors (e.g., DR4 and DR5) such as Apomab, conatumumab, ETR2-ST01, GDC0145 (lexatumumab), HGS-1029, LBY-135, PRO-1762 and trastuzumab.

Kinesin inhibitors include Eg5 inhibitors such as AZD4877, ARRY-520; CENPE inhibitors such as GSK923295A and the like.

JAK-2 inhibitors include CEP-701 (lesaurtinib), XL019 and INCB018424 and the like.

MEK inhibitors include ARRY-142886, ARRY-438162 PD-325901, PD-98059 and the like.

mTOR inhibitors include AP-23573, CCI-779, everolimus, RAD-001, rapamycin, temsirolimus, ATP-competitive TORC1/TORC2 inhibitors, including PI-103, PP242, PP30, Torin 1 and the like.

Non-steroidal anti-inflammatory drugs include AMIGESIC® (salsalate), DOLOBID® (diflunisal), MOTRIN® (ibuprofen), ORUDIS® (ketoprofen), RELAFEN® (nabumetone), FELDENE® (piroxicam), ibuprofen cream, ALEVE® (naproxen) and NAPROSYN® (naproxen), VOLTAREN® (diclofenac), INDOCIN® (indomethacin), CLINORIL® (sulindac), TOLECTIN® (tolmetin), LODINE® (etodolac), TORADOL® (ketorolac), DAYPRO® (oxaprozin) and the like.

PDGFR inhibitors include C-451, CP-673, CP-868596 and the like.

Platinum chemotherapeutics include cisplatin, ELOXATIN® (oxaliplatin) eptaplatin, lobaplatin, nedaplatin, PARAPLATIN® (carboplatin), satraplatin, picoplatin and the like.

Polo-like kinase inhibitors include BI-2536 and the like.

Phosphoinositide-3 kinase (PI3K) inhibitors include wortmannin, LY294002, XL-147, CAL-120, ONC-21, AEZS-127, ETP-45658, PX-866, GDC-0941, BGT226, BEZ235, XL765 and the like.

Thrombospondin analogs include ABT-510, ABT-567, ABT-898, TSP-1 and the like.

VEGFR inhibitors include AVASTIN® (bevacizumab), ABT-869, AEE-788, ANGIOZYME™ (a ribozyme that inhibits angiogenesis (Ribozyme Pharmaceuticals (Boulder, CO.) and Chiron, (Emeryville, CA)) , axitinib (AG-13736), AZD-2171, CP-547,632, IM-862, MACUGEN (pegaptamib), NEXAVAR® (sorafenib, BAY43-9006), pazopanib (GW-786034), vatalanib (PTK-787, ZK-222584), SUTENT® (sunitinib, SU-11248), VEGF trap, ZACTIMA™ (vandetanib, ZD-6474) and the like.

Antibiotics include intercalating antibiotics aclarubicin, actinomycin D, amrubicin, annamycin, adriamycin, BLENOXANE® (bleomycin), daunorubicin, CAELYX® or MYOCET® (liposomal doxorubicin), elsamitrucin, epirbucin, glarbuicin, ZAVEDOS® (idarubicin), mitomycin C, nemorubicin, neocarzinostatin, peplomycin, pirarubicin, rebeccamycin, stimalamer, streptozocin, VALSTAR® (valrubicin), zinostatin and the like.

Topoisomerase inhibitors include aclarubicin, 9-aminocamptothecin, amonafide, amsacrine, becatecarin, belotecan, BN-80915, CAMPTOSAR® (irinotecan hydrochloride), camptothecin, CARDIOXANE® (dexrazoxine), diflomotecan, edotecarin, ELLENCE® or PHARMORUBICIN® (epirubicin), etoposide, exatecan, 10-hydroxycamptothecin, gimatecan, lurtotecan, mitoxantrone, orathecin, pirarbucin, pixantrone, rubitecan, sobuzoxane, SN-38, tafluposide, topotecan and the like.

Antibodies include AVASTIN® (bevacizumab), CD40-specific antibodies, chTNT-1/B, denosumab, ERBITUX® (cetuximab), HUMAX-CD4® (zanolimumab), IGF1R-specific antibodies, lintuzumab, PANOREX® (edrecolomab), RENCAREX® (WX G250), RITUXAN® (rituximab), ticilimumab, trastuzimab, CD20 antibodies types I and II and the like.

Hormonal therapies include ARIMIDEX® (anastrozole), AROMASIN® (exemestane), arzoxifene, CASODEX® (bicalutamide), CETROTIDE® (cetrorelix), degarelix, deslorelin, DESOPAN® (trilostane), dexamethasone, DROGENIL® (flutamide), EVISTA® (raloxifene), AFEMA™ (fadrozole), FARESTON® (toremifene), FASLODEX® (fulvestrant), FEMARA® (letrozole), formestane, glucocorticoids, HECTOROL® (doxercalciferol), RENAGEL® (sevelamer carbonate), lasofoxifene, leuprolide acetate, MEGACE® (megesterol), MIFEPREX® (mifepristone), NILANDRON™ (nilutamide), NOLVADEX® (tamoxifen citrate), PLENAXIS™ (abarelix), prednisone, PROPECIA® (finasteride), rilostane, SUPREFACT® (buserelin), TRELSTAR® (luteinizing hormone releasing hormone (LHRH)),

VANTAS® (Histrelin implant), VETORYL® (trilostane or modrastane), ZOLADEX® (fosrelin, goserelin) and the like.

Deltoids and retinoids include seocalcitol (EB1089, CB1093), lexacalcitrol (KH1060), fenretinide, PANRETIN® (aliretinoin), ATRAGEN® (liposomal tretinoin), TARGRETIN® (bexarotene), LGD-1550 and the like.

PARP inhibitors include ABT-888 (veliparib), olaparib, KU-59436, AZD-2281, AG-014699, BSI-201, BGP-15, INO-1001, ONO-2231 and the like.

Plant alkaloids include, but are not limited to, vincristine, vinblastine, vindesine, vinorelbine and the like.

Proteasome inhibitors include VELCADE® (bortezomib), MG132, NPI-0052, PR-171 and the like.

Examples of immunologicals include interferons and other immune-enhancing agents. Interferons include interferon alpha, interferon alpha-2a, interferon alpha-2b, interferon beta, interferon gamma-1a, ACTIMMUNE® (interferon gamma-1b) or interferon gamma-n1, combinations thereof and the like. Other agents include ALFAFERONE® ,(IFN-α), BAM-002 (oxidized glutathione), BEROMUN® (tasonermin), BEXXAR® (tositumomab), CAMPATH® (alemtuzumab), CTLA4 (cytotoxic lymphocyte antigen 4), decarbazine, denileukin, epratuzumab, GRANOCYTE® (lenograstim), lentinan, leukocyte alpha interferon, imiquimod, MDX-010 (anti-CTLA-4), melanoma vaccine, mitumomab, molgramostim, MYLOTARG™ (gemtuzumab ozogamicin), NEUPOGEN® (filgrastim), OncoVAC-CL, OVAREX® (oregovomab), pemtumomab (Y-muHMFG1), PROVENGE® (sipuleucel-T), sargaramostim, sizofilan, teceleukin, THERACYS® (Bacillus Calmette-Guerin), ubenimex, VIRULIZIN® (immunotherapeutic, Lorus Pharmaceuticals), Z-100 (Specific Substance of Maruyama (SSM)), WF-10 (Tetrachlorodecaoxide (TCDO)), PROLEUKIN® (aldesleukin), ZADAXIN® (thymalfasin), ZENAPAX® (daclizumab), ZEVALIN® (90Y-Ibritumomab tiuxetan) and the like.

Biological response modifiers are agents that modify defense mechanisms of living organisms or biological responses, such as survival, growth or differentiation of tissue cells to direct them to have anti-tumor activity and include krestin, lentinan, sizofiran, picibanil PF-3512676 (CpG-8954), ubenimex and the like.

Pyrimidine analogs include cytarabine (ara C or Arabinoside C), cytosine arabinoside, doxifluridine, FLUDARA® (fludarabine), 5-FU (5-fluorouracil), floxuridine, GEMZAR® (gemcitabine), TOMUDEX® (ratitrexed), TROXATYL™ (triacetyluridine troxacitabine) and the like.

Purine analogs include LANVIS® (thioguanine) and PURI-NETHOL® (mercaptopurine).

Antimitotic agents include batabulin, epothilone D (KOS-862), N-(2-((4-hydroxyphenyl)amino)pyridin-3-yl)-4-methoxybenzenesulfonamide, ixabepilone (BMS 247550), paclitaxel, TAXOTERE® (docetaxel), PNU100940 (109881), patupilone, XRP-9881 (larotaxel), vinflunine, ZK-EPO (synthetic epothilone) and the like.

Ubiquitin ligase inhibitors include MDM2 inhibitors, such as nutlins, NEDD8 inhibitors such as MLN4924 and the like.

Compounds of this invention can also be used as radiosensitizers that enhance the efficacy of radiotherapy. Examples of radiotherapy include external beam radiotherapy, teletherapy, brachytherapy and sealed, unsealed source radiotherapy and the like.

Additionally, compounds having Formula (I) may be combined with other chemotherapeutic agents such as ABRAXANE™ (ABI-007), ABT-100 (farnesyl transferase inhibitor), ADVEXIN® (Ad5CMV-p53 vaccine), ALTOCOR® or MEVACOR® (lovastatin), AMPLIGEN® (poly I:poly C12U, a synthetic RNA), APTOSYN® (exisulind), AREDIA® (pamidronic acid), arglabin, L-asparaginase, atamestane (1-methyl-3,17-dione-androsta-1,4-diene), AVAGE® (tazarotene), AVE-8062 (combreastatin derivative) BEC2 (mitumomab), cachectin or cachexin (tumor necrosis factor), canvaxin (vaccine), CEAVAC® (cancer vaccine), CELEUK® (celmoleukin), CEPLENE® (histamine dihydrochloride), CERVARIX® (human papillomavirus vaccine), CHOP® (C: CYTOXAN® (cyclophosphamide); H: ADRIAMYCIN® (hydroxydoxorubicin); O: Vincristine (ONCOVIN®); P: prednisone), CYPAT™ (cyproterone acetate), combrestatin A4P, DAB(389)EGF (catalytic and translocation domains of diphtheria toxin fused via a His-Ala linker to human epidermal growth factor) or TransMID-107R™ (diphtheria toxins), dacarbazine, dactinomycin, 5,6-dimethylxanthenone-4-acetic acid (DMXAA), eniluracil, EVIZON™ (squalamine lactate), DIMERICINE® (T4N5 liposome lotion), discodermolide, DX-8951f (exatecan mesylate), enzastaurin, EPO906 (epithilone B), GARDASIL® (quadrivalent human papillomavirus (Types 6, 11, 16, 18) recombinant vaccine), GASTRIMMUNE®, GENASENSE®, GMK (ganglioside conjugate vaccine), GVAX® (prostate cancer vaccine), halofuginone, histerelin, hydroxycarbamide, ibandronic acid, IGN-101, IL-13-PE38, IL-13-PE38QQR (cintredekin besudotox), IL-13-pseudomonas exotoxin, interferon-α, interferon-γ, JUNOVAN™ or MEPACT™ (mifamurtide), lonafarnib, 5,10-methylenetetrahydrofolate, miltefosine (hexadecylphosphocholine), NEOVASTAT®(AE-941), NEUTREXIN® (trimetrexate glucuronate), NIPENT® (pentostatin), ONCONASE® (a ribonuclease enzyme), ONCOPHAGE® (melanoma vaccine treatment), ONCOVAX® (IL-2 Vaccine), ORATHECIN™ (rubitecan), OSIDEM® (antibody-based cell drug), OVAREX® MAb (murine monoclonal antibody), paclitaxel, PANDIMEX™ (aglycone saponins from ginseng comprising 20(S)protopanaxadiol (aPPD) and 20(S)protopanaxatriol (aPPT)), panitumumab, PANVAC®-VF (investigational cancer vaccine), pegaspargase, PEG Interferon A,

phenoxodiol, procarbazine, rebimastat, REMOVAB® (catumaxomab), REVLIMID® (lenalidomide), RSR13 (efaproxiral), SOMATULINE® LA (lanreotide), SORIATANE® (acitretin), staurosporine (Streptomyces staurospores), talabostat (PT100), TARGRETIN® (bexarotene), TAXOPREXIN® (DHA-paclitaxel), TELCYTA® (canfosfamide, TLK286), temilifene, TEMODAR® (temozolomide), tesmilifene, thalidomide, THERATOPE® (STn-KLH), thymitaq (2-amino-3,4-dihydro-6-methyl-4-oxo-5-(4-pyridylthio)quinazoline dihydrochloride), TNFERADE™ (adenovector: DNA carrier containing the gene for tumor necrosis factor-α), TRACLEER® or ZAVESCA® (bosentan), tretinoin (Retin-A), tetrandrine, TRISENOX® (arsenic trioxide), VIRULIZIN®, ukrain (derivative of alkaloids from the greater celandine plant), vitaxin (anti-alphavbeta3 antibody), XCYTRIN® (motexafin gadolinium), XINLAY™ (atrasentan), XYOTAX™ (paclitaxel poliglumex), YONDELIS® (trabectedin), ZD-6126, ZINECARD® (dexrazoxane), ZOMETA® (zolendronic acid), zorubicin and the like.

Data

Determination of the utility of compounds having Formula (I) as binders to and inhibitors of NAMPT was performed using Time-Resolved Fluorescence Resonance Energy Transfer (TR-FRET) binding assays.

Time-Resolved Fluorescence Resonance Energy Transfer (TR-FRET) Binding Assay of NAMPT

Test compounds were serially diluted (typically 11 half log dilutions) in neat DMSO to 50X final concentrations prior to dilution with assay buffer (50 mM HEPES (NaOH), pH 7.5, 100 mM NaCl, 10 mM $MgCl_2$, 1 mM DTT, 1% Glycerol) to 3X and 6% DMSO. Six µL were transferred to 384-well low-volume plates (Owens Corning #3673). To this, 12 µL of a 1.5X solution containing enzyme, probe and antibody were added. Final concentrations in the 18 µL reactions were 1X assay buffer, 2% DMSO, 6.8 nM NAMPT (human, recombinant, C-terminally His-tagged), 200 nM probe (a potent nicotinamide-competitive inhibitor conjugated to Oregon Green 488) and 1 nM Tb-anti-His antibody (Invitrogen # PV5895). Reactions were equilibrated at room temperature for 3 hours prior to reading on an Envision multi-label plate reader (Perkin Elmer; Ex = 337 nm, Em = 520 and 495 nm). Time-resolved FRET ratios (Em_{520}/Em_{495}) were normalized to controls, plotted as a function of compound concentration and fit with the four-parameter logistic equation to determine IC50s.

Time-Resolved Fluorescence Resonance Energy Transfer (TR-FRET) Binding Assay of NAMPT with PRPP

Compound handling and data processing were identical to the assay in the absence of substrates (above). Final concentrations were 1X assay buffer, 2% DMSO, 2 nM NAMPT, 2 nM probe, 1 nM Tb-anti-His antibody (Invitrogen # PV5895), 200 µM PRPP and 2.5 mM

ATP. Reactions were equilibrated for 16 hours prior to measurement to allow for potential enzymatic modification of test compounds.

Table 1 shows the utility of compounds having Formula I to functionally inhibit NAMPT.

TABLE 1

Example	TR-FRET Binding - IC50 (μM)	TR-FRET Binding - IC50 (with PRPP) (μM)	Example	TR-FRET Binding - IC50 (μM)	TR-FRET Binding - IC50 (with PRPP) (μM)
1	0.120000	0.000386	194	0.122000	0.062600
2	0.022300	0.020000	195	0.305000	0.094100
3	0.357000	0.019200	196	0.083800	0.098500
4	0.424000	0.024000	197	0.126000	0.079800
5	0.107000	0.010200	198	0.084500	0.103000
6	0.544000	0.002340	199	0.033700	0.028000
7	0.104000	0.084700	200	0.033100	0.034400
8	3.360000	0.005300	201	0.012100	0.018200
9	8.620000	0.017200	202	0.117000	0.089500
10	0.034500	0.000518	203	0.034200	0.021100
11	2.370000	0.001930	204	0.380000	0.002760
12	1.410000	0.002050	205	0.025100	0.034000
13	0.858000	0.002880	206	0.023800	0.024100
14	3.840000	0.003080	207	0.141000	0.086700
15	1.660000	0.002490	208	0.117000	0.049600
16	2.480000	0.004130	209	0.061700	0.028900
17	3.510000	0.002360	210	0.031700	0.038300
18	2.740000	0.005320	211	0.031900	0.000801
19	1.170000	0.000554	212	0.070400	0.000787
20	0.006740	0.000296	213	0.104000	0.000678
21	7.380000	0.000507	214	0.165000	0.000841
22	0.011700	0.000169	215	0.068200	0.001140
23	1.950000	0.000610	216	0.228000	0.001410
24	5.880000	0.000861	217	0.043900	0.001510
25	0.028100	0.000598	218	0.265000	0.001640
26	0.005050	0.000761	219	0.105000	0.000480
27	nd	0.011200	220	0.267000	0.001010
28	nd	0.002510	221	0.164000	0.000576
29	0.079800	0.016700	222	0.215000	0.001030
30	0.015000	0.000267	223	0.150000	0.000959
31	0.135000	0.000693	224	0.151000	0.001390
32	0.010200	0.000284	225	0.158000	0.001070

33	0.109000	0.000342	226	0.242000	0.000896
34	0.071400	0.000886	227	0.065900	0.000696
35	0.091600	0.000866	228	0.054600	0.000911
36	0.040100	0.000882	229	0.048000	0.000584
37	0.068900	0.000983	230	0.158000	0.000843
38	0.046500	0.000900	231	0.174000	0.000831
39	0.104000	0.001050	232	0.141000	0.000563
40	0.042800	0.000490	233	0.113000	0.000614
41	0.069200	0.000780	234	0.185000	0.000730
42	0.226000	0.002390	235	0.283000	0.001410
43	0.086500	0.000803	236	0.130000	0.001110
44	0.138000	0.001010	237	0.240000	0.001270
45	0.087300	0.001080	238	0.207000	0.000554
46	0.093400	0.001020	239	0.112000	0.000833
47	0.080500	0.001780	240	0.192000	0.000925
48	0.112000	0.000861	241	0.131000	0.000811
49	0.066100	0.001020	242	0.278000	0.001170
50	0.063500	0.001100	243	0.269000	0.000970
51	0.109000	0.001170	244	0.449000	0.000916
52	0.051000	0.000696	245	0.101000	0.000707
53	0.025600	0.000689	246	0.178000	0.000676
54	0.072100	0.000806	247	0.086000	0.001020
55	0.168000	0.002220	248	0.082600	0.000817
56	0.360000	0.000812	249	0.059900	0.000600
57	0.180000	0.001070	250	0.107000	0.000641
58	0.059500	0.000683	251	0.230000	0.000880
59	0.027900	0.000606	252	0.238000	0.001100
60	0.150000	0.001010	253	0.134000	0.000639
61	0.033700	0.000675	254	0.033900	0.011200
62	0.041600	0.000666	255	0.047300	0.037800
63	0.052700	0.000514	256	0.091100	0.038400
64	0.055200	0.000927	257	0.064700	0.041900
65	0.121000	0.000704	258	0.108000	0.034800
66	0.056600	0.000535	259	0.032500	0.017700
67	0.452000	0.000497	260	0.075400	0.019000
68	0.080600	0.000569	261	0.062900	0.023700
69	0.068600	0.000918	262	0.130000	0.034300
70	0.035700	0.000742	263	0.031300	0.020200
71	0.041200	0.014600	264	0.052800	0.013400
72	0.006540	0.007340	265	0.029500	0.021800
73	0.224000	0.071100	266	0.120000	0.053200
74	0.911000	0.000666	267	0.274000	0.056500
75	1.340000	0.000719	268	0.119000	0.042100
76	1.920000	0.000440	269	0.037700	0.022300
77	3.010000	0.000832	270	0.074800	0.035700

78	0.265000	0.000632	271	0.078000	0.025200
79	2.690000	0.000824	272	0.165000	0.052400
80	1.600000	0.000686	273	0.128000	0.042100
81	3.720000	0.001130	274	0.152000	0.064500
82	0.955000	0.000526	275	0.231000	0.045100
83	1.210000	0.000503	276	0.134000	0.034900
84	6.070000	0.001810	277	0.062400	0.026700
85	0.032200	0.017000	278	0.075800	0.033400
86	1.260000	0.000833	279	0.020200	0.015500
87	1.390000	0.001270	280	0.123000	0.051900
88	0.574000	0.000640	281	0.020500	0.014900
89	2.000000	0.000647	282	0.383000	0.090000
90	1.410000	0.000902	283	0.072300	0.032200
91	0.992000	0.000868	284	0.062400	0.038200
92	0.784000	0.000548	285	0.149000	0.086200
93	1.220000	0.001250	286	0.127000	0.066400
94	2.270000	0.001030	287	0.125000	0.063200
95	1.360000	0.001020	288	0.044900	0.019500
96	0.115000	0.282000	289	0.041600	0.032100
97	0.036600	0.131000	290	0.099300	0.045700
98	0.013000	0.000209	291	0.045600	0.018200
99	0.013500	0.000169	292	0.099000	0.064700
100	0.030600	0.000497	293	0.078200	0.025300
101	0.016500	0.000486	294	0.112000	0.055100
102	0.008840	0.000210	295	0.077600	0.051000
103	0.056200	0.000493	296	0.149000	0.057100
104	0.001200	0.000193	297	0.104000	0.047000
105	0.296000	0.000244	298	0.192000	0.061100
106	0.160000	0.000221	299	0.154000	0.086900
107	0.163000	0.000169	300	0.064200	0.039100
108	0.003330	0.000176	301	0.143000	0.048300
109	0.005030	0.000398	302	0.150000	0.048300
110	0.006630	0.000169	303	0.030900	0.015500
111	0.002840	0.000199	304	0.055400	0.024200
112	0.040200	0.000362	305	0.109000	0.035000
113	0.060600	0.000254	306	0.112000	0.046300
114	0.083900	0.000247	307	0.037700	0.015900
115	0.048200	0.000178	308	0.036900	0.018400
116	0.026500	0.000204	309	4.150000	0.000293
117	0.006270	0.000355	310	0.456000	0.005370
118	0.014100	0.000169	311	0.030200	0.003960
119	0.006120	0.000169	312	1.130000	0.008940
120	0.011600	0.000294	313	0.217000	0.004130
121	0.009940	0.000169	314	3.860000	0.000572
122	0.007940	0.000169	315	0.469000	0.000641

123	0.065600	0.000282	316	0.104000	0.000924
124	0.123000	0.000278	317	0.043900	0.000991
125	0.015400	0.000518	318	0.037700	0.000716
126	0.014900	0.000359	319	0.024900	0.000747
127	0.003640	0.000391	320	0.026400	0.000611
128	0.008360	0.000610	321	0.038700	0.000864
129	0.004490	0.000367	322	0.028600	0.000843
130	0.288000	0.000535	323	0.025300	0.000885
131	0.069900	0.000474	324	0.047300	0.001040
132	0.008460	0.000441	325	0.014000	0.001080
133	0.012000	0.000626	326	0.018300	0.000626
134	0.016900	0.000361	327	0.012600	0.000655
135	0.033900	0.000293	328	0.012200	0.000614
136	0.020400	0.000635	329	0.024200	0.000616
137	0.017600	0.000459	330	0.031700	0.000887
138	0.021800	0.000445	331	0.024900	0.000830
139	0.012000	0.000473	332	0.021900	0.000699
140	0.011000	0.008870	333	0.050900	0.000631
141	1.240000	0.075200	334	0.018200	0.000578
142	1.560000	0.032800	335	0.210000	0.001020
143	0.017000	0.031100	336	0.077300	0.000494
144	0.014600	0.034400	337	0.050000	0.000522
145	0.040600	0.058100	338	0.027600	0.000520
146	0.065900	0.109000	339	0.017900	0.000663
147	0.034600	0.001470	340	0.017600	0.000722
148	0.042900	0.020100	341	0.035100	0.000727
149	0.020700	0.054300	342	0.013100	0.000698
150	0.006530	0.043800	343	0.006180	0.000728
151	0.017400	0.043600	344	0.037800	0.000569
152	0.087600	0.101000	345	0.009540	0.000392
153	0.266000	0.122000	346	0.030800	0.000457
154	0.524000	0.016100	347	0.066200	0.000940
155	0.294000	0.044000	348	0.015300	0.000628
156	0.396000	0.084300	349	0.059500	0.000738
157	1.070000	0.192000	350	0.004620	0.000642
158	2.900000	0.224000	351	0.037100	0.000765
159	0.137000	0.061200	352	0.095800	0.000615
160	0.074500	0.070800	353	0.088200	0.000472
161	0.128000	0.059700	354	0.082800	0.000837
162	0.144000	0.071000	355	0.115000	0.000986
163	0.166000	0.083100	356	0.067700	0.000878
164	0.987000	0.124000	357	0.017700	0.001140
165	0.035200	0.068300	358	0.015900	0.000815
166	2.270000	0.206000	359	0.021300	0.000869
167	3.740000	0.204000	360	0.022000	0.000782

168	2.940000	0.171000	361	0.037400	0.000988
169	0.033700	0.067900	362	0.015200	0.000832
170	0.091500	0.089800	363	0.010400	0.000798
171	0.019700	0.037900	364	0.036900	0.000334
172	0.286000	0.170000	365	0.050100	0.001050
173	0.524000	0.154000	366	0.035100	0.000681
174	2.100000	0.158000	367	0.033700	0.000735
175	0.664000	0.161000	368	0.064000	0.000635
176	0.165000	0.111000	369	0.018300	0.000479
177	0.060400	0.091300	370	0.030535	0.000555
178	0.247000	0.065200	371	0.056700	0.000438
179	0.099200	0.070700	372	0.016600	0.000633
180	0.304000	0.123000	373	0.022400	0.000576
181	0.284000	0.128000	374	0.023900	0.000973
182	0.140000	0.104000	375	0.006720	0.000679
183	1.040000	0.185000	376	0.003220	0.000468
184	0.625000	0.078900	377	0.016200	0.000632
185	0.081300	0.044100	378	0.077100	0.000632
186	0.098900	0.118000	379	0.015900	0.000432
187	0.010200	0.027300	380	0.109000	0.000883
188	0.020500	0.049900	381	0.015100	0.001130
189	0.006910	0.026900	382	0.065800	0.000657
190	1.910000	0.103000	383	0.103000	0.000859
191	0.743000	0.184000	384	0.028800	0.000497
192	0.047300	0.072300	385	0.055100	0.001240
193	0.040200	0.054000	528	0.026200	0.017300

nd = no data

NAMPT cell proliferation assay

PC3 cells were seeded in 96-well black plates (Corning #3904) at 500 cells/well in 90 µl of RPMI media containing 10% heat-inactivated FBS and incubated overnight at 37°C and 5% CO_2 to allow cells to attach to wells. The following day, test compounds were serially diluted in neat DMSO to 1000X final concentrations prior to dilution with RPMI media to 10X and 1% DMSO. Ten µL of the 10X compounds were then transferred to wells containing cells to produce a dose response of 10-fold dilutions from 10 µM to 1 x 10^{-5} µM. Cells were incubated for 5 days at 37°C and 5% CO_2, then cell viability was measured using Cell Titer Glo reagent (Promega #G7571). Percent inhibition values were calculated and fitted to a sigmoidal dose response curves using Assay Explorer software to determine IC50s. To assess whether inhibition of cell viability was due to NAMPT inhibition, the proliferation assay was also performed in the presence of 0.3 mM nicotinamide mononucleotide.

Table 2 shows the results of the cell proliferation assay.

Table 2

Example	Cell Titer-Glo - IC50 (μM)	Example	Cell Titer-Glo - IC50 (μM)	Example	Cell Titer-Glo - IC50 (μM)	Example	Cell Titer-Glo - IC50 (μM)
1	0.00656	258	0.309	515	0.00085	772	0.0636
2	>10	259	0.0726	516	0.00226	773	0.0857
3	7.33	260	0.0746	517	0.00921	774	0.00252
4	0.112	261	0.0715	518	0.00087	775	0.00215
5	0.00675	262	0.119	519	0.00321	776	0.00764
6	0.0677	263	0.0595	520	0.00047	777	0.0192
7	0.876	264	0.1	521	0.00472	778	0.0197
8	0.0708	265	0.0701	522	0.00078	779	0.00148
9	0.739	266	0.083	523	0.00099	780	0.00407
10	0.00184	267	0.622	524	0.00573	781	0.01
11	0.0227	268	0.0829	525	0.00093	782	0.0669
12	0.0844	269	0.0604	526	0.00094	783	0.00646
13	0.0791	270	0.0627	527	0.00778	784	0.016
14	0.0548	271	0.0515	528	0.01923	785	0.00117
15	0.0347	272	0.0795	529	0.00933	786	0.012
16	0.0926	273	0.634	530	0.00202	787	0.0639
17	0.0937	274	0.107	531	0.0176	788	0.00759
18	0.148	275	0.683	532	0.00724	789	0.0284
19	0.0564	276	0.13	533	0.0246	790	0.0746
20	0.00028	277	0.0731	534	0.00546	791	0.00748
21	0.15	278	0.0791	535	0.00939	792	0.0088
22	0.00125	279	0.00972	536	0.00614	793	0.329
23	0.0725	280	0.0719	537	0.0033	794	0.196
24	0.169	281	0.0169	538	0.0137	795	0.773
25	0.00141	282	0.629	539	0.00257	796	0.0117
26	0.000682	283	0.0725	540	0.00391	797	0.0126
27	>10	284	0.0666	541	0.0042	798	0.0664
28	>10	285	0.0692	542	0.0676	799	0.0255
29	0.135	286	0.074	543	0.0077	800	0.06
30	0.00197	287	0.121	544	0.00717	801	0.024555
31	0.0069	288	0.0248	545	0.0152	802	0.0263
32	0.00654	289	0.0532	546	0.00141	803	0.00161
33	0.00366	290	0.0807	547	0.00302	804	0.00792
34	0.0068	291	0.0736	548	0.0649	805	0.065
35	0.00692	292	0.0934	549	0.00067	806	0.00313
36	0.00966	293	0.0723	550	0.00821	807	0.00415
37	0.00648	294	0.0832	551	0.00048	808	0.0411
38	0.00639	295	0.0715	552	0.00332	809	0.0024
39	0.00738	296	0.0689	553	0.0441	810	0.0611
40	0.00217	297	0.0932	554	0.00263	811	0.011
41	0.00376	298	0.0979	555	0.0239	812	0.0102

42	0.0646	299	0.0846	556	0.00598	813	0.0786
43	0.00688	300	0.0259	557	0.0102	814	0.0819
44	0.00547	301	0.0905	558	0.00066	815	0.185
45	0.00677	302	0.0824	559	0.00133	816	0.188
46	0.00301	303	0.0586	560	0.00585	817	0.0641
47	0.00335	304	0.0332	561	0.0622	818	0.0294
48	0.00288	305	0.102	562	0.00945	819	0.00856
49	0.00696	306	0.0347	563	0.0242	820	0.0754
50	0.00895	307	0.0208	564	0.0792	821	0.165
51	0.00362	308	0.0614	565	0.0741	822	0.0605
52	0.00628	309	8.2	566	0.0822	823	0.247
53	0.00367	310	0.0161	567	0.0765	824	0.0706
54	0.00331	311	0.0029	568	0.0482	825	0.0623
55	0.0211	312	0.0217	569	0.207	826	0.0983
56	0.00927	313	0.00603	570	0.631	827	0.0737
57	0.00875	314	0.621	571	0.118	828	0.000826
58	0.00648	315	0.0868	572	0.0598	829	0.00295
59	0.00614	316	0.00312	573	0.0819	830	0.00796
60	0.00507	317	0.00183	574	0.0553	831	0.00725
61	0.00352	318	0.00272	575	0.269	832	0.0167
62	0.0142	319	0.00124	576	0.0848	833	0.00667
63	0.00635	320	0.00237	577	0.093	834	0.0144
64	0.00632	321	0.00321	578	0.0887	835	0.00235
65	0.00638	322	0.00214	579	0.267	836	0.658
66	0.00581	323	0.00281	580	0.078	837	0.769
67	0.386	324	0.00708	581	0.0807	838	1.77
68	0.00354	325	0.00128	582	0.627	839	2
69	0.00422	326	0.00577	583	0.0874	840	0.0028
70	0.00397	327	0.00123	584	0.0872	841	0.00355
71	0.0729	328	0.00159	585	0.283	842	0.000665
72	0.00569	329	0.00283	586	0.107	843	0.00061
73	1.98	330	0.00138	587	0.0814	844	0.00252
74	0.0114	331	0.00209	588	0.113	845	0.00209
75	nd	332	0.00099	589	0.0979	846	0.00724
76	0.0191	333	0.00568	590	0.0822	847	0.115
77	nd	334	0.00097	591	0.0936	848	0.609
78	0.0212	335	0.00607	592	0.62	849	0.685
79	nd	336	0.00826	593	0.0634	850	0.0705
80	0.0255	337	0.00694	594	0.0478	851	0.00275
81	nd	338	0.00111	595	0.0806	852	0.0124
82	0.00955	339	0.00183	596	0.0846	853	>10
83	nd	340	0.00242	597	0.117	854	>10
84	0.0389	341	0.00198	598	0.208	855	0.747
85	0.0205	342	0.0023	599	0.0797	856	0.729
86	0.0697	343	0.00653	600	0.219	857	0.00252

87	0.0317	344	0.0089	601	0.0968	858	0.00436
88	0.0663	345	0.00199	602	0.002	859	0.0027
89	0.0646	346	0.0038	603	0.576	860	0.01
90	0.0601	347	0.00806	604	8.26127	861	0.00758
91	0.0599	348	0.002	605	1.4	862	0.00849
92	0.024	349	0.00728	606	0.0867	863	0.00567
93	0.0584	350	0.00075	607	7.65	864	0.00529
94	0.0657	351	0.00236	608	0.712	865	0.00406
95	0.0739	352	0.00888	609	0.00205	866	0.00792
96	7.61	353	0.00715	610	0.0079	867	0.00784
97	0.922	354	0.00751	611	0.09	868	0.00229
98	0.00605	355	0.00979	612	0.0536	869	0.00198
99	0.00572	356	0.00909	613	0.70691	870	0.0032
100	0.00613	357	0.00147	614	7.66	871	0.00361
101	0.00031	358	0.00186	615	6.15	872	0.0236
102	0.00059	359	0.00177	616	7.29	873	0.675
103	0.00144	360	0.00235	617	1.87	874	0.0711
104	0.00018	361	0.00277	618	>10	875	>10
105	0.00617	362	0.00261	619	>10	876	0.0292
106	0.0618	363	0.0056	620	2.83	877	0.02960
107	0.00688	364	0.00863	621	>10	878	0.0706
108	0.00013	365	0.00784	622	>10	879	0.00583
109	0.00066	366	0.00657	623	6.17	880	0.01540
110	0.00026	367	0.00638	624	>10	881	0.00818
111	0.00064	368	0.0077	625	1.9	882	0.00643
112	0.00076	369	0.00214	626	5.22	883	0.0309
113	0.00634	370	0.00879	627	0.853	884	0.00275
114	0.0181	371	0.00894	628	>10	885	0.00163
115	0.0004	372	0.00706	629	5.01	886	0.00766
116	0.00064	373	0.00595	630	0.00812	887	0.00847
117	0.00063	374	0.00632	631	0.00958	888	0.00976
118	0.00022	375	0.00087	632	0.00881	889	0.00285
119	0.00019	376	0.00062	633	0.00895	890	0.00409
120	0.00023	377	0.00213	634	0.00922	891	0.0656
121	0.00062	378	0.00709	635	0.0416	892	0.146
122	0.00061	379	0.00107	636	0.0828	893	0.681
123	0.00103	380	0.00757	637	0.00124	894	0.752
124	0.00144	381	0.00187	638	0.0299	895	0.00215
125	0.00024	382	0.00899	639	0.00816	896	0.00109
126	0.00026	383	0.0627	640	0.00292	897	0.00156
127	0.00014	384	0.00827	641	0.0726	898	.000851
128	0.00016	385	0.0232	642	0.00726	899	.000401
129	0.00016	386	0.00318	643	0.00846	900	0.00224
130	0.00181	387	0.0022	644	0.00823	901	0.00207
131	0.0003	388	0.00088	645	0.0033	902	0.00645

132	0.00023	389	0.00717	646	0.0587	903	.000618
133	0.00062	390	0.0015	647	0.00573	904	0.00195
134	0.00064	391	0.00599	648	0.0268	905	0.0133
135	0.0003	392	0.00354	649	0.00111	906	.000879
136	0.00023	393	0.00372	650	0.0869	907	6.75
137	0.00031	394	0.00199	651	0.0276	908	0.0925
138	0.00023	395	0.00214	652	0.00614	909	0.067
139	0.00018	396	0.06848	653	0.00972	910	0.00651
140	0.00354	397	0.00335	654	0.00276	911	>10
141	0.834	398	0.00819	655	0.000475	912	0.0642
142	0.7406	399	0.00635	656	0.061	913	0.0663
143	0.00496	400	0.0068	657	0.00844	914	0.0027
144	0.0184	401	0.00854	658	0.0144	915	0.139
145	0.0709	402	0.00168	659	0.0112	916	0.646
146	0.0707	403	0.0041	660	0.00523	917	0.101
147	0.00095	404	0.0027	661	0.0216	918	0.717
148	0.0761	405	0.00675	662	0.0159	919	0.0519
149	0.058	406	0.00742	663	0.0316	920	0.00543
150	0.0589	407	0.00101	664	1.15	921	0.0029
151	0.0609	408	0.0299	665	7.62	922	0.00338
152	0.116	409	0.00672	666	0.008059	923	0.0694
153	0.699	410	0.00868	667	0.01248	924	0.00117
154	0.803	411	0.00715	668	>10	925	0.0101
155	0.701	412	0.00137	669	0.00188	926	0.602
156	0.712	413	0.01	670	0.00853	927	0.0039
157	0.948	414	0.0074	671	0.00853	928	0.00256
158	1.3	415	0.00228	672	0.00405	929	0.0271
159	0.182	416	0.00112	673	0.0116	930	0.0027
160	0.173	417	0.00645	674	0.00572	931	0.00317
161	0.213	418	0.00826	675	0.0693	932	0.00582
162	0.225	419	0.00217	676	0.00202	933	0.00239
163	0.12	420	0.00235	677	0.0093	934	0.00245
164	0.202	421	0.00372	678	0.00609	935	0.002
165	0.0682	422	0.00112	679	0.0006	936	0.00218
166	1.07	423	0.00038	680	0.00355	937	0.00262
167	6.25	424	0.0015	681	0.00902	938	0.00875
168	1.01	425	0.00091	682	0.00273	939	0.00296
169	0.0654	426	0.00207	683	0.00902	940	0.00197
170	0.0655	427	0.00203	684	0.0766	941	0.0021
171	0.0681	428	0.00019	685	0.00828	942	0.00276
172	0.329	429	0.0008	686	0.0649	943	0.0076
173	0.627	430	0.00142	687	0.00611	944	0.00714
174	1.13	431	0.00167	688	0.0094	945	0.00451
175	0.683	432	0.008	689	0.00968	946	0.00289
176	0.218	433	0.00577	690	0.00314	947	0.00256

177	0.107	434	0.00635	691	0.03	948	0.00226
178	0.3	435	0.0003	692	0.00423	949	0.00595
179	0.192	436	0.00067	693	0.0136	950	0.00606
180	0.164	437	0.00098	694	0.0716	951	0.00277
181	0.238	438	0.00196	695	0.00616	952	0.00217
182	0.0879	439	0.00336	696	0.00467	953	0.00334
183	0.346	440	0.0018	697	0.00596	954	0.00638
184	0.604	441	0.00683	698	0.0679	955	0.00597
185	0.0742	442	0.00625	699	0.065	956	0.00640
186	0.627	443	0.00565	700	0.00876	957	0.00193
187	0.0206	444	0.078	701	0.0752	958	0.00263
188	0.0224	445	0.0191	702	0.00207	959	0.00233
189	0.0146	446	0.108	703	0.00843	960	0.00286
190	0.694	447	0.903	704	0.0053	961	0.00557
191	0.677	448	0.00932	705	0.0202	962	0.0024
192	0.0693	449	0.678	706	0.0077	963	0.00214
193	0.071	450	0.0509	707	0.00693	964	0.00184
194	0.124	451	0.0868	708	0.0142	965	0.00260
195	0.701	452	0.0632	709	0.0145	966	0.00323
196	0.111	453	0.105	710	0.0103	967	0.00305
197	0.103	454	0.106	711	0.0595	968	0.0037
198	0.0716	455	0.458	712	0.00679	969	.000347
199	0.0974	456	0.0395	713	0.00999	970	0.0285
200	0.0719	457	0.142	714	0.0176	971	0.0708
201	0.0609	458	0.0644	715	0.0118	972	0.667
202	0.168	459	0.0369	716	0.0692	973	0.00553
203	0.606	460	0.223	717	0.0121	974	0.00784
204	0.0245	461	0.646	718	0.00627	975	0.098
205	0.0387	462	0.214	719	0.00963	976	0.0612
206	0.0674	463	0.0709	720	0.00857	977	0.0124
207	0.671	464	0.0659	721	0.00839	978	1.07
208	0.593	465	0.616	722	0.0848	979	0.072
209	0.0816	466	0.00807	723	0.003507	980	0.0822
210	0.0627	467	0.0156	724	0.0809	981	1.06
211	0.00594	468	0.73	725	0.00401	982	0.0835
212	0.00579	469	0.00861	726	0.0327	983	0.604
213	0.00688	470	0.715	727	0.0046	984	0.696
214	0.00909	471	0.072	728	0.00697	985	0.635
215	0.00695	472	0.00656	729	0.0135	986	7.47
216	0.00599	473	0.0093	730	0.00681	987	0.609
217	0.00255	474	0.0685	731	0.00050	988	1.24
218	0.00886	475	0.594	732	0.0299	989	0.602
219	0.00886	476	0.0174	733	0.0375	990	6.81
220	0.0132	477	0.235	734	0.00833	991	0.76
221	0.00899	478	0.0143	735	0.0689	992	1.51

222	0.0155	479	0.0689	736	0.00809	993	0.809
223	0.0055	480	0.00424	737	1.86	994	0.059
224	0.00752	481	0.0121	738	0.853926	995	0.245
225	0.00876	482	0.0326	739	7.31	996	0.104
226	0.00889	483	0.00214	740	0.914369	997	0.0935
227	0.00453	484	0.00056	741	0.181262	998	1.28
228	0.00597	485	0.00635	742	0.734	999	0.25
229	0.00646	486	0.00624	743	6.62	1000	0.077
230	0.00905	487	0.072	744	2.72	1001	0.0532
231	0.00875	488	0.0642	745	>10	1002	0.911
232	0.00874	489	0.00207	746	>10	1003	1.07
233	0.00873	490	0.00068	747	5.92	1004	7.92
234	0.0105	491	0.00845	748	0.00258	1005	0.592
235	0.0124	492	0.00373	749	>10	1006	0.00536
236	0.00925	493	0.00673	750	0.226	1007	0.0567
237	0.0103	494	0.00105	751	0.00271	1008	0.299
238	0.0157	495	0.00706	752	2.45	1009	0.0818
239	0.0067	496	0.0063	753	0.00892	1010	0.0709
240	0.0103	497	0.0234	754	0.0948	1011	0.113
241	0.00773	498	0.00664	755	0.19	1012	0.782
242	0.00906	499	0.0121	756	0.00908	1013	0.213
243	0.00928	500	0.00102	757	0.0677	1014	0.219
244	0.0104	501	0.00607	758	0.857	1015	0.0901
245	0.00706	502	0.00474	759	0.0062	1016	0.212
246	0.00965	503	0.0582	760	0.253	1017	0.752
247	0.00798	504	0.00775	761	0.0923	1018	0.716
248	0.00658	505	0.00684	762	0.709	1019	2.46
249	0.00235	506	0.00128	763	0.00841	1020	7.27
250	0.00911	507	0.00834	764	0.022126	1021	0.0477
251	0.00787	508	0.00079	765	1.02	1022	8.16
252	0.00951	509	0.00119	766	0.787	1023	0.508
253	0.00809	510	0.0664	767	1.28	1024	nd
254	0.012	511	0.00082	768	0.111	1025	nd
255	0.0241	512	0.0155	769	0.0186		
256	0.145	513	0.0035	770	0.138		
257	0.0761	514	0.00032	771	0.0699		

nd = no data

Compounds which inhibit NAMPT are useful for treating diseases in which activation of NF-KB is implicated. Such methods are useful in the treatment of a variety of diseases including inflammatory and tissue repair disorders; particularly rheumatoid arthritis, inflammatory bowel disease, asthma and COPD (chronic obstructive pulmonary disease), osteoarthritis, osteoporosis and fibrotic diseases; dermatosis, including psoriasis, atopic dermatitis and ultra-violet induced skin damage; autoimmune diseases including systemic

lupus erythematosis, multiple sclerosis, psoriatic arthritis, ankylosing spondylitis, tissue and organ rejection, Alzheimer's disease, stroke, athersclerosis, restenosis, diabetes, glomerulonephritis, cancer, particularly wherein the cancer is selected from breast, prostate, lung, colon, cervix, ovary, skin, CNS, bladder, pancreas, leukaemia, lymphoma or Hodgkin's disease, cachexia, inflammation associated with infection and certain viral infections, including Acquired Immune Deficiency Syndrome (AIDS), adult respiratory distress syndrome, and ataxia telengiectasia.

Involvement of NAMPT in the treatment of cancer is described in WO 97/48696. Involvement of NAMPT in immuno-supression is described in WO 97/48397. Involvement of NAMPT for the treatment of diseases involving angiogenesis is described in WO 2003/80054. Involvement of NAMPT for the treatment of rheumatoid arthritis and septic shock is described in WO 2008/025857. Involvement of NAMPT for the prophlaxis and treatment of ischaemia is described in WO 2009/109610.

Cancers include, but are not limited to, hematologic and solid tumor types such as acoustic neuroma, acute leukemia, acute lymphoblastic leukemia, acute myelogenous leukemia (monocytic, myeloblastic, adenocarcinoma, angiosarcoma, astrocytoma, myelomonocytic and promyelocytic), acute t-cell leukemia, basal cell carcinoma, bile duct carcinoma, bladder cancer, brain cancer, breast cancer (including estrogen-receptor positive breast cancer), bronchogenic carcinoma, Burkitt's lymphoma, cervical cancer, chondrosarcoma, chordoma, choriocarcinoma, chronic leukemia, chronic lymphocytic leukemia, chronic myelocytic (granulocytic) leukemia, chronic myelogenous leukemia, colon cancer, colorectal cancer, craniopharyngioma, cystadenocarcinoma, dysproliferative changes (dysplasias and metaplasias), embryonal carcinoma, endometrial cancer, endotheliosarcoma, ependymoma, epithelial carcinoma, erythroleukemia, esophageal cancer, estrogen-receptor positive breast cancer, essential thrombocythemia, Ewing’s tumor, fibrosarcoma, gastric carcinoma, germ cell testicular cancer, gestational trophobalstic disease, glioblastoma, head and neck cancer, heavy chain disease, hemangioblastoma, hepatoma, hepatocellular cancer, hormone insensitive prostate cancer, leiomyosarcoma, liposarcoma, lung cancer (including small cell lung cancer and non-small cell lung cancer), lymphangioendothelio-sarcoma, lymphangiosarcoma, lymphoblastic leukemia, lymphoma (lymphoma, including diffuse large B-cell lymphoma, follicular lymphoma, Hodgkin’s lymphoma and non-Hodgkin’s lymphoma), malignancies and hyperproliferative disorders of the bladder, breast, colon, lung, ovaries, pancreas, prostate, skin and uterus, lymphoid malignancies of T-cell or B-cell origin, leukemia, medullary carcinoma, medulloblastoma, melanoma, meningioma, mesothelioma, multiple myeloma, myelogenous leukemia, myeloma, myxosarcoma, neuroblastoma, oligodendroglioma, oral cancer, osteogenic sarcoma, ovarian cancer, pancreatic cancer, papillary adenocarcinomas, papillary carcinoma, peripheral T-cell lymphoma, pinealoma,

polycythemia vera, prostate cancer (including hormone-insensitive (refractory) prostate cancer), rectal cancer, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, sebaceous gland carcinoma, seminoma, skin cancer, small cell lung carcinoma, solid tumors (carcinomas and sarcomas), stomach cancer, squamous cell carcinoma, synovioma, sweat gland carcinoma, testicular cancer (including germ cell testicular cancer), thyroid cancer, Waldenström's macroglobulinemia, testicular tumors, uterine cancer, Wilms' tumor and the like.

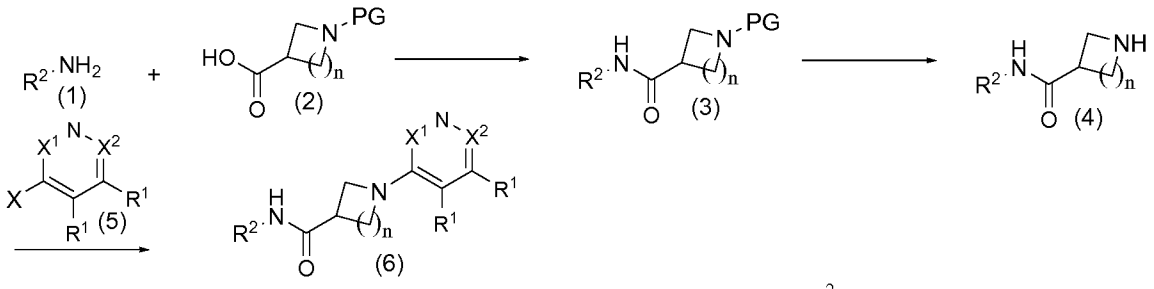
Schemes and Experimentals

The following abbreviations have the meanings indicated. ADDP means 1,1'-(azodicarbonyl)dipiperidine; AD-mix-β means a mixture of $(DHQD)_2PHAL$, $K_3Fe(CN)_6$, K_2CO_3, and K_2SO_4; 9-BBN means 9-borabicyclo(3.3.1)nonane; Boc means tert-butoxycarbonyl; $(DHQD)_2PHAL$ means hydroquinidine 1,4-phthalazinediyl diethyl ether; DBU means 1,8-diazabicyclo[5.4.0]undec-7-ene; DIBAL means diisobutylaluminum hydride; DIEA means diisopropylethylamine; DMAP means N,N-dimethylaminopyridine; DMF means N,N-dimethylformamide; dmpe means 1,2-bis(dimethylphosphino)ethane; DMSO means dimethylsulfoxide; dppb means 1,4-bis(diphenylphosphino)-butane; dppe means 1,2-bis(diphenylphosphino)ethane; dppf means 1,1'-bis(diphenylphosphino)ferrocene; dppm means 1,1-bis(diphenylphosphino)methane; EDAC·HCl means 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride; Fmoc means fluorenylmethoxycarbonyl; HATU means O-(7-azabenzotriazol-1-yl)-N,N'N'N'-tetramethyluronium hexafluorophosphate; HMPA means hexamethylphosphoramide; IPA means isopropyl alcohol; $MP\text{-}BH_3$ means macroporous triethylammonium methylpolystyrene cyanoborohydride; TEA means triethylamine; TFA means trifluoroacetic acid; THF means tetrahydrofuran; NCS means N-chlorosuccinimide; NMM means N-methylmorpholine; NMP means N-methylpyrrolidine; PPh_3 means triphenylphosphine.

The following schemes are presented to provide what is believed to be the most useful and readily understood description of procedures and conceptual aspects of this invention. Compounds of this invention may be made by synthetic chemical processes, examples of which are shown herein. It is meant to be understood that the order of the steps in the processes may be varied, that reagents, solvents and reaction conditions may be substituted for those specifically mentioned, and that vulnerable moieties may be protected and deprotected, as necessary.

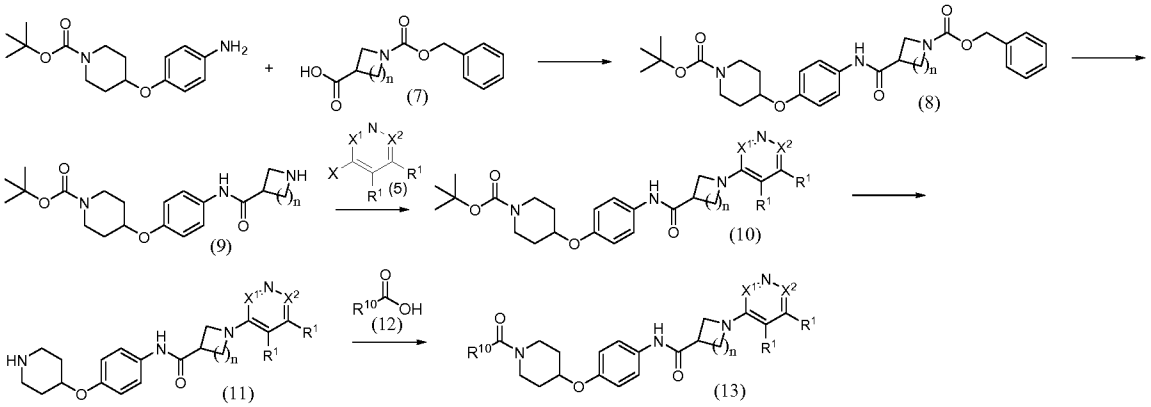
Schemes

Scheme 1



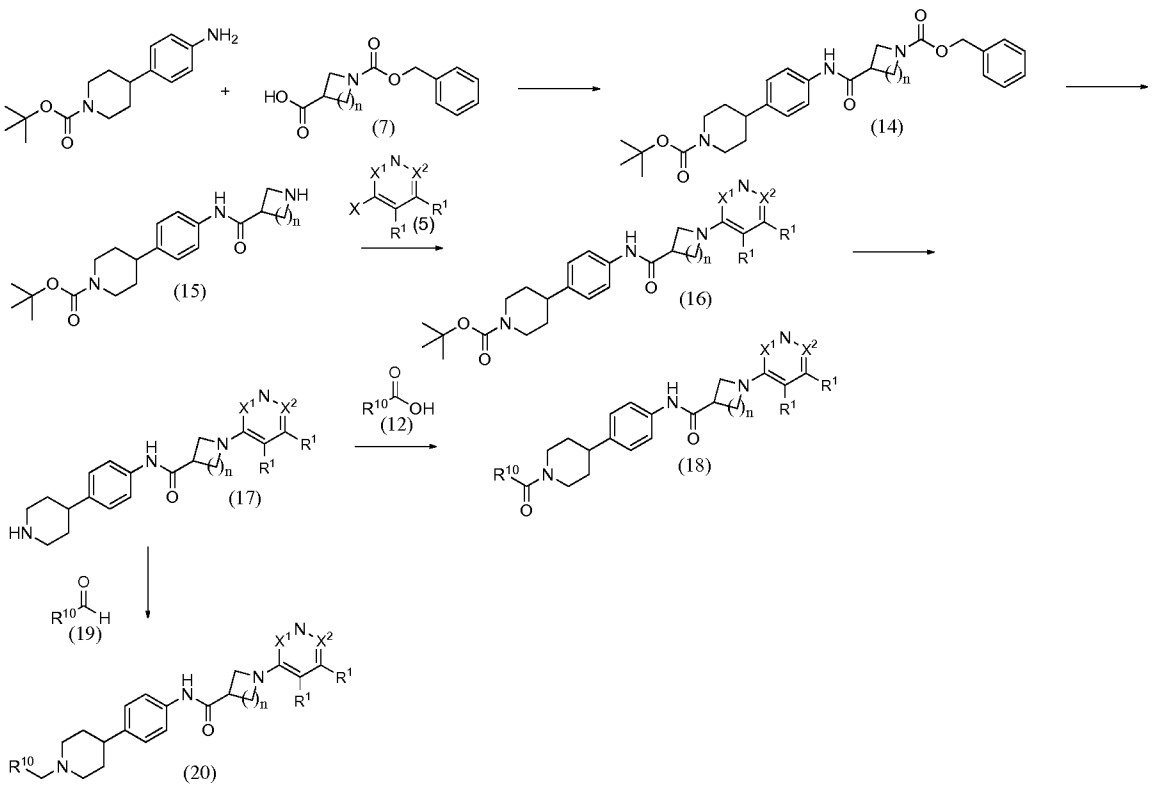
As shown in Scheme 1, compounds of formula (1), wherein R^2 is as described herein, can be reacted with acids of formula (2); wherein PG is a suitable protecting group and n is 1, 2, or 3, in the presence of a base such as but not limited to diisopropylethylamine, to provide compounds of formula (3). The reaction may involve the use of a carboxyl activating agent such as but not limited to N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride, and a ester activating agent such as but not limited to 1-hydroxybenzotriazole hydrate. The reaction is typically performed at ambient temperature in a solvent such as but not limited to N,N-dimethylformamide, N,N-dimethylacetamide, or mixtures thereof. Compounds of formula (4) can be prepared from compounds of formula (3) after removal of the suitable protecting group using standard reaction conditions known to those skilled in the art and readily available in the literature. Compounds of formula (5), wherein X^1, X^2, and R^1 are as described herein and X is an appropriate halide, can be reacted with compounds of formula (4) to provide compounds of formula (6) which are representative of compounds of Formula (I). This C-N cross coupling reaction typically employs a base such as but not limited to cesium carbonate, a palladium catalyst such as but not limited to bis(dibenzylideneacetone)palladium(0), and a ligand such as but not limited to (9,9-dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphine). The reaction is typically performed at an elevated temperature in a solvent such as but not limited to dioxane.

Scheme 2



tert-Butyl 4-(4-aminophenoxy)piperidine-1-carboxylate can be reacted with acids of formula (7); wherein n is 1, 2, or 3, in the presence of a base such as but not limited to diisopropylethylamine; to provide compounds of formula (8). The reaction may involve the use of a carboxyl activating agent such as but not limited to N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride, and a ester activating agent such as but not limited to 1-hydroxybenzotriazole hydrate. The reaction is typically performed at ambient temperature in a solvent such as but not limited to N,N-dimethylformamide, N,N-dimethylacetamide, or mixtures thereof. Compounds of formula (9) can be prepared from compounds of formula (8) by reacting the latter with hydrogen in the presence of palladium hydroxide. The reaction is typically performed at ambient temperature in a solvent such as but not limited to tetrahydrofuran. Compounds of formula (5), wherein X^1, X^2, and R^1 are as described herein and X is an appropriate halide, can be reacted with compounds of formula (9) to provide compounds of formula (10). The C-N cross coupling reaction typically employs a base such as but not limited to cesium carbonate, a palladium catalyst such as but not limited to bis(dibenzylideneacetone)palladium(0), and a ligand such as but not limited to (9,9-dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphine). The reaction is typically performed at an elevated temperature in a solvent such as but not limited to dioxane. Compounds of formula (11) can be prepared by treating compounds of formula (10) with an acid such as but not limited to trifluoroacetic acid in a solvent such as but not limited to dichloromethane. Compounds of formula (13), which are representative of compounds of Formula (I), can be prepared by reacting compounds of formula (11) with compounds of formula (12), wherein R^{10} is as described herein, in the presence of a base such as but not limited to diisopropylethylamine. The reaction may involve the use of a carboxyl activating agent such as but not limited to N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride, and a ester activating agent such as but not limited to 1-hydroxybenzotriazole hydrate. The reaction is typically performed at ambient temperature in a solvent such as but not limited to N,N-dimethylformamide, N,N-dimethylacetamide, or mixtures thereof.

Scheme 3



As shown in Scheme 3, tert-Butyl 4-(4-aminophenyl)piperidine-1-carboxylate can be reacted with acids of formula (7); wherein n is 1, 2, or 3, in the presence of a base such as but not limited to diisopropylethylamine; to provide compounds of formula (14). The reaction may involve the use of a carboxyl activating agent such as but not limited to N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride, and a ester activating agent such as but not limited to 1-hydroxybenzotriazole hydrate. The reaction is typically performed at ambient temperature in a solvent such as but not limited to N,N-dimethylformamide, N,N-dimethylacetamide, or mixtures thereof. Compounds of formula (15) can be prepared from compounds of formula (14) by reacting the latter with hydrogen in the presence of palladium hydroxide. The reaction is typically performed at ambient temperature in a solvent such as but not limited to tetrahydrofuran. Compounds of formula (5), wherein X^1, X^2, and R^1 are as described herein and X is an appropriate halide, can be reacted with compounds of formula (15) to provide compounds of formula (16). The C-N cross coupling reaction typically employs a base such as but not limited to cesium carbonate, a palladium catalyst such as but not limited to bis(dibenzylideneacetone)palladium(0), and a ligand such as but not limited to (9,9-dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphine). The reaction is typically performed at an elevated temperature in a solvent such as but not limited to dioxane. Compounds of formula (17) can be prepared by treating compounds of formula (16) with an acid such as but not limited to trifluoroacetic acid in a solvent such as but not limited to dichloromethane. Compounds of formula (18), which are representative of compounds of

Formula (I), can be prepared by reacting compounds of formula (17) with compounds of formula (12), wherein R^{10} is as described herein, in the presence of a base such as but not limited to diisopropylethylamine. The reaction may involve the use of a carboxyl activating agent such as but not limited to N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride, and a ester activating agent such as but not limited to 1-hydroxybenzotriazole hydrate. The reaction is typically performed at ambient temperature in a solvent such as but not limited to N,N-dimethylformamide, N,N-dimethylacetamide, or mixtures thereof. Alternatively, compounds of formula (17) can be reacted with compounds of formula (19), wherein R^{10} is as described herein, to provide compounds of formula (20), which are representative of compounds of Formula (I). The reaction is typically performed in the presence of a reducing agent such as but not limited to sodium triacetoxyborohydride and acetic acid in a solvent such as but not limited to methanol and may be performed at an elevated temperature.

Examples

The following examples are presented to provide what is believed to be the most useful and readily understood description of procedures and conceptual aspects of this invention. Each exemplified compound and intermediate was named using ACD/ChemSketch Version 12.5 (20 April 2011) or (03 Sept 2012), Advanced Chemistry Development Inc., Toronto, Ontario), or ChemDraw® Ver. 9.0.7 (CambridgeSoft, Cambridge, MA).

Experimentals

Example 1

1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide

Example 1A

tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate

1-(Benzyloxycarbonyl)azetidine-3-carboxylic acid (5.10 g, 21.67 mmol), 1-hydroxybenzotriazole hydrate (4.15 g, 27.1 mmol) and tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate (5.28 g, 18.06 mmol) were suspended in dimethylformamide (25 ml) followed by addition of diisopropylethylamine (9.64 ml, 54.2 mmol) and N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (5.19 g, 27.1 mmol). The mixture was stirred at room temperature overnight and the solution was diluted with water. The resulting turbid mixture was extracted with ethyl acetate and then ethyl acetate/tetrahydrofuran. The organics were combined and dried over magnesium sulfate, filtered and concentrated to give a solid which was triturated with ether and filtered to give the title compound.

Example 1B

tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate

tert-Butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate (50 mg, 0.098 mmol) and tetrahydrofuran (5 ml) were added to 20% wet palladium hydroxide on carbon (10 mg, 0.071 mmol) in a 50 ml pressure bottle and the mixture was stirred for 16 hours at 30 psi and room temperature. The mixture was filtered through a nylon membrane and the filtrate was concentrated to give the title compound.

Example 1C

tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate

tert-Butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate (4.97 g, 13.24 mmol), cesium carbonate (10.78 g, 33.1 mmol), 3-bromopyridine (1.307 ml, 13.24 mmol), (9,9-dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphine) (0.764 g, 1.32 mmol) and bis(dibenzylideneacetone)palladium(0) (0.606 g, 0.662 mmol) were suspended in dioxane (50 ml), bubbled with nitrogen for 30 minutes and heated at 100°C overnight. The mixture was filtered through a celite pad with dichloromethane washes and the filtrate was concentrated. Normal phase chromatography provided the title compound.

Example 1D

N-(4-(piperidin-4-yloxy)phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide

tert-Butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate (3.82 g, 8.44 mmol) was dissolved in 60 ml dichloromethane, cooled to 0°C and treated with trifluoroacetic acid (10 ml). The mixture was allowed to warm to room temperature and was stirred for 2 hours. Removal of the solvent under vacuum provided the title compound.

Example 1E

1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-yloxy)phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-(tetrahydro-2H-pyran-4-yl)acetic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.95 (bs, 1H), 7.93 (d, J = 4.2 Hz, 1H), 7.88 – 7.83 (m, 1H), 7.55 – 7.47 (m, 2H), 7.26 – 7.08 (m, 1H), 7.01 – 6.78 (m, 3H), 4.14 – 4.04 (m, 2H), 4.02 – 3.62 (m, 6H), 2.37 – 1.73 (m, 6H), 1.66 – 1.00 (m, 8H); MS (ESI(+)) m/e 479 $(M+H)^+$.

Table 1.

The following Examples were prepared essentially as described in Example 1, substituting the appropriate bromopyridine in Example 1C and the appropriate carboxylic acid in Example 1E. Some products were purified by flash chromatography while others were

purified by reverse-phase HPLC. Accordingly, some Examples were isolated as trifluoroacetic acid salts.

Ex		Name	^{1}H NMR	MS
3		N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-[2-(trifluoromethyl)pyridin-3-yl]azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.96 (s, 1H), 8.02 (dd, J = 4.3, 1.2 Hz, 1H), 7.55 – 7.45 (m, 3H), 7.15 (d, J = 8.5 Hz, 1H), 6.97 – 6.90 (m, 2H), 4.59 – 4.47 (m, 1H), 4.28 – 4.05 (m, 4H), 3.93 – 3.53 (m, 6H), 2.27 (d, J = 1.3 Hz, 2H), 2.00 – 1.78 (m, 4H), 1.64 – 1.38 (m, 5H), 1.39 – 1.04 (m, 3H)	(ESI(+)) m/e 547 $(M+H)^+$
4		1-(2-methylpyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.92 (s, 1H), 7.88 (dd, J = 4.7, 1.4 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.07 (dd, J = 8.0, 4.7 Hz, 1H), 6.97 – 6.92 (m, 1H), 6.94 – 6.81 (m, 2H), 4.58 – 4.47 (m, 1H), 4.10 (t, J = 7.7 Hz, 2H), 3.98 (t, J = 6.8 Hz, 2H), 3.93 – 3.50 (m, 6H), 3.29 – 3.14 (m, 2H), 2.35 (s, 3H), 2.26 (d, J = 6.9 Hz, 2H), 2.05 – 1.79 (m, 3H), 1.66 – 1.32 (m, 5H), 1.31 – 1.06 (m, 2H)	(ESI(+)) m/e 493 $(M+H)^+$
5		1-(4-methylpyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.93 (s, 1H), 7.90 (d, J = 4.7 Hz, 1H), 7.76 (s, 1H), 7.55 – 7.48 (m, 2H), 7.03 – 6.89 (m, 3H), 4.58 – 4.47 (m, 1H), 4.20 – 3.95 (m, 4H), 3.95 – 3.53 (m, 5H), 3.26 – 3.15 (m, 4H), 2.26 (d, J = 6.9 Hz, 2H), 2.18 (s, 3H), 2.05 – 1.78 (m, 3H), 1.66 – 1.35 (m, 4H), 1.32 – 1.08 (m, 2H)	(ESI(+)) m/e 493 $(M+H)^+$
6		1-(4-fluoropyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.93 (bs, 1H), 7.95 (t, J = 11.6 Hz, 2H), 7.55 – 7.47 (m, 2H), 7.16 (dd, J = 12.7, 5.2 Hz, 1H), 6.97 – 6.90 (m, 2H), 4.59 – 4.48 (m, 1H), 4.29 – 4.00 (m, 5H), 3.93 – 3.41 (m, 5H), 2.30 – 2.23 (m, 2H), 1.99 – 1.78 (m, 4H), 1.66 – 1.39 (m, 5H), 1.40 – 1.00 (m, 3H)	(ESI(+)) m/e 497 $(M+H)^+$
7		N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.93 (bs, 1H), 7.95 (t, J = 11.6 Hz, 2H), 7.55 – 7.47 (m, 2H), 7.16 (dd, J = 12.7, 5.2 Hz, 1H), 6.97 – 6.90 (m, 2H), 4.59 – 4.48 (m, 1H), 4.29 – 4.00 (m, 5H), 3.93 – 3.41 (m, 5H), 2.30 – 2.23 (m, 2H), 1.99 – 1.78 (m, 4H), 1.66 – 1.39 (m, 5H), 1.40 – 1.00 (m,	(ESI(+)) m/e 547 $(M+H)^+$

		)-1-[4-(trifluoromethyl)pyridin-3-yl]azetidine-3-carboxamide	3H)	
31		N-(4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.94 (s, 1H), 7.97 – 7.70 (m, 2H), 7.55 – 7.47 (m, 2H), 7.18 (dd, J = 8.2, 4.6 Hz, 1H), 7.00 – 6.78 (m, 3H), 5.39 (s, 1H), 4.58 – 4.41 (m, 1H), 4.09 (t, J = 7.8 Hz, 2H), 3.95 (t, J = 6.7 Hz, 2H), 3.78 – 3.47 (m, 2H), 1.99 – 1.82 (m, 2H), 1.62 – 1.34 (m, 2H), 1.35 – 1.02 (m, 8H)	(ESI(+)) m/e 439 $(M+H)^+$
32		N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.94 (s, 1H), 7.94 (d, J = 4.7 Hz, 1H), 7.86 (d, J = 2.8 Hz, 1H), 7.55 – 7.47 (m, 2H), 7.24 – 7.04 (m, 1H), 7.02 – 6.80 (m, 3H), 4.59 – 4.48 (m, 1H), 4.09 (t, J = 7.8 Hz, 2H), 4.03 – 3.62 (m, 5H), 3.38 (dd, J = 13.6, 6.6 Hz, 1H), 2.80 – 2.64 (m, 1H), 2.01 – 1.78 (m, 2H), 1.64 – 1.36 (m, 3H), 1.38 – 1.15 (m, 1H), 1.15 – 0.86 (m, 4H), 0.81 (t, J = 7.3 Hz, 3H)	(ESI(+)) m/e 437 $(M+H)^+$
33		1-(pyridin-3-yl)-N-[4-({1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.94 (s, 1H), 7.98 – 7.82 (m, 2H), 7.55 – 7.48 (m, 2H), 7.20 (dd, J = 8.3, 4.6 Hz, 1H), 7.00 – 6.80 (m, 3H), 4.67 (t, J = 6.5 Hz, 1H), 4.53 (s, 1H), 4.10 (t, J = 7.8 Hz, 2H), 3.96 (t, J = 6.6 Hz, 2H), 3.89 – 3.58 (m, 4H), 3.46 – 3.08 (m, 4H), 2.12 – 1.68 (m, 5H), 1.66 – 1.38 (m, 2H)	(ESI(+)) m/e 451 $(M+H)^+$
34		N-{4-[(1-pentanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.39, 2.29 Hz, 1 H) 7.51 (d, J=9.16 Hz, 2 H) 6.96 (d, J=8.85 Hz, 2 H) 4.51 - 4.59 (m, 1 H) 4.25 (t, J=8.24 Hz, 2 H) 4.14 (dd, J=7.93, 5.80 Hz, 2 H) 3.80 - 3.90 (m, 1 H) 3.73 - 3.79 (m, 2 H) 3.31 - 3.41 (m, 1 H) 3.19 - 3.27 (m, 1 H) 2.29 - 2.36 (m, 2 H) 1.83 - 2.00 (m, 2 H) 1.53 - 1.62 (m, 1 H) 1.42 - 1.51 (m, 3 H) 1.24 - 1.35 (m, 2 H) 0.87 (t, 3 H)	(ESI(+)) m/e 437 $(M+H)^+$
35		N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.59 (dd, J=8.70, 1.98 Hz, 1 H) 7.52 (d, J=8.85 Hz, 2 H) 6.97 (d, J=8.85 Hz, 2 H) 4.51 - 4.62 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 5.80 Hz, 2 H) 3.79 - 4.01 (m, 2 H) 3.73 - 3.78 (m, 1 H) 3.46 - 3.54 (m, 1 H) 3.16 - 3.28 (m, 1 H) 1.89 (d, J=1.53 Hz, 2 H) 1.70 - 1.76 (m, 1 H) 1.53 (d, J=55.85 Hz, 2 H) 1.03 - 1.17 (m, 4 H) 0.89 - 0.97 (m, 1 H) 0.49 - 0.59 (m, 1 H)	(ESI(+)) m/e 435 $(M+H)^+$
36		N-[4-({1-	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12	(ESI(+))

		[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide	(d, J=5.19 Hz, 1 H) 8.04 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.54, 2.14 Hz, 1 H) 7.47 - 7.54 (m, 2 H) 6.93 - 6.99 (m, 2 H) 4.49 - 4.58 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.10 - 4.16 (m, J=8.09, 5.95 Hz, 2 H) 3.81 - 3.89 (m, 1 H) 3.73 - 3.79 (m, 2 H) 3.18 - 3.39 (m, 2 H) 2.27 - 2.36 (m, 1 H) 2.11 - 2.21 (m, 2 H) 1.73 - 1.99 (m, 4 H) 1.38 - 1.60 (m, 5 H) 1.34 (d, J=9.77 Hz, 1 H) 0.97 - 1.19 (m, 4 H)	m/e 489 $(M+H)^+$
37		N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.19 Hz, 1 H) 8.04 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.70, 5.34 Hz, 1 H) 7.59 (dd, J=8.70, 1.98 Hz, 1 H) 7.47 - 7.54 (m, 2 H) 6.93 - 6.99 (m, 2 H) 4.51 - 4.57 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.10 - 4.16 (m, J=8.09, 5.95 Hz, 2 H) 3.80 - 3.87 (m, J=17.70 Hz, 1 H) 3.74 - 3.79 (m, 2 H) 3.17 - 3.38 (m, 2 H) 2.27 - 2.36 (m, J=8.85, 6.71 Hz, 2 H) 1.83 - 1.99 (m, J=22.89 Hz, 2 H) 1.32 - 1.62 (m, 5 H) 0.87 (d, J=6.41 Hz, 6 H)	(ESI(+)) m/e 451 $(M+H)^+$
38		N-(4-{[1-(3-methylpentanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.19 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.54, 2.14 Hz, 1 H) 7.49 - 7.53 (m, 2 H) 6.93 - 6.97 (m, 2 H) 4.51 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.83 - 3.91 (m, 1 H) 3.73 - 3.79 (m, 2 H) 3.19 - 3.39 (m, 2 H) 2.27 - 2.34 (m, 1 H) 2.10 - 2.18 (m, 1 H) 1.84 - 1.98 (m, 2 H) 1.73 - 1.81 (m, 1 H) 1.42 - 1.59 (m, 2 H) 1.29 - 1.39 (m, 1 H) 1.11 - 1.21 (m, 1 H) 0.82 - 0.89 (m, 6 H)	(ESI(+)) m/e 451 $(M+H)^+$
39		N-(4-{[1-(3-ethoxypropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.85, 1.83 Hz, 1 H) 7.51 (d, J=9.16 Hz, 2 H) 6.92 - 6.98 (m, 2 H) 4.49 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 5.80 Hz, 2 H) 3.80 - 3.89 (m, 1 H) 3.74 - 3.79 (m, 2 H) 3.59 (t, J=6.56 Hz, 2 H) 3.42 (q, J=7.02 Hz, 2 H) 3.20 - 3.38 (m, 2 H) 2.55 - 2.63 (m, 2 H) 1.83 - 1.99 (m, 2 H) 1.41 - 1.63 (m, 2 H) 1.09 (t, J=7.02 Hz, 3 H)	(ESI(+)) m/e 453 $(M+H)^+$
40		N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.81 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.85, 1.83 Hz, 1 H) 7.49 - 7.53 (m, 2 H) 6.96 (d, J=9.16 Hz, 2 H) 4.53 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.12 - 4.18 (m, J=7.93, 6.10 Hz, 2 H) 3.87 - 3.93 (m, 1 H) 3.75 - 3.80 (m, 2 H) 3.28 - 3.38 (m, 2 H) 1.89 - 1.97 (m, 2 H) 1.60 (q, J=7.53 Hz, 2 H) 1.46 - 1.54 (m, 2 H) 1.16 (s, 6 H) 0.80 (t, J=7.48 Hz, 3 H)	(ESI(+)) m/e 451 $(M+H)^+$
41		N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.49 - 7.52 (m, 2 H) 6.92 - 6.99 (m, 2 H)	(ESI(+)) m/e 451 $(M+H)^+$

		yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	4.47 - 4.58 (m, 1 H) 4.22 - 4.29 (m, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.85 - 3.92 (m, 1 H) 3.74 - 3.80 (m, 2 H) 3.34 - 3.43 (m, 1 H) 3.20 - 3.27 (m, 1 H) 2.26 (s, 2 H) 1.82 - 2.01 (m, 2 H) 1.38 - 1.60 (m, 2 H) 0.99 (s, 9 H)	
42		N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.59 - 7.61 (m, 1 H) 7.49 - 7.54 (m, 2 H) 6.93 - 6.98 (m, 2 H) 4.51 - 4.61 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.85 - 3.92 (m, 2 H) 3.73 - 3.79 (m, 1 H) 3.29 - 3.38 (m, 2 H) 1.89 - 1.99 (m, 2 H) 1.45 - 1.56 (m, 2 H) 1.20 (s, 9 H)	(ESI(+)) m/e 437 $(M+H)^+$
43		N-{4-[(1-butanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.85, 1.83 Hz, 1 H) 7.49 - 7.53 (m, 2 H) 6.93 - 6.98 (m, 2 H) 4.49 - 4.60 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.82 - 3.90 (m, 1 H) 3.73 - 3.79 (m, 2 H) 3.20 - 3.37 (m, 2 H) 2.31 (t, J=7.17 Hz, 2 H) 1.82 - 1.98 (m, 2 H) 1.41 - 1.63 (m, 4 H) 0.89 (t, J=7.32 Hz, 3 H)	(ESI(+)) m/e 423 $(M+H)^+$
44		N-(4-{[1-(ethoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.54, 1.83 Hz, 1 H) 7.51 (d, J=9.16 Hz, 2 H) 6.96 (d, J=9.16 Hz, 2 H) 4.50 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.10 - 4.16 (m, 4 H) 3.80 - 3.87 (m, 1 H) 3.73 - 3.78 (m, 2 H) 3.47 (q, J=7.02 Hz, 2 H) 3.20 - 3.35 (m, 2 H) 1.86 - 1.98 (m, J=21.67 Hz, 2 H) 1.45 - 1.64 (m, 2 H) 1.13 (t, J=7.02 Hz, 3 H)	(ESI(+)) m/e 439 $(M+H)^+$
45		N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.47 - 7.55 (m, 2 H) 6.93 - 6.98 (m, 2 H) 4.51 - 4.57 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.83 - 3.90 (m, 1 H) 3.74 - 3.79 (m, 2 H) 3.19 - 3.37 (m, 2 H) 2.19 - 2.24 (m, 2 H) 1.82 - 2.03 (m, 3 H) 1.41 - 1.60 (m, 2 H) 0.90 (d, J=6.71 Hz, 6 H)	(ESI(+)) m/e 437 $(M+H)^+$
46		N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.49 - 7.54 (m, 2 H) 6.93 - 6.99 (m, 2 H) 4.52 - 4.60 (m, 1 H) 4.25 (t, J=8.24 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.84 (s, 1 H) 3.75 - 3.79 (m, 2 H) 3.18 - 3.42 (m, 2 H) 2.86 - 2.93 (m, 1 H) 1.84 - 1.99 (m, 2 H) 1.42 - 1.63 (m, 2 H) 1.00 (d, J=6.71 Hz, 6 H)	(ESI(+)) m/e 423 $(M+H)^+$
47		N-(4-{[1-(N-acetyl-L-leucyl)piperidin-4-yl]oxy}phenyl	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.81 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.85, 1.83 Hz, 1 H) 7.52 (d, J=8.85 Hz, 2 H) 6.95 - 6.99 (m, 2 H) 4.77 (dd, J=9.00, 3.81 Hz, 1 H) 4.53 - 4.62	(ESI(+)) m/e 508 $(M+H)^+$

		)-1-(pyridin-3-yl)azetidine-3-carboxamide	(m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.12 - 4.17 (m, 2 H) 3.92 (d, J=13.12 Hz, 1 H) 3.74 - 3.79 (m, 2 H) 3.31 - 3.47 (m, 2 H) 3.14 - 3.21 (m, 1 H) 1.92 - 2.01 (m, 1 H) 1.85 (s, 3 H) 1.28 - 1.63 (m, 5 H) 0.85 - 0.91 (m, 6 H)	
48		N-[4-({1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.19 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.54, 2.14 Hz, 1 H) 7.51 (d, J=9.16 Hz, 2 H) 6.93 - 6.99 (m, J=9.61, 9.61 Hz, 2 H) 4.51 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.09 - 4.18 (m, 4 H) 3.80 - 3.86 (m, 1 H) 3.74 - 3.77 (m, 1 H) 3.54 - 3.57 (m, 2 H) 3.47 (dd, J=5.65, 3.51 Hz, 2 H) 3.20 - 3.33 (m, 6 H) 1.87 - 1.96 (m, 2 H) 1.45 - 1.66 (m, 2 H)	(ESI(+)) m/e 469 $(M+H)^+$
49		N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.51 (d, J=8.85 Hz, 2 H) 6.94 - 6.97 (m, 2 H) 4.49 - 4.58 (m, 1 H) 4.25 (t, J=8.24 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.84 (dd, 1 H) 3.73 - 3.78 (m, 2 H) 3.33 - 3.40 (m, J=9.77 Hz, 1 H) 3.17 - 3.27 (m, 1 H) 2.58 - 2.63 (m, 1 H) 1.82 - 1.99 (m, 2 H) 1.09 - 1.73 (m, 12 H)	(ESI(+)) m/e 463 $(M+H)^+$
50		N-(4-{[1-(cyclohexylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.81 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.85, 1.83 Hz, 1 H) 7.48 - 7.53 (m, 2 H) 6.91 - 7.00 (m, 2 H) 4.51 - 4.57 (m, 1 H) 4.25 (t, J=8.24 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.84 (d, J=4.27 Hz, 1 H) 3.74 - 3.79 (m, 2 H) 3.31 - 3.38 (m, 1 H) 3.16 - 3.27 (m, 1 H) 2.18 - 2.23 (m, J=6.56, 2.90 Hz, 2 H) 1.83 - 1.97 (m, 2 H) 1.41 - 1.71 (m, 8 H) 1.06 - 1.27 (m, 3 H) 0.88 - 0.98 (m, 2 H)	(ESI(+)) m/e 477 $(M+H)^+$
51		1-(pyridin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.59 (dd, J=8.70, 1.98 Hz, 1 H) 7.49 - 7.54 (m, 2 H) 6.93 - 6.99 (m, 2 H) 4.52 - 4.60 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.81 - 3.89 (m, 1 H) 3.74 - 3.78 (m, 2 H) 3.25 - 3.39 (m, 2 H) 2.61 - 2.68 (m, 2 H) 2.43 - 2.51 (m, 2 H) 1.84 - 2.00 (m, 2 H) 1.44 - 1.65 (m, 2 H)	(ESI(+)) m/e 477 $(M+H)^+$
52		N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.51 (d, J=8.85 Hz, 2 H) 6.96 (d, J=8.85 Hz, 2 H) 4.51 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.09 - 4.18 (m, 2 H) 3.81 - 3.90 (m, 1 H) 3.75 - 3.79 (m, 2 H) 3.33 - 3.42 (m, 1 H) 3.20 - 3.29 (m, 1 H) 2.96 - 3.02 (m, 1 H) 1.46 - 1.98 (m, 12 H)	(ESI(+)) m/e 449 $(M+H)^+$
53		N-[4-({1-[(1-methylcyclohexyl)carbonyl]piperidin-4-	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.19 Hz, 1 H) 8.04 (d, J=2.44 Hz, 1 H) 7.79 (dd, J=8.54, 5.49 Hz, 1 H) 7.59 (dd, J=8.70, 1.98 Hz, 1 H) 7.49 - 7.53 (m, 2 H) 6.96 (d, J=8.85 Hz,	(ESI(+)) m/e 477 $(M+H)^+$

		yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide	2 H) 4.50 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.90 (dd, J=9.00, 5.95 Hz, 2 H) 3.74 - 3.78 (m, 1 H) 3.27 - 3.36 (m, 2 H) 1.85 - 1.99 (m, 4 H) 1.24 - 1.55 (m, 10 H) 1.18 (s, 3 H)	
54		N-(4-{[1-(furan-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.44 Hz, 1 H) 8.02 (s, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.71 - 7.73 (m, 1 H) 7.59 (dd, J=8.70, 2.29 Hz, 1 H) 7.52 (d, J=8.85 Hz, 2 H) 6.97 (d, J=8.85 Hz, 2 H) 6.67 (s, 1 H) 4.56 - 4.62 (m, 1 H) 4.25 (t, J=8.24 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.82 - 3.92 (m, 2 H) 3.73 - 3.77 (m, 1 H) 3.39 - 3.49 (m, 2 H) 1.91 - 2.00 (m, 2 H) 1.55 - 1.65 (m, 2 H)	(ESI(+)) m/e 447 $(M+H)^+$
55		1-(pyridin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.09 (d, J=4.58 Hz, 1 H) 8.02 (s, 1 H) 7.73 (dd, J=8.54, 5.49 Hz, 1 H) 7.48 - 7.54 (m, J=9.16 Hz, 3 H) 6.96 (d, J=8.85 Hz, 2 H) 4.57 (s, 1 H) 4.23 (t, J=8.24 Hz, 2 H) 4.09 - 4.14 (m, 2 H) 3.80 - 3.87 (m, 1 H) 3.72 - 3.78 (m, 2 H) 3.59 - 3.63 (m, 2 H) 3.26 - 3.39 (m, 2 H) 1.93 (s, 2 H) 1.51 (s, 2 H)	(ESI(+)) m/e 463 $(M+H)^+$
56		N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.19 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.81 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.49 - 7.53 (m, 2 H) 6.92 - 6.98 (m, 2 H) 4.50 - 4.58 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.79 - 3.85 (m, 1 H) 3.75 - 3.79 (m, 2 H) 3.19 - 3.40 (m, 2 H) 2.02 (s, 3 H) 1.83 - 1.99 (m, 2 H) 1.41 - 1.68 (m, 2 H)	(ESI(+)) m/e 395 $(M+H)^+$
57		N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.54, 2.44 Hz, 1 H) 7.51 (d, J=9.16 Hz, 2 H) 6.96 (d, J=9.16 Hz, 2 H) 4.51 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 4.10 (d, J=3.05 Hz, 2 H) 3.80 - 3.86 (m, 1 H) 3.74 - 3.77 (m, 1 H) 3.57 - 3.64 (m, 1 H) 3.18 - 3.34 (m, 5 H) 1.85 - 1.99 (m, 2 H) 1.44 - 1.64 (m, 2 H)	(ESI(+)) m/e 425 $(M+H)^+$
58		1-(pyridin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.11 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.75 Hz, 1 H) 7.76 - 7.78 (m, 1 H) 7.59 - 7.61 (m, 2 H) 7.52 (d, J=8.85 Hz, 2 H) 7.44 (d, J=4.88 Hz, 1 H) 7.22 (d, J=5.19 Hz, 1 H) 6.97 (d, J=9.16 Hz, 2 H) 4.56 - 4.62 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.12 - 4.16 (m, 2 H) 3.87 - 3.96 (m, 1 H) 3.72 - 3.79 (m, 2 H) 3.33 - 3.46 (m, 2 H) 1.90 - 2.01 (m, J=1.83 Hz, 2 H) 1.54 - 1.70 (m, 2 H)	(ESI(+)) m/e 463 $(M+H)^+$
59		N-[4-({1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.48 - 7.62 (m, 4 H) 6.93 - 6.99 (m, 3 H) 4.54 - 4.66 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H)	(ESI(+)) m/e 477 $(M+H)^+$

		yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide	3.72 - 3.85 (m, 3 H) 3.34 - 3.45 (m, 2 H) 2.20 (s, 3 H) 1.91 - 2.00 (m, J=9.77 Hz, 2 H) 1.53 - 1.64 (m, 2 H)	
60		N-(4-{[1-(morpholin-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.13 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.54, 2.14 Hz, 1 H) 7.53 (d, J=8.85 Hz, 2 H) 6.97 (d, J=9.16 Hz, 2 H) 4.54 - 4.64 (m, 1 H) 4.35 (s, 2 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.76 - 4.04 (m, 6 H) 3.52 - 3.60 (m, 1 H) 3.25 - 3.49 (m, 4 H) 3.08 - 3.22 (m, 2 H) 1.89 - 2.08 (m, 2 H) 1.50 - 1.77 (m, 2 H)	(ESI(+)) m/e 480 $(M+H)^+$
61		1-(pyridin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=1.83 Hz, 1 H) 7.79 (dd, J=8.85, 5.49 Hz, 1 H) 7.58 (dd, J=8.54, 2.14 Hz, 1 H) 7.52 (d, J=9.16 Hz, 2 H) 7.42 (d, J=3.66 Hz, 1 H) 7.18 - 7.22 (m, 1 H) 7.14 (dd, J=4.88, 3.66 Hz, 1 H) 6.99 (d, 2 H) 4.58 - 4.66 (m, 1 H) 4.25 (t, J=8.24 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.89 - 3.96 (m, 2 H) 3.74 - 3.80 (m, 1 H) 3.52 (m, 2 H) 1.95 - 2.04 (m, 2 H) 1.59 - 1.70 (m, 2 H)	(ESI(+)) m/e 463 $(M+H)^+$
62		N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.59 (dd, J=8.24, 2.14 Hz, 1 H) 7.52 (d, J=9.16 Hz, 2 H) 7.23 (d, J=3.36 Hz, 1 H) 6.98 (d, J=9.16 Hz, 2 H) 6.80 - 6.86 (m, 1 H) 4.56 - 4.65 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.12 - 4.17 (m, 2 H) 3.90 - 3.95 (m, 2 H) 3.74 - 3.79 (m, 1 H) 3.45 - 3.55 (m, 2 H) 2.47 (s, 3 H) 1.94 - 2.05 (m, 2 H) 1.58 - 1.67 (m, 2 H)	(ESI(+)) m/e 477 $(M+H)^+$
63		N-(4-{[1-(furan-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.78 - 7.83 (m, 2 H) 7.60 (dd, J=8.39, 2.29 Hz, 1 H) 7.52 (d, J=9.16 Hz, 2 H) 6.96 - 7.02 (m, 3 H) 6.63 (dd, J=3.36, 1.83 Hz, 1 H) 4.58 - 4.67 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 5.80 Hz, 2 H) 3.92 - 3.99 (m, 2 H) 3.75 - 3.80 (m, 1 H) 3.41 - 3.59 (m, 2 H) 1.95 - 2.04 (m, 2 H) 1.58 - 1.67 (m, 2 H)	(ESI(+)) m/e 447 $(M+H)^+$
64		N-[4-({1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.11 (s, 1 H) 8.04 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.70, 5.34 Hz, 1 H) 7.59 (dd, J=8.85, 1.83 Hz, 1 H) 7.52 (d, J=9.16 Hz, 2 H) 6.97 (d, J=9.16 Hz, 2 H) 6.88 (s, 1 H) 6.33 (dd, J=3.81, 1.68 Hz, 1 H) 6.01 - 6.05 (m, 1 H) 4.52 - 4.63 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.11 - 4.17 (m, 2 H) 3.90 - 3.96 (m, 2 H) 3.74 - 3.79 (m, 1 H) 3.66 (s, 3 H) 3.41 - 3.50 (m, 2 H) 1.91 - 2.04 (m, 2 H) 1.52 - 1.67 (m, 2 H)	(ESI(+)) m/e 460 $(M+H)^+$
65		N-{4-[(1-propanoylpiperidin-4-yl)oxy]phenyl	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.39, 2.29 Hz, 1 H) 7.51 (d, J=8.85 Hz, 2 H) 6.96 (d, 2 H)	(ESI(+)) m/e 409 $(M+H)^+$

		}-1-(pyridin-3-yl)azetidine-3-carboxamide	4.48 - 4.60 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.81 - 3.90 (m, 1 H) 3.72 - 3.80 (m, 2 H) 3.17 - 3.41 (m, 2 H) 2.34 (q, J=7.53 Hz, 2 H) 1.82 - 2.01 (m, 2 H) 1.35 - 1.63 (m, 2 H) 1.00 (t, J=7.48 Hz, 3 H)	
66		N-[4-({1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.55, 1.83 Hz, 1 H) 7.52 (d, J=8.85 Hz, 2 H) 6.96 (d, J=8.85 Hz, 2 H) 4.51 - 4.60 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 5.80 Hz, 2 H) 3.82 - 3.92 (m, 2 H) 3.74 - 3.78 (m, 1 H) 3.31 - 3.46 (m, 2 H) 1.85 - 1.96 (m, 2 H) 1.47 - 1.58 (m, J=7.32 Hz, 2 H) 1.23 (s, 3 H) 0.76 - 0.81 (m, 2 H) 0.52 - 0.56 (m, 2 H)	(ESI(+)) m/e 435 $(M+H)^+$
67		N-(4-{[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.19 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.39, 2.29 Hz, 1 H) 7.53 (d, J=9.16 Hz, 2 H) 6.99 (d, J=8.85 Hz, 2 H) 4.56 - 4.64 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 5.80 Hz, 2 H) 3.72 - 3.82 (m, 3 H) 3.67 - 3.70 (m, 2 H) 3.19 - 3.54 (m, J=87.28 Hz, 4 H) 2.92 (d, J=10.68 Hz, 6 H) 1.97 - 2.16 (m, 2 H) 1.66 - 1.85 (m, 2 H)	N/A
68		1-(pyridin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.98 - 8.02 (m, 2 H) 7.81 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.39, 2.29 Hz, 1 H) 7.53 (d, 2 H) 6.99 (d, 2 H) 4.55 - 4.69 (m, 2 H) 4.25 (t, J=8.39 Hz, 2 H) 4.15 (dd, J=7.93, 5.80 Hz, 2 H) 3.94 - 4.08 (m, J=41.20, 9.46 Hz, 2 H) 3.74 - 3.79 (m, 1 H) 3.49 - 3.58 (m, 1 H) 1.98 - 2.08 (m, 2 H) 1.67 (s, 2 H)	(ESI(+)) m/e 464 $(M+H)^+$
69		N-(4-{[1-(cyclopentylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.77 - 7.82 (m, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.51 (d, J=8.85 Hz, 2 H) 6.96 (d, J=8.85 Hz, 2 H) 4.50 - 4.58 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.11 - 4.15 (m, 2 H) 3.81 - 3.90 (m, 1 H) 3.73 - 3.79 (m, 2 H) 3.18 - 3.40 (m, 2 H) 2.35 (dd, J=7.17, 2.59 Hz, 2 H) 2.05 - 2.16 (m, 1 H) 1.83 - 1.98 (m, 2 H) 1.68 - 1.77 (m, 2 H) 1.42 - 1.63 (m, 6 H) 1.05 - 1.19 (m, 2 H)	(ESI(+)) m/e 463 $(M+H)^+$
70		N-(4-{[1-(2,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 2.29 Hz, 1 H) 7.50 - 7.53 (m, 2 H) 6.96 (d, J=9.16 Hz, 2 H) 4.50 - 4.61 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.92 - 3.97 (m, 1 H) 3.74 - 3.87 (m, 3 H) 3.20 - 3.43 (m, 2 H) 2.55 - 2.61 (m, 1 H) 1.38 - 2.03 (m, 5 H) 0.95 (d, J=6.71 Hz, 2 H) 0.81 - 0.88 (m, 6 H)	(ESI(+)) m/e 451 $(M+H)^+$

Example 8

tert-butyl 4-[4-({[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate

The title compound was prepared as described in Example 1A-C, substituting (S)-1-(benzyloxycarbonyl)pyrrolidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid in Example 1A. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.96 (s, 1H), 7.95 (d, J = 2.9 Hz, 1H), 7.85 (dd, J = 4.6, 1.3 Hz, 1H), 7.54 – 7.48 (m, 2H), 7.15 (dd, J = 8.4, 4.6 Hz, 1H), 6.98 – 6.86 (m, 3H), 4.53 – 4.41 (m, 1H), 3.73 – 3.46 (m, 3H), 3.45 – 3.30 (m, 2H), 3.24 (dd, J = 17.5, 10.0 Hz, 2H), 3.12 (dd, J = 24.9, 15.2 Hz, 2H), 2.35 – 2.10 (m, 2H), 2.01 – 1.78 (m, 2H), 1.68 – 1.42 (m, 2H), 1.40 (s, 9H); MS (ESI(+)) m/e 467 $(M+H)^+$.

Example 9

tert-butyl 4-[4-({[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate

The title compound was prepared as described in Example 1A-C, substituting (R)-1-(benzyloxycarbonyl)pyrrolidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid in Example 1A. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.97 (s, 1H), 7.95 (d, J = 2.9 Hz, 1H), 7.85 (dd, J = 4.6, 1.3 Hz, 1H), 7.54 – 7.48 (m, 2H), 7.16 (dd, J = 8.4, 4.6 Hz, 1H), 6.98 – 6.86 (m, 3H), 4.53 – 4.41 (m, 1H), 3.75 – 3.45 (m, 3H), 3.45 – 3.34 (m, 3H), 3.25 (dd, J = 8.8, 6.2 Hz, 1H), 3.23 – 3.09 (m, 2H), 2.34 – 2.07 (m, 2H), 1.95 – 1.75 (m, 2H), 1.59 – 1.41 (m, 2H), 1.40 (s, 9H); MS (ESI(+)) m/e 467 $(M+H)^+$.

Example 10

1-(pyridin-3-yl)-N-(4-{1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide

Example 10A

tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(4-aminophenyl)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate.

Example 10B

tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1B, substituting tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 10C

tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1C, substituting tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 10D

N-(4-(piperidin-4-yl)phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 10E

1-(pyridin-3-yl)-N-(4-{1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and (S)-tetrahydrofuran-2-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.01 (s, 1H), 7.93 (dd, J = 4.6, 1.3 Hz, 1H), 7.85 (d, J = 2.8 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.22 – 7.14 (m, 3H), 6.86 (ddd, J = 8.2, 2.9, 1.4 Hz, 1H), 4.68 (dd, J = 7.5, 5.7 Hz, 1H), 4.53 – 4.43 (m, 1H), 4.10 (d, J = 8.0 Hz, 2H), 3.95 (d, J = 13.3 Hz, 2H), 3.89 – 3.64 (m, 3H), 3.15 – 3.00 (m, 1H), 2.82 – 2.59 (m, 2H), 2.19 – 1.68 (m, 6H), 1.61 – 1.29 (m, 3H); MS (ESI(+)) m/e 435 $(M+H)^+$.

Table 2.

The following Examples were prepared essentially as described in Example 10, substituting the appropriate bromopyridine in Example 10C and the appropriate carboxylic acid in Example 10E. Some products were purified by flash chromatography while others were purified by reverse-phase HPLC. Accordingly, some Examples were isolated as trifluoroacetic acid salts.

Ex		Name	^{1}H NMR	MS
2		1-(2-cyanopyridin-3-yl)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.04 (s, 1H), 8.12 – 7.94 (m, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.48 – 7.37 (m, 1H), 7.21 – 7.16 (m, 2H), 7.14 (dt, J = 7.7, 1.9 Hz, 1H), 5.36 (s, 1H), 4.97 – 4.53 (m, 2H), 4.43 – 4.31 (m, 2H), 4.30 – 4.13 (m, 2H), 3.78 – 3.56 (m, 1H), 2.85 – 2.65 (m, 2H), 1.81 – 1.63 (m, 2H), 1.59 – 1.42 (m, 2H), 1.33 (s, 6H)	(ESI(+)) m/e 448 $(M+H)^+$
20		N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.01 (s, 1H), 7.93 (dd, J = 4.6, 1.3 Hz, 1H), 7.85 (d, J = 2.8 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.26 – 7.09 (m, 3H), 6.86 (ddd, J = 8.2, 2.9, 1.4 Hz, 1H), 5.37 (s, 1H), 4.77 (bs, 1H), 4.09 (t, J = 7.8 Hz, 2H), 3.95 (t, J = 6.6 Hz, 2H), 3.77 – 3.55 (m, 1H), 3.18 –	(ESI(+)) m/e 423 $(M+H)^+$

		yl)azetidine-3-carboxamide	2.62 (m, 2H), 1.81 – 1.71 (m, 2H), 1.67 – 1.35 (m, 2H), 1.33 (s, 6H), 1.30 – 1.00 (m, 1H)	
22		N-(4-{1-[(2S)-2-methylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.01 (s, 1H), 7.93 (dd, J = 4.6, 1.4 Hz, 1H), 7.86 (d, J = 2.8 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.25 – 7.09 (m, 3H), 6.90 – 6.82 (m, 1H), 4.63 – 4.52 (m, 1H), 4.18 – 3.87 (m, 5H), 3.78 – 3.63 (m, 1H), 3.16 – 2.99 (m, 1H), 2.81 – 2.67 (m, 2H), 2.59 (d, J = 12.4 Hz, 1H), 1.88 – 1.67 (m, 2H), 1.68 – 1.07 (m, 4H), 1.05 – 0.94 (m, 3H), 0.91 – 0.72 (m, 3H)	(ESI(+)) m/e 421 $(M+H)^+$
25		1-(pyridin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.01 (s, 1H), 7.93 (dd, J = 4.6, 1.3 Hz, 1H), 7.85 (d, J = 2.8 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.22 – 7.14 (m, 3H), 6.86 (ddd, J = 8.2, 2.8, 1.4 Hz, 1H), 4.60 – 4.49 (m, 1H), 4.09 (t, J = 7.8 Hz, 2H), 3.97 (dd, J = 16.6, 10.2 Hz, 2H), 3.88 – 3.62 (m, 3H), 3.14 – 3.00 (m, 1H), 2.77 – 2.65 (m, 1H), 2.57 (t, J = 11.1 Hz, 1H), 2.27 (d, J = 6.8 Hz, 2H), 1.91 (dd, J = 9.4, 5.6 Hz, 1H), 1.74 (d, J = 11.3 Hz, 3H), 1.59 (d, J = 12.9 Hz, 2H), 1.43 (dd, J = 31.3, 12.2 Hz, 3H), 1.20 (dd, J = 24.5, 12.0 Hz, 3H)	(ESI(+)) m/e 463 $(M+H)^+$
26		N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.01 (s, 1H), 7.93 (dd, J = 4.7, 1.3 Hz, 1H), 7.86 (d, J = 2.7 Hz, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.48 – 7.36 (m, 5H), 7.27 – 7.11 (m, 3H), 6.86 (ddd, J = 8.3, 2.8, 1.3 Hz, 1H), 4.62 (s, 1H), 4.13 – 4.01 (m, 2H), 3.97 (dd, J = 12.1, 5.8 Hz, 2H), 3.71 (ddd, J = 14.3, 8.1, 6.1 Hz, 2H), 3.13 (s, 1H), 2.76 (t, J = 11.7 Hz, 2H), 1.85 (d, J = 32.6 Hz, 2H), 1.66 – 1.40 (m, 2H)	(ESI(+)) m/e 441 $(M+H)^+$
29		N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.00 (s, 1H), 7.88 (dd, J = 4.7, 1.4 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.22 – 7.14 (m, 2H), 7.07 (dd, J = 8.0, 4.7 Hz, 1H), 6.85 (dd, J = 8.1, 1.4 Hz, 1H), 4.60 – 4.49 (m, 1H), 4.15 – 3.85 (m, 4H), 3.68 – 3.53 (m, 1H), 3.21 – 3.02 (m, 1H), 2.97 – 2.61 (m, 2H), 2.35 (s, 3H), 2.32 – 1.66 (m, 3H), 1.60 – 1.14 (m, 3H), 1.12 – 0.92 (m, 6H)	(ESI(+)) m/e 421 $(M+H)^+$
30		N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.01 (s, 1H), 8.11 – 7.82 (m, 2H), 7.80 – 7.31 (m, 2H), 7.33 – 7.07 (m, 2H), 6.86 (ddd, J = 8.3, 2.9, 1.4 Hz, 1H), 4.61 – 4.49 (m, 1H), 4.16 – 3.87 (m, 4H), 3.77 – 3.64 (m, 1H), 3.20 – 2.99 (m, 1H), 2.89 (p, J = 6.7 Hz, 1H), 2.80 – 2.61 (m, 1H), 2.64 – 2.47 (m, 1H), 1.89 – 1.60 (m, 2H), 1.61 – 1.30 (m, 2H), 1.08 (d, J = 6.8 Hz, 2H), 1.05 – 0.97 (m, 6H)	(ESI(+)) m/e 407 $(M+H)^+$
71		N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.00 (s, 1H), 7.88 (dd, J = 4.7, 1.4 Hz, 1H), 7.57 – 7.50 (m, 2H), 7.21 – 7.14 (m, 2H), 7.07 (dd, J = 8.0, 4.6 Hz, 1H), 6.85 (dd, J = 8.1, 1.4 Hz, 1H), 5.37 (s, 1H), 4.65 (bs, 1H), 4.10 (t, J = 7.7 Hz, 2H), 3.97 (t, J = 6.8 Hz, 2H), 3.70 – 3.56 (m, 1H),	(ESI(+)) m/e 437 $(M+H)^+$

		yl)azetidine-3-carboxamide	3.05 – 2.63 (m, 2H), 2.35 (s, 3H), 1.81 – 1.71 (m, 2H), 1.66 – 1.36 (m, 3H), 1.33 (s, 6H), 1.28 – 1.13 (m, 1H)	
72		N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.99 (s, 1H), 7.90 (d, J = 4.7 Hz, 1H), 7.76 (s, 1H), 7.57 – 7.50 (m, 2H), 7.21 – 7.14 (m, 2H), 7.00 (d, J = 4.7 Hz, 1H), 5.35 (s, 1H), 4.71 (bs, 2H), 4.15 (t, J = 7.7 Hz, 2H), 4.05 (t, J = 6.8 Hz, 2H), 3.72 – 3.58 (m, 1H), 3.22 – 2.63 (m, 1H), 2.18 (s, 3H), 1.82 – 1.72 (m, 2H), 1.62 – 1.36 (m, 2H), 1.33 (s, 6H), 1.20 (d, J = 18.3 Hz, 1H), 0.89 – 0.72 (m, 1H)	(ESI(+)) m/e 437 $(M+H)^+$
73		N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methoxypyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.94 (s, 1H), 7.56 – 7.49 (m, 3H), 7.21 – 7.13 (m, 2H), 6.84 (dd, J = 7.5, 4.9 Hz, 1H), 6.72 (dd, J = 7.5, 1.6 Hz, 1H), 5.35 (s, 1H), 4.72 (bs, 2H), 4.07 (t, J = 7.9 Hz, 2H), 3.95 (d, J = 6.9 Hz, 2H), 3.83 (s, 3H), 3.66 – 3.52 (m, 1H), 2.73 (t, J = 11.9 Hz, 2H), 1.82 – 1.71 (m, 2H), 1.59 – 1.36 (m, 2H), 1.33 (s, 6H)	(ESI(+)) m/e 453 $(M+H)^+$
96		N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methoxypyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.94 (s, 1H), 7.93 (d, J = 5.3 Hz, 1H), 7.63 (s, 1H), 7.56 – 7.49 (m, 2H), 7.21 – 7.13 (m, 2H), 6.88 (d, J = 5.4 Hz, 1H), 5.35 (s, 1H), 4.71 (bs, 1H), 4.09 (t, J = 7.9 Hz, 2H), 3.96 (dd, J = 12.1, 4.8 Hz, 2H), 3.79 (s, 3H), 3.71 – 3.54 (m, 2H), 2.73 (t, J = 11.8 Hz, 1H), 1.76 (d, J = 11.4 Hz, 3H), 1.51 (s, 3H), 1.33 (s, 6H)	(ESI(+)) m/e 453 $(M+H)^+$
97		1-(4-cyanopyridin-3-yl)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.04 (s, 1H), 8.09 (s, 1H), 7.96 (d, J = 5.0 Hz, 1H), 7.54 (d, J = 8.6 Hz, 2H), 7.46 (dd, J = 5.1, 0.5 Hz, 1H), 7.18 (d, J = 8.6 Hz, 2H), 5.36 (s, 1H), 4.74 (s, 1H), 4.43 (t, J = 8.3 Hz, 2H), 4.31 (dd, J = 8.0, 5.8 Hz, 2H), 3.79 – 3.66 (m, 1H), 2.74 (dd, J = 13.8, 10.3 Hz, 2H), 1.81 – 1.72 (m, 3H), 1.65 – 1.45 (m, 3H), 1.33 (s, 6H)	(ESI(+)) m/e 448 $(M+H)^+$
98		N-[4-(1-pentanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 421 $(M+H)^+$
99		N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 435 $(M+H)^+$
100		N-(4-{1-[(1S,4R)-bicyclo[2.2.1]hept-2-		(ESI(+)) m/e 473 $(M+H)^+$

		ylacetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide		
101		N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 447 $(M+H)^+$
102		N-(4-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 419 $(M+H)^+$
103		N-{4-[1-(morpholin-4-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 464 $(M+H)^+$
104		N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 431 $(M+H)^+$
105		1-(pyridin-3-yl)-N-{4-[1-(pyrrolidin-1-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		(ESI(+)) m/e 474 $(M+H)^+$
106		N-{4-[1-(5-oxo−D-prolyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 448 $(M+H)^+$
107		N-{4-[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-		(ESI(+)) m/e 436 $(M+H)^+$

		carboxamide		
108		1-(pyridin-3-yl)-N-{4-[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		(ESI(+)) m/e 448 $(M+H)^+$
109		1-(pyridin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		(ESI(+)) m/e 447 $(M+H)^+$
110		N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 419 $(M+H)^+$
111		N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 461 $(M+H)^+$
112		1-(pyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		(ESI(+)) m/e 461 $(M+H)^+$
113		N-(4-{1-[(4-methylpiperazin-1-yl)acetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 477 $(M+H)^+$
114		N-{4-[1-(5-oxo-L-prolyl)piperidin-4-yl]phenyl}-1-(pyridin-3-		(ESI(+)) m/e 448 $(M+H)^+$

		yl)azetidine-3-carboxamide		
115		N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 437 $(M+H)^+$
116		N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 435 $(M+H)^+$
117		N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 461 $(M+H)^+$
118		N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 379 $(M+H)^+$
119		N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 461 $(M+H)^+$
120		N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 492 $(M+H)^+$
121		N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 393 $(M+H)^+$
122		1-(pyridin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidi		(ESI(+)) m/e 447 $(M+H)^+$

		ne-3-carboxamide		
123		N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 453 $(M+H)^+$
124		N-(4-{1-[3-(morpholin-4-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 478 $(M+H)^+$
125		N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 421 $(M+H)^+$
126		N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 461 $(M+H)^+$
127		1-(pyridin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		(ESI(+)) m/e 447 $(M+H)^+$
128		N-(4-{1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 444 $(M+H)^+$
129		N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-		(ESI(+)) m/e 431 $(M+H)^+$

		yl)azetidine-3-carboxamide		
130		N-(4-{1-[3-(piperidin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 476 $(M+H)^+$
131		N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 423 $(M+H)^+$
132		N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 435 $(M+H)^+$
133		N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 435 $(M+H)^+$
134		N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 407 $(M+H)^+$
135		N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 409 $(M+H)^+$
136		N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 447 $(M+H)^+$
137		N-{4-[1-(3-methylbutanoyl)piperidin-4-		(ESI(+)) m/e 421 $(M+H)^+$

		yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		
138		N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 433 $(M+H)^+$
139		N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 435 $(M+H)^+$
149		N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 455 $(M+H)^+$
150		N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 473 $(M+H)^+$
151		N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 489 $(M+H)^+$
152		N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 473 $(M+H)^+$
153		N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 489 $(M+H)^+$
154		N-{4-[1-(3,5-		(ESI(+))

		dichlorobenzoyl) piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		m/e 523 $(M+H)^+$
155		N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 473 $(M+H)^+$
156		N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 489 $(M+H)^+$
157		1-(2-methylpyridin-3-yl)-N-(4-{1-[4-(trifluoromethyl) benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide		(ESI(+)) m/e 523 $(M+H)^+$
158		1-(2-methylpyridin-3-yl)-N-{4-[1-(pyridazin-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		(ESI(+)) m/e 457 $(M+H)^+$
159		1-(2-methylpyridin-3-yl)-N-[4-(1-pentanoylpiperidin-4-yl)phenyl]azetidine-3-carboxamide		(ESI(+)) m/e 435 $(M+H)^+$
160		N-{4-[1-(3-methylpentanoyl) piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 449 $(M+H)^+$
161		N-(4-{1-		(ESI(+))

		[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		m/e 487 $(M+H)^+$
162		N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 461 $(M+H)^+$
163		N-(4-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 433 $(M+H)^+$
164		1-(2-methylpyridin-3-yl)-N-{4-[1-(morpholin-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		(ESI(+)) m/e 478 $(M+H)^+$
165		N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 445 $(M+H)^+$
166		1-(2-methylpyridin-3-yl)-N-{4-[1-(pyrrolidin-1-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		(ESI(+)) m/e 462 $(M+H)^+$
167		1-(2-methylpyridin-3-yl)-N-{4-[1-(5-oxo−D-prolyl)piperidin-		(ESI(+)) m/e 462 $(M+H)^+$

		4-yl]phenyl}azetidine-3-carboxamide		
168		N-{4-[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 450 $(M+H)^+$
169		1-(2-methylpyridin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		(ESI(+)) m/e 461 $(M+H)^+$
170		N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 433 $(M+H)^+$
171		1-(2-methylpyridin-3-yl)-N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide		(ESI(+)) m/e 475 $(M+H)^+$
172		1-(2-methylpyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		(ESI(+)) m/e 475 $(M+H)^+$
173		N-(4-{1-[(4-methylpiperazin-1-yl)acetyl]piperidin-4-yl}phenyl)-1-(2-		(ESI(+)) m/e 491 $(M+H)^+$

		methylpyridin-3-yl)azetidine-3-carboxamide		
174		1-(2-methylpyridin-3-yl)-N-{4-[1-(5-oxo-L-prolyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		(ESI(+)) m/e 462 $(M+H)^+$
175		N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 451 $(M+H)^+$
176		N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 449 $(M+H)^+$
177		N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 475 $(M+H)^+$
178		N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 393 $(M+H)^+$
179		N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 475 $(M+H)^+$
180		N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-		(ESI(+)) m/e 506 $(M+H)^+$

		yl)azetidine-3-carboxamide		
181		1-(2-methylpyridin-3-yl)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]azetidine-3-carboxamide		(ESI(+)) m/e 407 $(M+H)^+$
182		1-(2-methylpyridin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		(ESI(+)) m/e 461 $(M+H)^+$
183		N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 467 $(M+H)^+$
184		1-(2-methylpyridin-3-yl)-N-(4-{1-[3-(morpholin-4-yl)propanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide		(ESI(+)) m/e 492 $(M+H)^+$
185		N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 435 $(M+H)^+$
186		1-(2-methylpyridin-3-yl)-N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide		(ESI(+)) m/e 475 $(M+H)^+$
187		1-(2-methylpyridin-3-		(ESI(+)) m/e 461

		yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide		$(M+H)^+$
188		1-(2-methylpyridin-3-yl)-N-(4-{1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide		(ESI(+)) m/e 458 $(M+H)^+$
189		N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 445 $(M+H)^+$
190		1-(2-methylpyridin-3-yl)-N-(4-{1-[3-(piperidin-1-yl)propanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide		(ESI(+)) m/e 490 $(M+H)^+$
191		N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 437 $(M+H)^+$
192		N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 449 $(M+H)^+$
193		N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 449 $(M+H)^+$

194		N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 421 $(M+H)^+$
195		N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 423 $(M+H)^+$
196		N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 461 $(M+H)^+$
197		N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 435 $(M+H)^+$
198		N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 449 $(M+H)^+$

Example 11

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1D-E, substituting tert-butyl 4-[4-({[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate in Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.98 (s, 1H), 7.99 (d, J = 2.9 Hz, 1H), 7.91 (d, J = 4.8 Hz, 1H), 7.50 (s, 2H), 7.33 (dd, J = 8.5, 4.8 Hz, 1H), 7.16 – 7.09 (m, 1H), 6.97 – 6.89 (m, 2H), 4.58 – 4.47 (m, 1H), 3.95 – 3.65 (m, 4H), 3.56 (d, J = 8.6 Hz, 1H), 3.50 – 3.32 (m, 6H), 2.36 – 2.11 (m, 4H), 2.01 – 1.79 (m, 3H), 1.66 – 1.38 (m, 4H), 1.32 – 1.08 (m, 3H); MS (ESI(+)) m/e 493 $(M+H)^+$.

Table 3.

The following Examples were prepared essentially as described in Example 1D-E, substituting tert-butyl 4-[4-({[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate in Example 1D and the appropriate carboxylic acid for 2-(tetrahydro-2H-pyran-4-yl)acetic acid in Example 1E. Some products were purified by flash chromatography while others were purified by reverse-phase HPLC. Accordingly, some Examples were isolated as trifluoroacetic acid salts.

Ex		Name	^{1}H NMR	MS
12		(3S)-N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.97 (s, 1H), 7.96 (d, J = 2.9 Hz, 1H), 7.86 (dd, J = 4.6, 1.3 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.19 (dd, J = 8.4, 4.6 Hz, 1H), 6.99 – 6.90 (m, 3H), 4.59 – 4.48 (m, 1H), 4.03 – 3.67 (m, 3H), 3.54 (d, J = 8.6 Hz, 1H), 3.47 – 3.38 (m, 2H), 3.35 (d, J = 7.4 Hz, 2H), 3.28 – 3.18 (m, 1H), 2.95 – 2.82 (m, 1H), 2.38 – 2.03 (m, 2H), 2.00 – 1.80 (m, 2H), 1.64 – 1.37 (m, 2H), 1.00 (d, J = 6.7 Hz, 6H)	(ESI(+)) m/e 437 $(M+H)^+$
13		(3S)-1-(pyridin-3-yl)-N-[4-({1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]pyrrolidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.97 (s, 1H), 7.97 (d, J = 2.8 Hz, 1H), 7.88 (d, J = 5.1 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.33 – 7.19 (m, 1H), 7.05 – 6.88 (m, 3H), 4.67 (t, J = 6.5 Hz, 1H), 4.57 – 4.50 (m, 1H), 3.94 – 3.67 (m, 4H), 3.55 (d, J = 8.6 Hz, 1H), 3.47 – 3.38 (m, 4H), 2.38 – 2.12 (m, 2H), 2.07 – 1.74 (m, 7H), 1.65 – 1.00 (m, 3H)	(ESI(+)) m/e 465 $(M+H)^+$
14		(3S)-1-(pyridin-3-yl)-N-[4-({1-[(2R)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]pyrrolidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.97 (s, 1H), 7.96 (d, J = 2.9 Hz, 1H), 7.87 (dd, J = 4.6, 1.2 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.21 (dd, J = 8.4, 4.6 Hz, 1H), 7.02 – 6.93 (m, 2H), 6.92 (s, 1H), 4.67 (t, J = 6.6 Hz, 1H), 4.57 – 4.50 (m, 1H), 3.94 – 3.62 (m, 4H), 3.54 (d, J = 8.6 Hz, 1H), 3.44 (d, J = 6.7 Hz, 2H), 3.41 (d, J = 5.4 Hz, 2H), 3.23 (d, J = 7.8 Hz, 1H), 2.36 – 2.07 (m, 3H), 2.09 – 1.76 (m, 6H), 1.65 – 1.39 (m, 2H)	(ESI(+)) m/e 465 $(M+H)^+$
15		(3S)-1-(pyridin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.97 (s, 1H), 7.97 (d, J = 2.9 Hz, 1H), 7.88 (dd, J = 4.7, 1.2 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.25 (dd, J = 8.4, 4.7 Hz, 1H), 7.02 (dd, J = 8.5, 2.8 Hz, 1H), 6.97 – 6.90 (m, 2H), 4.60 – 4.48 (m, 1H), 3.98 – 3.61 (m, 7H), 3.55 (d, J = 8.6 Hz, 1H), 3.45 (d, J = 6.9 Hz, 2H), 3.44 – 3.39 (m, 2H), 3.38 – 3.32 (m, 2H), 2.38 – 2.09 (m, 2H), 2.10 – 1.81 (m, 4H), 1.65 – 1.40 (m, 2H)	(ESI(+)) m/e 465 $(M+H)^+$
16		(3S)-N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.96 (s, 1H), 7.99 – 7.93 (m, 1H), 7.85 (dd, J = 4.6, 1.3 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.16 (dd, J = 8.4, 4.5 Hz, 1H), 6.98 – 6.87 (m, 3H), 4.59 – 4.47 (m, 1H), 3.92 – 3.80 (m, 1H), 3.73 – 3.61 (m, 1H),	(ESI(+)) m/e 449 $(M+H)^+$

		yl)pyrrolidine-3-carboxamide	3.54 (d, J = 8.6 Hz, 1H), 3.47 – 3.37 (m, 2H), 3.26 – 3.07 (m, 3H), 2.27 (d, J = 6.8 Hz, 3H), 2.23 – 2.12 (m, 1H), 1.97 – 1.79 (m, 2H), 1.62 – 1.32 (m, 2H), 1.04 – 0.83 (m, 1H), 0.49 – 0.36 (m, 2H), 0.19 – 0.07 (m, 2H)	
17		(3S)-N-(4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.96 (s, 1H), 7.96 (d, J = 3.1 Hz, 1H), 7.87 (d, J = 4.7 Hz, 1H), 7.57 – 7.39 (m, 2H), 7.21 (dd, J = 8.4, 4.6 Hz, 1H), 7.03 – 6.88 (m, 3H), 5.38 (s, 1H), 4.59 – 3.79 (m, 3H), 3.65 – 3.38 (m, 4H), 2.35 – 2.10 (m, 2H), 1.99 – 1.84 (m, 2H), 1.63 – 1.34 (m, 3H), 1.35 – 1.19 (m, 7H)	(ESI(+)) m/e 453 $(M+H)^+$
18		(3S)-1-(pyridin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.96 (s, 1H), 7.95 (d, J = 2.9 Hz, 1H), 7.85 (dd, J = 4.6, 1.3 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.16 (dd, J = 8.4, 4.5 Hz, 1H), 6.98 – 6.88 (m, 3H), 4.55 (dq, J = 7.7, 3.8 Hz, 1H), 3.83 (ddd, J = 13.2, 6.8, 3.9 Hz, 1H), 3.74 – 3.49 (m, 5H), 3.48 – 3.38 (m, 2H), 2.38 – 2.06 (m, 3H), 2.02 – 1.80 (m, 2H), 1.71 – 1.36 (m, 3H)	(ESI(+)) m/e 477 $(M+H)^+$
19		(3S)-N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)pyrrolidine-3-carboxamide	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.96 (s, 1H), 7.95 (d, J = 2.9 Hz, 1H), 7.85 (d, J = 4.6 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.16 (dd, J = 8.4, 4.5 Hz, 1H), 6.98 – 6.88 (m, 3H), 4.60 – 4.48 (m, 1H), 4.03 – 3.69 (m, 2H), 3.54 (d, J = 8.6 Hz, 1H), 3.47 – 3.37 (m, 2H), 3.33 (d, J = 4.6 Hz, 1H), 3.27 – 3.17 (m, 1H), 2.72 (h, J = 6.7 Hz, 1H), 2.35 – 2.01 (m, 2H), 2.02 – 1.79 (m, 2H), 1.65 – 1.10 (m, 5H), 0.98 (d, J = 6.7 Hz, 3H), 0.81 (t, J = 7.4 Hz, 3H)	(ESI(+)) m/e 451 $(M+H)^+$

Example 21

N-[1-(pyridin-3-yl)azetidin-3-yl]-4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}benzamide

Example 21A

tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidin-3-ylcarbamoyl)phenoxy)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting benzyl 3-aminoazetidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 4-(1-(tert-butoxycarbonyl)piperidin-4-yloxy)benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 21B

benzyl 3-(4-(piperidin-4-yloxy)benzamido)azetidine-1-carboxylate

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidin-3-ylcarbamoyl)phenoxy)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 21C

benzyl 3-(4-(1-(2-(tetrahydro-2H-pyran-4-yl)acetyl)piperidin-4-yloxy)benzamido)azetidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting benzyl 3-(4-(piperidin-4-yloxy)benzamido)azetidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-(tetrahydro-2H-pyran-4-yl)acetic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 21D

N-(azetidin-3-yl)-4-(1-(2-(tetrahydro-2H-pyran-4-yl)acetyl)piperidin-4-yloxy)benzamide

The title compound was prepared as described in Example 1B, substituting benzyl 3-(4-(1-(2-(tetrahydro-2H-pyran-4-yl)acetyl)piperidin-4-yloxy)benzamido)azetidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 21E

N-[1-(pyridin-3-yl)azetidin-3-yl]-4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}benzamide

The title compound was prepared as described in Example 1C, substituting N-(azetidin-3-yl)-4-(1-(2-(tetrahydro-2H-pyran-4-yl)acetyl)piperidin-4-yloxy)benzamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.83 (d, J = 6.8 Hz, 1H), 7.93 (d, J = 4.0 Hz, 1H), 7.85 (d, J = 8.4 Hz, 3H), 7.27 (s, 2H), 7.26 – 7.11 (m, 1H), 7.05 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.1 Hz, 1H), 4.86 (d, J = 6.9 Hz, 1H), 4.71 (s, 1H), 4.28 – 4.19 (m, 2H), 3.93 – 3.64 (m, 6H), 2.30 – 2.23 (m, 2H), 2.05 – 1.67 (m, 3H), 1.52 (t, J = 29.3 Hz, 5H), 1.32 – 0.81 (m, 3H); MS (ESI(+)) m/e 479 $(M+H)^+$.

Example 23

4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)-N-[1-(pyridin-3-yl)azetidin-3-yl]benzamide

The title compound was prepared as described in Example 21, substituting (S)-2-methylbutanoic acid for 2-(tetrahydro-2H-pyran-4-yl)acetic acid in Example 21C. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.84 (d, J = 7.0 Hz, 1H), 7.99 – 7.84 (m, 3H), 7.83 (s, 1H), 7.18 (dd, J = 8.2, 4.6 Hz, 1H), 7.09 – 7.01 (m, 2H), 6.87 (ddd, J = 8.2, 2.8, 1.4 Hz, 1H), 4.94 – 4.64 (m, 2H), 4.24 (t, J = 7.5 Hz, 2H), 3.98 – 3.72 (m, 4H), 2.73 (h, J = 6.7 Hz, 1H), 2.04 – 1.83 (m, 2H), 1.67 – 1.20 (m, 4H), 1.06 – 0.87 (m, 4H), 0.87 – 0.77 (m, 4H); MS (ESI(+)) m/e 437 $(M+H)^+$.

Example 24

4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}-N-[1-(pyridin-3-yl)azetidin-3-yl]benzamide

The title compound was prepared as described in Example 21, substituting 2-hydroxy-2-methylpropanoic acid for 2-(tetrahydro-2H-pyran-4-yl)acetic acid in Example 21C. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 8.84 (d, J = 7.0 Hz, 1H), 7.93 (dd, J = 4.6, 1.3 Hz, 1H), 7.87 – 7.86 (m, 1H), 7.86 (s, 1H), 7.84 (s, 1H), 7.18 (dd, J = 8.2, 4.6 Hz, 1H), 7.08 – 7.02 (m, 2H), 6.87 (ddd, J = 8.2, 2.8, 1.4 Hz, 1H), 5.40 (s, 1H), 4.92 – 4.81 (m, 1H), 4.76 – 4.67 (m, 1H), 4.24 (t, J = 7.5 Hz, 3H), 3.82 (dd, J = 7.6, 5.9 Hz, 3H), 1.98 – 1.94 (m, 3H), 1.72 – 1.41 (m, 3H), 1.32 (s, 6H); MS (ESI(+)) m/e 439 $(M+H)^+$.

Example 27

tert-butyl 4-(4-{[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbamoyl}phenoxy)piperidine-1-carboxylate

The title compound was prepared as described in Example 21A, D and E, substituting (S)-benzyl 3-aminopyrrolidine-1-carboxylate for benzyl 3-aminoazetidine-1-carboxylate in Example 21A. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.43 (d, J = 6.8 Hz, 1H), 7.94 (d, J = 2.9 Hz, 1H), 7.87 – 7.80 (m, 3H), 7.15 (dd, J = 8.4, 4.5 Hz, 1H), 7.03 (s, 1H), 7.00 (s, 1H), 6.90 (ddd, J = 8.4, 3.0, 1.3 Hz, 1H), 4.71 – 4.55 (m, 2H), 3.73 – 3.53 (m, 3H), 3.44 (t, J = 7.5 Hz, 1H), 3.18 (d, J = 13.4 Hz, 2H), 3.17 (d, J = 12.2 Hz, 2H), 2.34 – 2.19 (m, 1H), 2.14 – 1.97 (m, 1H), 1.98 – 1.82 (m, 2H), 1.63 – 1.43 (m, 2H), 1.40 (s, 9H) ; MS (ESI(+)) m/e 467$(M+H)^+$.

Example 28

tert-butyl 4-(4-{[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbamoyl}phenoxy)piperidine-1-carboxylate

The title compound was prepared as described in Example 21A, D and E, substituting (R)-benzyl 3-aminopyrrolidine-1-carboxylate for benzyl 3-aminoazetidine-1-carboxylate in Example 21A. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.44 (d, J = 6.8 Hz, 1H), 7.94 (d, J = 2.9 Hz, 1H), 7.88 – 7.79 (m, 3H), 7.15 (dd, J = 8.3, 4.5 Hz, 1H), 7.06 – 6.98 (m, 2H), 6.90 (ddd, J = 8.4, 3.0, 1.4 Hz, 1H), 4.72 – 4.54 (m, 2H), 3.74 – 3.50 (m, 3H), 3.51 – 3.39 (m, 1H), 3.18 (d, J = 13.6 Hz, 2H), 3.16 (d, J = 11.9 Hz, 1H), 2.33 – 2.18 (m, 1H), 2.07 (dq, J = 12.9, 6.5 Hz, 1H), 2.00 – 1.82 (m, 2H), 1.67 – 1.43 (m, 2H), 1.40 (s, 9H); MS (ESI(+)) m/e 467$(M+H)^+$.

Example 74

N-(4-{[1-(cyclopropylmethyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide

In a 20 mL vial was added N-(4-(piperidin-4-yloxy)phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide bis(2,2,2-trifluoroacetate) (67 mg, 0.12 mmol) dissolved in methanol (2.0 mL) followed by the addition of cyclopropanecarbaldehyde (10 mg, 0.14 mmol) dissolved in methanol (0.45mL), followed by the addition of neat acetic acid (66 µL, 1.2 mmol). The mixture was shaken for 1 hour at 70°C. After that, 265 mg of MP-cyanoborohydride resin (2-

3 mmol/g) was added and the resulting mixture was shaken at 70°C overnight. The reaction mixture was filtered, checked by LC/MS and concentrated to dryness. The residues were dissolved in 1:1 DMSO/CH_3OH and purified by reverse phase HPLC. ^{1}H NMR (500 MHz, pyridine-d_5/D_2O) δ ppm 8.20 - 8.25 (m, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.98 - 8.03 (m, 2 H) 7.11 (dd, J=8.24, 4.58 Hz, 1 H) 7.02 - 7.07 (m, 2 H) 6.72 - 6.78 (m, 1 H) 4.58 (d, J=2.75 Hz, 1 H) 4.34 (t, J=6.71 Hz, 2 H) 4.05 (t, J=7.63 Hz, 2 H) 3.80 - 3.92 (m, 1 H) 3.34 (s, 4 H) 2.92 (d, J=7.32 Hz, 2 H) 2.32 - 2.44 (m, 2 H) 2.12 (s, 2 H) 1.09 - 1.22 (m, 1 H) 0.51 - 0.58 (m, 2 H) 0.28 - 0.34 (m, 2 H); MS (ESI(+)) m/e 407 (M+H).

Table 4.

The following Examples were prepared essentially as described in Example 74, substituting the appropriate aldehyde for cyclopropanecarbaldehyde. Some products were purified by flash chromatography while others were purified by reverse-phase HPLC. Accordingly, some Examples were isolated as trifluoroacetic acid salts.

Ex		Name	^{1}H NMR	MS
75		N-(4-{[1-(2-methylpentyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O Temp=27 °C) δ ppm 8.23 (dd, J=4.58, 1.22 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.97 - 8.03 (m, 2 H) 7.06 - 7.13 (m, 3 H) 6.71 - 6.77 (m, 1 H) 4.44 (s, 1 H) 4.34 (t, J=6.56 Hz, 2 H) 4.00 - 4.08 (m, 2 H) 3.78 - 3.88 (m, 1 H) 2.96 (s, 2 H) 2.67 (s, 1 H) 2.34 - 2.48 (m, J=2.44 Hz, 3 H) 2.21 (s, 2 H) 1.97 (s, 2 H) 1.72 - 1.83 (m, 1 H) 1.15 - 1.45 (m, 3 H) 1.00 - 1.10 (m, 1 H) 0.96 (d, J=6.71 Hz, 3 H) 0.85 (t, J=7.17 Hz, 3 H)	(ESI(+)) m/e 437 $(M+H)^+$
76		N-(4-{[1-(2-methylpropyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O Temp=27 °C) δ ppm 8.23 (dd, J=4.73, 1.37 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.97 - 8.04 (m, 2 H) 7.04 - 7.15 (m, 3 H) 6.72 - 6.76 (m, 1 H) 4.40 - 4.47 (m, 1 H) 4.34 (t, J=6.56 Hz, 2 H) 3.99 - 4.09 (m, 2 H) 3.79 - 3.89 (m, 1 H) 2.91 - 3.00 (m, 2 H) 2.61 - 2.82 (m, 2 H) 2.36 - 2.45 (m, 2 H) 2.13 - 2.26 (m, J=9.46 Hz, 2 H) 1.79 - 2.04 (m, 3 H) 0.92 (d, J=6.41 Hz, 6 H)	(ESI(+)) m/e 409 $(M+H)^+$
77		N-(4-{[1-(3-methylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O Temp=27 °C) δ ppm 8.21 - 8.26 (m, 1 H) 8.14 (d, J=3.05 Hz, 1 H) 7.98 - 8.03 (m, 2 H) 7.05 - 7.13 (m, 3 H) 6.71 - 6.77 (m, 1 H) 4.47 - 4.54 (m, 1 H) 4.34 (t, J=6.56 Hz, 2 H) 4.00 - 4.07 (m, 2 H) 3.80 - 3.89 (m, 1 H) 3.11 (s, 2 H) 2.87 - 3.06 (m, 2 H) 2.77 - 2.86 (m, 2 H) 2.22 - 2.33 (m, 2 H) 2.04 (s, 2 H) 1.47 - 1.61 (m, 3 H) 0.82 (d, J=6.41 Hz, 6 H)	(ESI(+)) m/e 423 $(M+H)^+$
78		N-(4-{[1-(2-ethylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O Temp=27 °C) δ ppm 8.23 (dd, J=4.58, 1.22 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.98 - 8.03 (m, 2 H) 7.06 - 7.13 (m, 3 H) 6.71 - 6.76 (m, 1 H) 4.40 - 4.49 (m, 1 H) 4.34 (t, J=6.56 Hz, 2 H) 4.00 - 4.06 (m, 2 H) 3.78 - 3.88 (m, 1 H) 2.91 - 3.03 (m, 2 H) 2.57 - 2.77 (m, 2 H) 2.40 - 2.49 (m, J=4.27, 2.14 Hz, 2 H)	(ESI(+)) m/e 437 $(M+H)^+$

			2.14 - 2.28 (m, 2 H) 1.90 - 2.01 (m, J=14.04 Hz, 2 H) 1.58 (s, 1 H) 1.29 - 1.45 (m, 4 H) 0.84 (t, J=7.48 Hz, 6 H)	
79		N-(4-{[1-(2,2-dimethylpropyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O Temp=27 °C) δ ppm 8.23 (dd, J=4.58, 1.22 Hz, 1 H) 8.14 (d, J=2.75 Hz, 1 H) 7.99 - 8.01 (m, 2 H) 7.07 - 7.13 (m, 3 H) 6.74 (d, J=5.49 Hz, 1 H) 4.33 (t, J=6.56 Hz, 2 H) 4.00 - 4.06 (m, 2 H) 3.80 - 3.86 (m, 1 H) 2.73 - 2.81 (m, 2 H) 2.34 - 2.43 (m, 2 H) 1.93 - 2.03 (m, 4 H) 1.76 - 1.88 (m, 2 H) 1.24 - 1.34 (m, 1 H) 0.87 (s, 9 H)	(ESI(+)) m/e 423 $(M+H)^+$
80		N-(4-{[1-(2-methylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O Temp=27 °C) δ ppm 8.21 - 8.24 (m, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 8.00 (d, J=9.16 Hz, 2 H) 7.07 - 7.14 (m, 3 H) 6.70 - 6.77 (m, 1 H) 4.29 - 4.39 (m, 3 H) 3.97 - 4.06 (m, 2 H) 3.77 - 3.86 (m, 1 H) 2.75 - 2.88 (m, 2 H) 2.45 - 2.56 (m, 4 H) 2.04 - 2.25 (m, 3 H) 1.85 - 1.97 (m, 2 H) 1.38 - 1.64 (m, 2 H) 0.81 - 0.93 (m, 6 H)	(ESI(+)) m/e 423 $(M+H)^+$
81		N-{4-[(1-propylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide		(ESI(+)) m/e 395 $(M+H)^+$
82		N-(4-{[1-(2-cyclopropylethyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O Temp=27 °C) δ ppm 8.23 (dd, J=4.58, 1.53 Hz, 1 H) 8.14 (d, J=2.44 Hz, 1 H) 7.95 - 8.04 (m, 2 H) 7.05 - 7.14 (m, 3 H) 6.69 - 6.78 (m, 1 H) 4.42 - 4.51 (m, 1 H) 4.34 (t, J=6.56 Hz, 2 H) 3.95 - 4.11 (m, 2 H) 3.79 - 3.89 (m, J=8.24, 8.24 Hz, 1 H) 3.00 - 3.13 (m, 2 H) 2.73 - 2.93 (m, 3 H) 2.40 - 2.48 (m, 1 H) 2.15 - 2.30 (m, 2 H) 2.01 (s, 2 H) 1.50 - 1.61 (m, J=8.54 Hz, 2 H) 0.54 - 0.70 (m, 1 H) 0.33 - 0.42 (m, 2 H) 0.06 (t, J=4.73 Hz, 2 H)	(ESI(+)) m/e 421 $(M+H)^+$
83		1-(pyridin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylmethyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O Temp=27 °C) δ ppm 8.23 (dd, J=4.58, 1.22 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.98 - 8.04 (m, 2 H) 7.03 - 7.15 (m, 3 H) 6.70 - 6.77 (m, 1 H) 4.44 - 4.53 (m, 1 H) 4.34 (t, J=6.56 Hz, 2 H) 3.96 - 4.09 (m, 3 H) 3.77 - 3.92 (m, 2 H) 3.55 - 3.74 (m, 2 H) 3.03 - 3.19 (m, 2 H) 2.86 - 3.04 (m, 2 H) 2.75 - 2.88 (m, 2 H) 2.57 - 2.72 (m, 1 H) 2.19 - 2.34 (m, 2 H) 1.94 - 2.08 (m, 3 H) 1.56 - 1.71 (m, 1 H)	(ESI(+)) m/e 437 $(M+H)^+$
84		N-(4-{[1-(2,2-dimethylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O Temp=27 °C) δ ppm 8.23 (dd, J=4.73, 1.37 Hz, 1 H) 8.14 (d, J=2.44 Hz, 1 H) 7.97 - 8.02 (m, 2 H) 7.07 - 7.13 (m, 3 H) 6.71 - 6.76 (m, 1 H) 4.28 - 4.38 (m, 2 H) 4.00 - 4.06 (m, 2 H) 3.82 (s, 1 H) 2.72 - 2.82 (m, 2 H) 2.29 - 2.43 (m, 2 H) 1.91 - 2.07 (m, 4 H) 1.75 - 1.88 (m, 2 H) 1.19 - 1.29 (m, J=7.22, 7.22, 7.22 Hz, 3 H) 0.72 - 0.86 (m, 9 H)	(ESI(+)) m/e 437 $(M+H)^+$

Example 85

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 10, substituting 4-bromopyridazine for 3-bromopyridine in Example 10C and 2-hydroxy-2-methylpropanoic acid for (S)-tetrahydrofuran-2-carboxylic acid in Example 10E. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.04 (s, 1H), 8.60 (d, J = 6.0 Hz, 1H), 8.51 (d, J = 3.0 Hz, 1H), 7.57 – 7.50 (m, 2H), 7.22 – 7.14 (m, 2H), 6.54 (dd, J = 6.0, 3.0 Hz, 1H), 5.36 (s, 1H), 4.73 (bs, 2H), 4.30 – 3.96 (m, 4H), 3.87 – 3.60 (m, 1H), 2.71 (d, J = 11.9 Hz, 1H), 1.82 – 1.72 (m, 2H), 1.67 – 1.42 (m, 2H), 1.35 – 1.31 (m, 8H); MS (ESI(+)) m/e 424 $(M+H)^+$.

Table 5.

The following Examples were essentially prepared as described in Example 10, substituting 4-bromopyridazine for 3-bromopyridine in Example 10C and the appropriate acid for (S)-tetrahydrofuran-2-carboxylic acid in Example 10E. Some products were purified by flash chromatography while others were purified by reverse-phase HPLC. Accordingly, some Examples were isolated as trifluoroacetic acid salts.

Ex		Name	MS
140		N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
143		N-(4-{1-[(2S)-2-methylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
144		N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 448 $(M+H)^+$
145		1-(pyridazin-4-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 464 $(M+H)^+$
146		1-(pyridazin-4-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 564 $(M+H)^+$
525		N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
526		1-(pyridazin-4-yl)-N-{4-[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 449 $(M+H)^+$
527		N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 420 $(M+H)^+$
528		N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 408 $(M+H)^+$
529		N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 460 $(M+H)^+$
530		1-(pyridazin-4-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-	(ESI(+))

		yl]phenyl}azetidine-3-carboxamide	m/e 448 $(M+H)^+$
531		N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
532		N-(4-{1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
533		N-{4-[1-(3,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
534		N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
535		1-(pyridazin-4-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 510 $(M+H)^+$
536		N-(4-{1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
537		1-(pyridazin-4-yl)-N-{4-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 449 $(M+H)^+$
538		1-(pyridazin-4-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
539		N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
540		N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
541		N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 406 $(M+H)^+$
542		1-(pyridazin-4-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
543		1-(pyridazin-4-yl)-N-{4-[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 443 $(M+H)^+$
544		N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
545		N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
546		N-{4-[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
547		N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
548		N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-	(ESI(+))

		yl)azetidine-3-carboxamide	m/e 410 $(M+H)^+$
549		1-(pyridazin-4-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 448 $(M+H)^+$
550		1-(pyridazin-4-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
551		N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 460 $(M+H)^+$
552		N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
553		1-(pyridazin-4-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 510 $(M+H)^+$
554		N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 460 $(M+H)^+$
555		1-(pyridazin-4-yl)-N-(4-{1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 526 $(M+H)^+$
556		N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
557		1-(pyridazin-4-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 448 $(M+H)^+$
558		N-(4-{1-[difluoro(phenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
559		N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
560		N-(4-{1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
561		1-(pyridazin-4-yl)-N-[4-(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 540 $(M+H)^+$
562		1-(pyridazin-4-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 526 $(M+H)^+$
563		1-(pyridazin-4-yl)-N-[4-(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$

Example 86

N-{4-[1-(cyclohexylmethyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 74, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide for N-(4-(piperidin-4-yloxy)phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide and cyclohexanecarbaldehyde for

cyclopropanecarbaldehyde. ^{1}H NMR (500 MHz, pyridine-d_5/D_2O) δ ppm 8.23 (dd, J=4.58, 1.22 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.31 - 7.36 (m, 2 H) 7.11 (dd, J=8.24, 4.27 Hz, 1 H) 6.71 - 6.75 (m, 1 H) 4.32 (t, J=6.56 Hz, 2 H) 3.98 - 4.05 (m, 2 H) 3.79 - 3.89 (m, 1 H) 3.62 - 3.71 (m, 2 H) 2.69 - 2.95 (m, 5 H) 2.37 - 2.49 (m, 2 H) 1.75 - 2.00 (m, 5 H) 1.46 - 1.65 (m, 3 H) 0.90 - 1.24 (m, 5 H) ; (ESI(+)) m/e 433 (M+H).

Table 6.

The following Examples were prepared essentially as described in Example 74, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide for N-(4-(piperidin-4-yloxy)phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide and the appropriate aldehyde for cyclopropanecarbaldehyde. Some products were purified by flash chromatography while others were purified by reverse-phase HPLC. Accordingly, some Examples were isolated as trifluoroacetic acid salts.

Ex		Name	^{1}H NMR	MS
87		N-{4-[1-(3,3-dimethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O) δ ppm 8.23 (dd, J=4.73, 1.37 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.98 (d, J=8.54 Hz, 2 H) 7.29 - 7.32 (m, 2 H) 7.11 (dd, J=7.93, 4.88 Hz, 1 H) 6.69 - 6.75 (m, 1 H) 4.32 (t, J=6.71 Hz, 2 H) 3.98 - 4.04 (m, 2 H) 3.79 - 3.87 (m, 1 H) 3.68 (s, 2 H) 3.08 - 3.15 (m, 2 H) 2.80 - 2.92 (m, 2 H) 2.71 - 2.79 (m, 1 H) 2.34 - 2.46 (m, 2 H) 1.90 - 1.99 (m, 2 H) 1.71 - 1.78 (m, 2 H) 0.87 (s, 9 H)	(ESI(+)) m/e 421 $(M+H)^+$
88		N-{4-[1-(cyclopentylmethyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O) δ ppm 8.23 (dd, J=4.88, 1.22 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.31 - 7.35 (m, 2 H) 7.11 (dd, J=8.09, 4.73 Hz, 1 H) 6.70 - 6.75 (m, 1 H) 4.33 (t, J=6.56 Hz, 2 H) 3.97 - 4.05 (m, 2 H) 3.77 - 3.85 (m, 1 H) 3.56 - 3.71 (m, 2 H) 2.98 (d, J=6.71 Hz, 2 H) 2.69 - 2.86 (m, J=12.21, 12.21 Hz, 3 H) 2.34 - 2.49 (m, 2 H) 2.19 - 2.31 (m, 1 H) 1.78 - 1.97 (m, 4 H) 1.35 - 1.57 (m, 4 H) 1.17 - 1.28 (m, 2 H)	(ESI(+)) m/e 419 $(M+H)^+$
89		N-{4-[1-(2,2-dimethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O) δ ppm 8.23 (dd, J=4.58, 1.22 Hz, 1 H) 8.14 (d, J=2.75 Hz, 1 H) 8.02 (d, J=8.54 Hz, 2 H) 7.32 (d, J=8.24 Hz, 2 H) 7.11 (dd, J=8.24, 4.58 Hz, 1 H) 6.71 - 6.75 (m, 1 H) 4.33 (t, J=6.56 Hz, 2 H) 3.99 - 4.05 (m, 2 H) 3.79 - 3.86 (m, 1 H) 2.89 - 2.97 (m, 2 H) 2.29 - 2.50 (m, J=59.51 Hz, 3 H) 2.14 (d, J=3.97 Hz, 2 H) 1.84 - 1.97 (m, 2 H) 1.71 - 1.78 (m, 2 H) 1.30 (q, J=7.63 Hz, 2 H) 0.88 (s, 6 H) 0.82 (t, J=7.48 Hz, 3 H)	(ESI(+)) m/e 421 $(M+H)^+$
90		N-{4-[1-(2-methylpentyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O) δ ppm 8.23 (dd, J=4.73, 1.37 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.30 - 7.37 (m, 2 H) 7.11 (dd, J=8.24, 4.27 Hz, 1 H) 6.69 - 6.77 (m, 1 H) 4.28 - 4.36 (m, 2 H) 3.96 - 4.06 (m, 2 H) 3.77 - 3.87 (m, 1 H) 3.53 (s, 2 H) 2.55 - 2.91 (m, 5 H) 2.23 - 2.42 (m, 2 H) 1.81 - 1.95 (m, J=6.71 Hz, 3 H) 1.04 - 1.47 (m, 4 H) 1.03 (t, J=6.41 Hz, 3 H) 0.85 (t, J=7.17 Hz, 3 H)	(ESI(+)) m/e 421 $(M+H)^+$

91		N-[4-(1-butylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O) δ ppm 8.20 - 8.27 (m, 1 H) 8.13 (d, J=3.05 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.30 - 7.35 (m, 2 H) 7.08 - 7.12 (m, 1 H) 6.68 - 6.74 (m, 1 H) 4.32 (t, J=6.56 Hz, 2 H) 3.97 - 4.06 (m, 2 H) 3.78 - 3.86 (m, 1 H) 3.56 - 3.69 (m, 2 H) 2.92 - 3.03 (m, 2 H) 2.66 - 2.87 (m, 3 H) 2.29 - 2.45 (m, 2 H) 1.91 (d, J=13.73 Hz, 2 H) 1.65 - 1.77 (m, 2 H) 1.10 - 1.31 (m, 2 H) 0.79 (t, J=7.32 Hz, 3 H)	(ESI(+)) m/e 393 $(M+H)^+$
92		N-{4-[1-(2-ethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O) δ ppm 8.23 (d, J=4.58 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.33 (d, J=8.54 Hz, 2 H) 7.09 - 7.11 (m, 1 H) 6.70 - 6.74 (m, 1 H) 4.32 (t, J=6.56 Hz, 2 H) 3.97 - 4.05 (m, 2 H) 3.78 - 3.86 (m, 1 H) 3.43 - 3.61 (m, 2 H) 2.55 - 2.95 (m, 5 H) 2.22 - 2.43 (m, 2 H) 1.90 (d, J=13.12 Hz, 2 H) 1.67 - 1.78 (m, 1 H) 1.30 - 1.50 (m, 4 H) 0.85 (t, J=7.48 Hz, 6 H)	(ESI(+)) m/e 421 $(M+H)^+$
93		N-{4-[1-(3-methylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O) δ ppm 8.19 - 8.26 (m, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.29 - 7.34 (m, 2 H) 7.11 (dd, J=8.24, 4.58 Hz, 1 H) 6.67 - 6.76 (m, 1 H) 4.32 (t, J=6.56 Hz, 2 H) 3.98 - 4.04 (m, 2 H) 3.77 - 3.87 (m, 1 H) 3.57 - 3.69 (m, 2 H) 2.95 - 3.05 (m, 2 H) 2.67 - 2.87 (m, 3 H) 2.29 - 2.44 (m, 2 H) 1.84 - 1.98 (m, 2 H) 1.60 - 1.71 (m, 2 H) 1.39 - 1.58 (m, 1 H) 0.82 (d, J=6.71 Hz, 6 H)	(ESI(+)) m/e 407 $(M+H)^+$
94		N-{4-[1-(2-methylpropyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O) δ ppm 8.21 - 8.27 (m, 1 H) 8.14 (d, J=2.75 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.32 (d, J=8.54 Hz, 2 H) 7.11 (dd, J=8.09, 4.73 Hz, 1 H) 6.70 - 6.75 (m, 1 H) 4.33 (t, J=6.56 Hz, 2 H) 3.97 - 4.04 (m, 2 H) 3.78 - 3.87 (m, 1 H) 3.27 - 3.41 (m, 2 H) 2.62 (s, 1 H) 2.38 - 2.52 (m, 4 H) 2.10 - 2.26 (m, J=22.28 Hz, 2 H) 1.90 - 1.99 (m, 1 H) 1.81 - 1.88 (m, 2 H) 0.95 (d, J=6.41 Hz, 6 H)	(ESI(+)) m/e 393 $(M+H)^+$
95		N-[4-(1-propylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide	^{1}H NMR (500 MHz, pyridine-d_5/D_2O) δ ppm 8.21 - 8.25 (m, 1 H) 8.10 - 8.15 (m, 1 H) 7.98 (d, J=8.54 Hz, 2 H) 7.31 (d, J=8.54 Hz, 2 H) 7.11 (dd, J=8.24, 4.58 Hz, 1 H) 6.71 - 6.76 (m, 1 H) 4.32 (t, J=6.56 Hz, 2 H) 3.99 - 4.04 (m, 2 H) 3.77 - 3.89 (m, 1 H) 3.55 - 3.66 (m, 2 H) 2.86 - 2.98 (m, 2 H) 2.64 - 2.86 (m, 3 H) 2.30 - 2.46 (m, 2 H) 1.90 (d, J=14.04 Hz, 2 H) 1.70 - 1.81 (m, 2 H) 0.78 (t, J=7.32 Hz, 3 H)	(ESI(+)) m/e 379 $(M+H)^+$

Example 141

(3S)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide

Example 141A

(S)-tert-butyl 4-(4-(1-((benzyloxy)carbonyl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting (S)-1-((benzyloxy)carbonyl)pyrrolidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-

carboxylic acid and tert-butyl 4-(4-aminophenyl)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate.

Example 141B

(S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1B, substituting (S)-tert-butyl 4-(4-(1-((benzyloxy)carbonyl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 141C

(S)-tert-butyl 4-(4-(1-(pyridazin-4-yl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1C, substituting (S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate and 4-bromopyridazine for 3-bromopyridine.

Example 141D

(S)-N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 141E

(3S)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-hydroxy-2-methylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.07 (s, 1H), 8.68 – 8.61 (m, 1H), 8.61 – 8.50 (m, 1H), 7.52 (t, J = 6.8 Hz, 2H), 7.17 (d, J = 8.6 Hz, 2H), 6.62 (dd, J = 6.3, 3.2 Hz, 1H), 5.35 (s, 1H), 3.73 – 3.34 (m, 8H), 2.73 (dd, J = 13.9, 10.2 Hz, 2H), 2.40 – 2.06 (m, 2H), 1.76 (d, J = 11.0 Hz, 2H), 1.64 – 1.38 (m, 2H), 1.33 (s, 6H); MS (ESI(+)) m/e 438 $(M+H)^+$.

Example 142

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and cyclopentylacetic acid for 1-

(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.07 (s, 1H), 8.64 (dd, J = 3.1, 0.9 Hz, 1H), 8.57 (dd, J = 6.2, 0.9 Hz, 1H), 7.54 (s, 1H), 7.51 (s, 1H), 7.21 – 7.13 (m, 2H), 6.61 (dd, J = 6.2, 3.1 Hz, 1H), 3.68 – 3.41 (m, 8H), 3.18 – 3.00 (m, 1H), 2.78 – 2.64 (m, 1H), 2.42 – 2.06 (m, 5H), 1.83 – 1.69 (m, 4H), 1.65 – 1.20 (m, 6H), 1.22 – 1.04 (m, 2H); MS (ESI(+)) m/e 462 $(M+H)^+$.

Example 147

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 147A

tert-butyl 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

In a 50 mL round-bottomed flask was added tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate (918 mg, 2.55 mmol) and diisopropylethylamine (0.558 ml, 3.19 mmol) in ethanol (10.6 ml). 3,6–dichloropyridazine (317 mg, 2.128 mmol) was added as a solid in a single portion. The reaction was stirred overnight at 45°C; and the reaction was cooled and concentrated. Dichloromethane and water were added and the layers were separated. The aqueous layer was extracted three times with dichloromethane and the combined organics were dried with magnesium sulfate, filtered and concentrated by rotary evaporation. The residue was purified by regular phase flash column chromatography to give the title compound.

Example 147B

tert-butyl 4-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

To a 50 mL round-bottomed flask was added tert-butyl 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate (550 mg, 1.165 mmol) and Pd/C (93 mg, 0.087 mmol). The flask was flushed with nitrogen for 10 minutes and ethanol (11.7 ml) was added. Triethylamine (0.162 ml, 1.165 mmol) and cyclohexa-1,4-diene (654 mg, 8.16 mmol) were added and the reaction was stirred at 80 °C for 1 hour, cooled and filtered through diatomaceous earth. The filtrate was concentrated in vacuo and the residue was purified by regular phase flash column chromatography to give the title compound.

Example 147C

N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 147D

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-methylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.03 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.52 (dd, J = 9.2, 4.7 Hz, 2H), 7.40 (ddd, J = 13.5, 7.9, 2.8 Hz, 1H), 7.18 (d, J = 8.6 Hz, 2H), 6.82 (dd, J = 8.9, 1.3 Hz, 1H), 4.55 (d, J = 12.0 Hz, 1H), 4.32 – 3.90 (m, 5H), 3.83 – 3.54 (m, 1H), 3.10 (t, J = 12.9 Hz, 1H), 2.89 (hept, J = 6.7 Hz, 1H), 2.71 (ddd, J = 28.5, 16.0, 11.7 Hz, 1H), 1.77 (d, J = 12.3 Hz, 2H), 1.60 – 1.10 (m, 4H), 1.01 (t, J = 6.0 Hz, 6H); MS (ESI(+)) m/e 408 $(M+H)^+$.

Table 7.

The following Examples were prepared essentially as described in Example 1A, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and the appropriate carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. Some products were purified by flash chromatography while others were purified by reverse-phase HPLC. Accordingly, some Examples were isolated as trifluoroacetic acid salts.

Ex		Name	MS
316		N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 380 $(M+H)^+$
317		N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 408 $(M+H)^+$
318		N-[4-(1-pentanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
319		N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
320		N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
321		N-[4-(1-hexanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
322		N-{4-[1-(2-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
323		N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
324		N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
325		N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436

			$(M+H)^+$
326		N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
327		N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
328		N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
329		N-[4-(1-heptanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
330		N-{4-[1-(but-3-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 406 $(M+H)^+$
331		N-{4-[1-(pent-4-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 420 $(M+H)^+$
332		1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 448 $(M+H)^+$
333		N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 410 $(M+H)^+$
334		N-(4-{1-[(methylsulfanyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 426 $(M+H)^+$
335		N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 454 $(M+H)^+$
336		N-{4-[1-(3-nitropropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 439 $(M+H)^+$
337		N-(4-{1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 440 $(M+H)^+$
338		N-{4-[1-(pent-4-ynoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 418 $(M+H)^+$
339		N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 448 $(M+H)^+$
340		N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
341		N-{4-[1-(3-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 456 $(M+H)^+$
342		N-{4-[1-(2-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 458 $(M+H)^+$
343		N-{4-[1-(3-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 458

			$(M+H)^+$
344		N-{4-[1-(4-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 458 $(M+H)^+$
345		N-{4-[1-(2-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 472 $(M+H)^+$
346		N-{4-[1-(3-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 472 $(M+H)^+$
347		N-{4-[1-(4-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 472 $(M+H)^+$
348		N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 460 $(M+H)^+$
349		N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 460 $(M+H)^+$
350		N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
351		N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
352		N-{4-[1-(3-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 467 $(M+H)^+$
353		N-{4-[1-(4-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 467 $(M+H)^+$
354		1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 510 $(M+H)^+$
355		1-(pyridazin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 510 $(M+H)^+$
356		1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 526 $(M+H)^+$
357		N-{4-[1-(2,3-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 470 $(M+H)^+$
358		N-{4-[1-(2,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 470 $(M+H)^+$
359		N-{4-[1-(2,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 470 $(M+H)^+$
360		N-{4-[1-(3,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 470 $(M+H)^+$
361		N-{4-[1-(3,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 470

			$(M+H)^+$
362		N-{4-[1-(2,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 510 $(M+H)^+$
363		N-{4-[1-(2,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 510 $(M+H)^+$
364		N-{4-[1-(3,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 510 $(M+H)^+$
365		N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 510 $(M+H)^+$
366		N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
367		N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
368		N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
369		N-(4-{1-[(2-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
370		N-(4-{1-[(4-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
371		1-(pyridazin-3-yl)-N-[4-(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
372		N-(4-{1-[(3,5-dimethylphenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
373		N-(4-{1-[(2,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
374		N-(4-{1-[(3,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 525 $(M+H)^+$
375		N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 432 $(M+H)^+$
376		1-(pyridazin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 448 $(M+H)^+$
377		N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
378		N-(4-{1-[(5-methylpyrazin-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 458 $(M+H)^+$
379		N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 420

			$(M+H)^+$
380		N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
381		N-(4-{1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 482 $(M+H)^+$
382		1-(pyridazin-3-yl)-N-(4-{1-[(pyrimidin-2-ylsulfanyl)acetyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
383		N-(4-{1-[(1-acetylpiperidin-4-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 491 $(M+H)^+$
384		N-(4-{1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
385		N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 493 $(M+H)^+$
386		N-{4-[1-(diphenylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 532 $(M+H)^+$
387		N-{4-[1-(3-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
388		N-{4-[1-(5-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
389		N-{4-[1-(3-fluoro-4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
390		N-{4-[1-(2,3-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
391		N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
392		N-(4-{1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
393		N-{4-[1-(4-tert-butylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 498 $(M+H)^+$
394		N-(4-{1-[2-fluoro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 528 $(M+H)^+$
395		N-(4-{1-[2-chloro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 544 $(M+H)^+$
397		N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 448 $(M+H)^+$
398		N-(4-{1-[(4-methylphenoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 486

			$(M+H)^+$
399		N-(4-{1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
400		N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
401		N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
402		N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
403		1-(pyridazin-3-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
404		N-(4-{1-[(3-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
405		N-(4-{1-[(2,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
406		N-{4-[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
407		N-(4-{1-[(2R)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 486 $(M+H)^+$
408		N-(4-{1-[N-(furan-2-ylcarbonyl)glycyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 489 $(M+H)^+$
409		N-(4-{1-[(benzyloxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 486 $(M+H)^+$
410		N-{4-[1-(naphthalen-1-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 506 $(M+H)^+$
411		N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 406 $(M+H)^+$
412		1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
413		N-{4-[1-(N-benzoylglycyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 499 $(M+H)^+$
414		1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
415		1-(pyridazin-3-yl)-N-(4-{1-[4-(thiophen-2-yl)butanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
416		N-{4-[1-(2,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478

			$(M+H)^+$
417		N-{4-[1-(cyclobutylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 420 $(M+H)^+$
418		N-[4-(1-{N-[(4-methylphenyl)sulfonyl]glycyl}piperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 549 $(M+H)^+$
419		N-(4-{1-[(2,3-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
420		N-(4-{1-[(2S)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 486 $(M+H)^+$
421		N-{4-[1-(naphthalen-2-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 506 $(M+H)^+$
422		N-{4-[1-(3-phenylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 470 $(M+H)^+$
423		N-(4-{1-[(2,6-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
424		N-(4-{1-[3-(phenylsulfonyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 534 $(M+H)^+$
425		1-(pyridazin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 448 $(M+H)^+$
426		N-(4-{1-[(2,5-dimethylfuran-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 460 $(M+H)^+$
427		N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 420 $(M+H)^+$
428		N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 460 $(M+H)^+$
429		N-{4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 456 $(M+H)^+$
430		1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 449 $(M+H)^+$
431		1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 449 $(M+H)^+$
432		N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
433		1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
434		N-(4-{1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 457

			$(M+H)^+$
435		N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 442 $(M+H)^+$
436		N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 432 $(M+H)^+$
437		N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
438		N-{4-[1-(2-oxopropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 408 $(M+H)^+$
439		N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 434 $(M+H)^+$
440		N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 394 $(M+H)^+$
441		N-{4-[1-(4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 456 $(M+H)^+$

Example 148

N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide

Example 148A

4-(1-isobutyl-1H-pyrazol-4-yl)aniline

A suspension of 4-bromoaniline (406 mg, 2.362 mmol), 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (650 mg, 2.60 mmol), $PdCl_2$(dppf)-dichloromethane adduct (57.9 mg, 0.071 mmol) and sodium carbonate (526 mg, 4.96 mmol) in a 6:2:1 mixture of tetrahydrofuran/methanol/water (12 ml) was taken through three vacuum/nitrogen purge cycles; and the reaction mixture was heated in an oil bath at 85°C overnight. The mixture was diluted with ethyl acetate and water; the separated aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with brine, dried with magnesium sulfate, filtered and concentrated. The residue was purified by normal phase chromatography to give the title compound .

Example 148B

benzyl 3-((4-(1-isobutyl-1H-pyrazol-4-yl)phenyl)carbamoyl)azetidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting 4-(1-isobutyl-1H-pyrazol-4-yl)aniline for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate.

Example 148C

N-(4-(1-isobutyl-1H-pyrazol-4-yl)phenyl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1B, substituting benzyl 3-((4-(1-isobutyl-1H-pyrazol-4-yl)phenyl)carbamoyl)azetidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 148D

N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1C, substituting 4-bromopyridazine for 3-bromopyridine and N-(4-(1-isobutyl-1H-pyrazol-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.10 (s, 1H), 8.61 (d, J = 6.0 Hz, 1H), 8.51 (d, J = 3.0 Hz, 1H), 8.08 (s, 1H), 7.81 (s, 1H), 7.64 – 7.56 (m, 2H), 7.55 – 7.48 (m, 2H), 6.55 (dd, J = 6.0, 3.0 Hz, 1H), 4.31 – 3.96 (m, 4H), 3.91 (d, J = 7.1 Hz, 2H), 3.74 (s, 1H), 2.12 (dd, J = 13.3, 6.5 Hz, 1H), 0.86 (d, J = 6.7 Hz, 6H); MS (ESI(+)) m/e 377 $(M+H)^+$.

Example 199

N-(4-{[1-(4-fluorobenzoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1, substituting tert-butyl 4-(4-aminophenoxy)azetidinyl-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate in Example 1A, 4-bromopyridazine for 3-bromopyridyl in Example 1C and 4-fluorobenzoic acid for 2-(tetrahydro-2H-pyran-4-yl)acetic acid in Example 1E. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.01 (s, 1H), 8.67 – 8.44 (m, 1H), 7.83 – 7.63 (m, 2H), 7.62 – 7.43 (m, 2H), 7.43 – 7.18 (m, 2H), 6.90 – 6.77 (m, 2H), 6.55 (dd, J = 6.1, 3.1 Hz, 1H), 5.13 – 4.94 (m, 1H), 4.61 (d, J = 52.0 Hz, 2H), 4.36 – 4.04 (m, 4H), 3.99 (s, 1H), 3.70 (ddt, J = 33.0, 30.2, 15.0 Hz, 1H), 1.21 (t, J = 15.0 Hz, 3H); MS (ESI(+)) m/e 448 $(M+H)^+$.

Table 8.

The following Examples were prepared essentially as described in Example 1, substituting the appropriate amine for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate in Example 1A, 4-bromopyridazine for 3-bromopyridyl in Example 1C and the appropriate carboxylic acid for 2-(tetrahydro-2H-pyran-4-yl)acetic acid in Example 1E. Some products were purified by flash chromatography while others were purified by reverse-phase HPLC. Accordingly, some Examples were isolated as trifluoroacetic acid salts.

Ex		Name	MS
200		N-(4-{[1-(2,4-difluorobenzoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 466 $(M+H)^+$
201		N-[4-({1-[difluoro(phenyl)acetyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 480 $(M+H)^+$

202		N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 472 $(M+H)^+$
203		N-[4-({1-[(4-fluorophenyl)acetyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
205		1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]azetidin-3-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 498 $(M+H)^+$
206		N-{4-[(1-benzoylazetidin-3-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 430 $(M+H)^+$
207		N-(4-{[1-(2-hydroxy-2-methylpropanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 412 $(M+H)^+$
208		1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
209		N-(4-{[1-(furan-3-ylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 420 $(M+H)^+$
210		N-{4-[(1-pentanoylazetidin-3-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 410 $(M+H)^+$
254		N-(4-{[1-(3,3-dimethylbutanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
255		N-(4-{[1-(cyclohexylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
256		1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 452 $(M+H)^+$
257		N-[4-({1-[(2-methylcyclopropyl)carbonyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 408 $(M+H)^+$
258		1-(pyridazin-4-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
259		N-(4-{[1-(cyclopentylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
260		N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 452 $(M+H)^+$
261		N-(4-{[1-(cyclobutylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 408 $(M+H)^+$
262		1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
263		N-(4-{[1-(4-methylpentanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$

264		N-(4-{[1-(2-methylpropanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 396 $(M+H)^+$
265		N-[4-({1-[(2S)-2-methylbutanoyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 410 $(M+H)^+$
266		N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
267		N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 426 $(M+H)^+$
268		1-(pyridazin-4-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 464 $(M+H)^+$
269		N-[4-({1-[difluoro(phenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 508 $(M+H)^+$
270		N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 500 $(M+H)^+$
271		N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
272		1-(pyridazin-4-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 465 $(M+H)^+$
273		1-(pyridazin-4-yl)-N-{4-[(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 540 $(M+H)^+$
274		N-(4-{[1-(3,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$
275		1-(pyridazin-4-yl)-N-{4-[(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 556 $(M+H)^+$
276		N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
277		N-[4-({1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 508 $(M+H)^+$
278		1-(pyridazin-4-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 464 $(M+H)^+$
279		N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
280		N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
281		N-(4-{[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 500 $(M+H)^+$

282		N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 396 $(M+H)^+$
283		1-(pyridazin-4-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 465 $(M+H)^+$
284		N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$
285		1-(pyridazin-4-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 526 $(M+H)^+$
286		N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
287		1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 526 $(M+H)^+$
288		N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
289		N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
290		1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 542 $(M+H)^+$
291		N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 508 $(M+H)^+$
292		1-(pyridazin-4-yl)-N-[4-({1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 542 $(M+H)^+$
293		N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
294		N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
295		N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
296		1-(pyridazin-4-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 459 $(M+H)^+$
297		N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
298		1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 452 $(M+H)^+$
299		N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$

300		N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 452 $(M+H)^+$
301		N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
302		1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 452 $(M+H)^+$
303		1-(pyridazin-4-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 464 $(M+H)^+$
304		N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
305		1-(pyridazin-4-yl)-N-{4-[(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 540 $(M+H)^+$
306		1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 466 $(M+H)^+$
307		N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
308		N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
396		N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
442		N-(4-{[(3R)-1-(2-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
443		1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(1,3-thiazol-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 451 $(M+H)^+$
444		N-(4-{[(3R)-1-(cyclopropylacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
445		N-[4-({(3R)-1-[(2S)-2-methylbutanoyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
446		1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydro-2H-pyran-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 452 $(M+H)^+$
447		1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethoxy)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 542 $(M+H)^+$
448		1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(thiophen-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
449		N-[4-({(3R)-1-[(4-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$

450		N-[4-({(3R)-1-[(3,5-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$
451		N-(4-{[(3R)-1-(3,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 480 $(M+H)^+$
452		N-[4-({(3R)-1-[(3-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
453		1-(pyridazin-4-yl)-N-[4-({(3R)-1-[3-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 512 $(M+H)^+$
454		N-[4-({(3R)-1-[(2,4-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$
455		1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 526 $(M+H)^+$
456		1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 451 $(M+H)^+$
457		1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
458		N-[4-({(3R)-1-[(5-methylthiophen-2-yl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 464 $(M+H)^+$
459		N-[4-({(3R)-1-[(2-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
460		N-(4-{[(3R)-1-(cyclopropylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 408 $(M+H)^+$
461		1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
462		1-(pyridazin-4-yl)-N-[4-({(3R)-1-[3-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 528 $(M+H)^+$
463		1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(pyridin-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 445 $(M+H)^+$
464		N-(4-{[(3R)-1-(3-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
465		N-(4-{[(3R)-1-(4-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
466		N-(4-{[(3R)-1-(2-methyl-2-phenylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 486 $(M+H)^+$
467		N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 480 $(M+H)^+$

468		N-(4-{[(3R)-1-(methoxyacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 412 $(M+H)^+$
469		1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(thiophen-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
470		1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[3-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 526 $(M+H)^+$
471		N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 410 $(M+H)^+$
472		N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
473		N-(4-{[(3R)-1-(2,2-dimethylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
474		N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 480 $(M+H)^+$
475		1-(pyridazin-4-yl)-N-[4-({(3R)-1-[4-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 512 $(M+H)^+$
476		N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
477		1-(pyridazin-4-yl)-N-[4-({(3R)-1-[4-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 528 $(M+H)^+$
478		N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
479		1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(3,3,3-trifluoropropanoyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
480		N-[4-({(3R)-1-[difluoro(phenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$
481		N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
482		N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide	(ESI(+)) m/e 486 $(M+H)^+$

Example 204

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1, substituting (S)-1-((benzyloxy)carbonyl)pyrrolidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid acid and tert-butyl 4-(4-aminophenyl)piperidine-1-carboxylate for tert-butyl

4-(4-aminophenoxy)piperidine-1-carboxylate in Example 1A, and cyclopentylbenzoic acid for 2-(tetrahydro-2H-pyran-4-yl)acetic acid in Example 1E. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.03 (s, 1H), 7.95 (d, J = 2.8 Hz, 1H), 7.85 (dd, J = 4.6, 1.2 Hz, 1H), 7.55 (t, J = 10.1 Hz, 2H), 7.16 (dd, J = 8.3, 4.3 Hz, 3H), 6.92 (ddd, J = 8.4, 2.9, 1.3 Hz, 1H), 4.54 (d, J = 12.7 Hz, 1H), 3.98 (d, J = 13.7 Hz, 1H), 3.64 – 3.48 (m, 1H), 3.48 – 3.38 (m, 1H), 3.22 – 2.87 (m, 2H), 2.68 (dd, J = 24.3, 12.3 Hz, 1H), 2.41 – 2.01 (m, 6H), 1.77 (s, 4H), 1.68 – 1.04 (m, 9H); MS (ESI(+)) m/e 461 $(M+H)^+$.

Example 211

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 147, substituting tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate for 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate in Example 147A and 2-chlorobenzoic acid for 2-methylpropanoic acid in Example 147D. ^{1}H NMR (400 MHz, DMSO/D_2O) δ ppm 8.51 (dd, J = 4.4, 1.2 Hz, 1H), 7.78 – 7.66 (m, 1H), 7.55 – 7.45 (m, 3H), 7.45 – 7.37 (m, 2H), 7.37 – 7.28 (m, 2H), 7.01 – 6.89 (m, 2H), 4.63 – 4.34 (m, 6H), 4.03 – 3.86 (m, 1H), 3.86 – 3.72 (m, 1H), 3.63 – 3.43 (m, 1H), 3.43 – 3.31 (m, 1H), 3.26 – 3.07 (m, 1H), 2.06 – 1.80 (m, 2H), 1.80 – 1.53 (m, 2H), 1.28 – 1.21 (m, 1H); MS (ESI(+)) m/e 492 $(M+H)^+$.

Table 9.

The following Examples were prepared essentially as described in Example 147, substituting the appropriate amine in Example 147A and the appropriate carboxylic acid in Example 147D. Some products were purified by flash chromatography while others were purified by reverse-phase HPLC. Accordingly, some Examples were isolated as trifluoroacetic acid salts.

Ex		Name	MS
212		N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
213		1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 465 $(M+H)^+$
214		1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 466 $(M+H)^+$
215		N-[4-({1-[difluoro(phenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 508 $(M+H)^+$
216		N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 500 $(M+H)^+$
217		N-(4-{[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 500

			$(M+H)^+$
218		1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 465 $(M+H)^+$
219		N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
220		1-(pyridazin-3-yl)-N-{4-[(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 540 $(M+H)^+$
221		1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 452 $(M+H)^+$
222		1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 526 $(M+H)^+$
223		1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 464 $(M+H)^+$
224		1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 542 $(M+H)^+$
225		N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
226		1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 452 $(M+H)^+$
227		N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
228		N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
229		N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$
230		N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
231		N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
232		N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
233		N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
234		N-(4-{[1-(3,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$
235		1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 542

			$(M+H)^+$
236		N-[4-({1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 508 $(M+H)^+$
237		1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 526 $(M+H)^+$
238		1-(pyridazin-3-yl)-N-{4-[(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 556 $(M+H)^+$
239		N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 508 $(M+H)^+$
240		1-(pyridazin-3-yl)-N-{4-[(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 540 $(M+H)^+$
241		N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
242		1-(pyridazin-3-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 459 $(M+H)^+$
243		N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$
244		-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 396 $(M+H)^+$
245		N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
246		N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 426 $(M+H)^+$
247		N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
248		N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 452 $(M+H)^+$
249		1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 464 $(M+H)^+$
250		N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
251		N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
252		1-(pyridazin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 464 $(M+H)^+$
253		N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 424

			$(M+H)^+$
483		N-(4-{[(3R)-1-(2-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
484		1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 451 $(M+H)^+$
485		N-(4-{[(3R)-1-(cyclopropylacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
486		N-[4-({(3R)-1-[(2S)-2-methylbutanoyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
487		1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydro-2H-pyran-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 452 $(M+H)^+$
488		1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethoxy)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 542 $(M+H)^+$
489		N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
490		1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(thiophen-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
491		N-[4-({(3R)-1-[(4-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
492		N-[4-({(3R)-1-[(3,5-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$
493		N-(4-{[(3R)-1-(3,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 480 $(M+H)^+$
494		N-[4-({(3R)-1-[(3-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
495		1-(pyridazin-3-yl)-N-[4-({(3R)-1-[3-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 512 $(M+H)^+$
496		N-[4-({(3R)-1-[(2,4-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$
497		1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 526 $(M+H)^+$
498		1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 451 $(M+H)^+$
499		1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
500		N-[4-({(3R)-1-[(5-methylthiophen-2-yl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 464

			$(M+H)^+$
501		N-[4-({(3R)-1-[(2-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
502		N-(4-{[(3R)-1-(cyclopropylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 408 $(M+H)^+$
503		1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
504		1-(pyridazin-3-yl)-N-[4-({(3R)-1-[3-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 528 $(M+H)^+$
505		1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(pyridin-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 445 $(M+H)^+$
506		N-(4-{[(3R)-1-(3-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
507		N-(4-{[(3R)-1-(4-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
508		N-(4-{[(3R)-1-(2-methyl-2-phenylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 486 $(M+H)^+$
509		N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 480 $(M+H)^+$
510		N-(4-{[(3R)-1-(methoxyacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 412 $(M+H)^+$
511		1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(thiophen-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
512		1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[3-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 526 $(M+H)^+$
513		N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 410 $(M+H)^+$
514		N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
515		N-(4-{[(3R)-1-(2,2-dimethylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
516		N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 480 $(M+H)^+$
517		1-(pyridazin-3-yl)-N-[4-({(3R)-1-[4-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 512 $(M+H)^+$
518		N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 462

			$(M+H)^+$
519		1-(pyridazin-3-yl)-N-[4-({(3R)-1-[4-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 528 $(M+H)^+$
520		N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
521		1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(3,3,3-trifluoropropanoyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
522		N-[4-({(3R)-1-[difluoro(phenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$
523		N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
524		N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 486 $(M+H)^+$

Example 309

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]furan-2-carboxamide

Example 309A

tert-butyl (1-(6-chloropyridazin-3-yl)azetidin-3-yl)carbamate

tert-Butyl azetidin-3-ylcarbamate (500 mg, 2.90 mmol) and 3,6-dichloropyridazine (454 mg, 3.05 mmol) were combined in DMSO (5 mL) and N-ethyl-N-isopropylpropan-2-amine (563 mg, 4.35 mmol), and the mixture was heated overnight at 100°C. The mixture was cooled to room temperature and diluted with water. Filtration provided the title compound.

Example 309B

tert-butyl (1-(pyridazin-3-yl)azetidin-3-yl)carbamate

A mixture of tert-butyl 1-(6-chloropyridizan-3-yl)azetidin-3-ylcarbamate (413 mg, 1.45 mmol), 1,4-cyclohexadiene (1.10 mL, 11.6 mmol) and triethylamine (0.61 mL, 1.45 mmol) was purged with nitrogen and 5% palladium on carbon (20 mg) was added. The reaction mixture was heated to 80 °C overnight, cooled to room temperature and filtered through diatomaceous earth, rinsing with methanol. Concentration provided the title compound.

Example 309C

1-(pyridazin-3-yl)azetidin-3-amine

Tert-butyl 1-(pyridazin-3-yl)azetidin-3-ylcarbamate•triethylamine hydrochloride (200 mg, 0.516 mmol) was dissolved in methanol (1.5 mL) and a 4N solution of HCl in dioxane (1.5 mL, 6.00 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 1 hour then concentrated to dryness to give the title compound.

Example 309D

5-(1-isobutyl-1H-pyrazol-4-yl)furan-2-carboxylic acid

The title compound was prepared as described as described in Example 148A, substituting 5-bromofuran-2-carboxylic acid for 4-bromoaniline.

Example 309E

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]furan-2-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(pyridazin-3-yl)azetidin-3-amine for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 5-(1-isobutyl-1H-pyrazol-4-yl)furan-2-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.83 (d, J = 7.5 Hz, 1H), 8.57 (dd, J = 4.5, 1.3 Hz, 1H), 8.15 (d, J = 0.7 Hz, 1H), 7.88 (d, J = 0.7 Hz, 1H), 7.39 (dd, J = 8.9, 4.5 Hz, 1H), 7.16 (d, J = 3.5 Hz, 1H), 6.84 (dd, J = 8.9, 1.4 Hz, 1H), 6.64 (d, J = 3.5 Hz, 1H), 4.97 – 4.84 (m, 1H), 4.38 (t, J = 8.1 Hz, 2H), 4.06 (dd, J = 8.6, 5.7 Hz, 2H), 3.95 (d, J = 7.2 Hz, 2H), 2.21 – 2.05 (m, 1H), 0.85 (d, J = 6.7 Hz, 6H); MS (ESI(+)) m/e 367 $(M+H)^+$.

Example 310

(3S)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 147, substituting (S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate in Example 147A. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.06 (s, 1H), 8.48 (dd, J = 4.4, 1.2 Hz, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.43 – 7.25 (m, 1H), 7.18 (d, J = 8.6 Hz, 2H), 6.87 (dd, J = 9.2, 1.2 Hz, 1H), 4.64 – 4.48 (m, 1H), 4.15 – 3.97 (m, 1H), 3.76 (dd, J = 10.4, 8.0 Hz, 1H), 3.69 – 3.54 (m, 2H), 3.54 – 3.38 (m, 1H), 3.20 – 3.03 (m, 1H), 3.02 – 2.83 (m, 2H), 2.79 – 2.64 (m, 1H), 2.64 – 2.52 (m, 1H), 2.37 – 2.13 (m, 2H), 1.90 – 1.68 (m, 2H), 1.59 – 1.29 (m, 2H), 0.99 (dt, J = 14.5, 7.0 Hz, 6H); MS (ESI(+)) m/e 422 $(M+H)^+$.

Example 311

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 147, substituting (S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate in Example 147A and benzoic acid for 2-methylpropanoic acid in Example 147D. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.06 (s, 1H), 8.48 (dd, J = 4.4, 1.3 Hz, 1H), 7.55 (d, J = 8.6 Hz, 1H), 7.51 – 7.39 (m, 5H), 7.34 (dd, J = 9.1, 4.5 Hz, 1H), 7.25 – 7.19 (m, 2H), 6.87 (dd, J = 9.1, 1.3 Hz, 1H), 4.65 – 4.48

(m, 1H), 3.84 – 3.53 (m, 4H), 3.48 (dt, J = 10.2, 7.4 Hz, 1H), 3.22 – 2.69 (m, 3H), 2.36 – 2.13 (m, 2H), 1.98 – 1.48 (m, 4H); MS (ESI(+)) m/e 456 $(M+H)^+$.

Example 312

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 147, substituting (S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate in Example 147A and tetrahydro-2H-pyran-4-ylacetic acid for 2-methylpropanoic acid in Example 147D. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.06 (s, 1H), 8.48 (dd, J = 4.4, 1.2 Hz, 1H), 7.54 (d, J = 8.6 Hz, 2H), 7.39 – 7.27 (m, 1H), 7.17 (d, J = 8.6 Hz, 2H), 6.87 (dd, J = 9.2, 1.2 Hz, 1H), 4.65 – 4.45 (m, 1H), 4.07 – 3.92 (m, 1H), 3.89 – 3.68 (m, 3H), 3.68 – 3.54 (m, 2H), 3.54 – 3.39 (m, 1H), 3.22 – 2.93 (m, 2H), 2.80 – 2.65 (m, 1H), 2.64 – 2.52 (m, 1H), 2.38 – 2.13 (m, 4H), 2.00 – 1.84 (m, 1H), 1.80 (dt, J = 27.7, 7.7 Hz, 2H), 1.68 – 1.14 (m, 7H); MS (ESI(+)) m/e 478 $(M+H)^+$.

Example 313

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 147, substituting (S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate in Example 147A and 2,2-dimethylpropanoic acid for 2-methylpropanoic acid in Example 147D. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.05 (s, 1H), 8.47 (dd, J = 4.4, 1.0 Hz, 1H), 7.52 (d, J = 8.5 Hz, 2H), 7.32 (dd, J = 9.1, 4.5 Hz, 1H), 7.16 (d, J = 8.5 Hz, 2H), 6.86 (dd, J = 9.2, 1.0 Hz, 1H), 4.39 (d, J = 13.2 Hz, 2H), 3.75 (dd, J = 10.4, 8.0 Hz, 1H), 3.69 – 3.54 (m, 2H), 3.46 (dt, J = 10.1, 7.5 Hz, 1H), 3.27 (dd, J = 14.8, 7.4 Hz, 1H), 2.96 (dd, J = 12.8, 7.0 Hz, 1H), 2.84 (dd, J = 22.1, 9.6 Hz, 2H), 2.78 – 2.64 (m, 1H), 2.27 (dt, J = 7.1, 5.0 Hz, 1H), 2.18 (ddd, J = 14.3, 11.6, 7.3 Hz, 1H), 1.77 (d, J = 11.3 Hz, 2H), 1.54 – 1.31 (m, 3H), 1.18 (d, J = 16.8 Hz, 9H); MS (ESI(+)) m/e 436 $(M+H)^+$.

Table 10.

The following Examples were essentially prepared as described in Example 313, substituting the appropriate carboxylic acid for 2,2-dimethylpropanoic acid.

Ex		Name	MS
630		(3S)-1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide	(ESI(+)) m/e 463 $(M+H)^+$
631		(3S)-N-{4-[1-(4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 470 $(M+H)^+$
632		(3S)-N-(4-{1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}phenyl)-1-	(ESI(+))

		(pyridazin-3-yl)pyrrolidine-3-carboxamide	m/e 498 $(M+H)^+$
633		(3S)-N-(4-{1-[(2S)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 500 $(M+H)^+$
634		(3S)-N-(4-{1-[(2R)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 500 $(M+H)^+$
635		(3S)-N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
636		(3S)-N-(4-{1-[(4-methylphenoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 500 $(M+H)^+$
637		(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
638		(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
639		(3S)-N-{4-[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 506 $(M+H)^+$
640		(3S)-N-(4-{1-[(2,6-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 538 $(M+H)^+$
641		(3S)-N-{4-[1-(naphthalen-1-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 520 $(M+H)^+$
642		(3S)-1-(pyridazin-3-yl)-N-(4-{1-[4-(thiophen-2-yl)butanoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 504 $(M+H)^+$
643		(3S)-N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 434 $(M+H)^+$
644		(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
645		(3S)-N-{4-[1-(2,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
646		(3S)-N-{4-[1-(naphthalen-2-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 520 $(M+H)^+$
647		(3S)-N-(4-{1-[3-(phenylsulfonyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 548 $(M+H)^+$
648		(3S)-1-(pyridazin-3-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]pyrrolidine-3-carboxamide	(ESI(+)) m/e 538 $(M+H)^+$
649		(3S)-N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 446 $(M+H)^+$
650		(3S)-N-{4-[1-(N-benzoylglycyl)piperidin-4-yl]phenyl}-1-	(ESI(+))

		(pyridazin-3-yl)pyrrolidine-3-carboxamide	m/e 513 $(M+H)^+$
651		(3S)-N-(4-{1-[(2,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 538 $(M+H)^+$
652		(3S)-N-{4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 470 $(M+H)^+$
653		(3S)-1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
654		(3S)-N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
655		(3S)-1-(pyridazin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
656		(3S)-N-(4-{1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 471 $(M+H)^+$
657		(3S)-N-(4-{1-[(3-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 504 $(M+H)^+$
658		(3S)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 408 $(M+H)^+$
659		(3S)-N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
660		(3S)-N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 448 $(M+H)^+$
661		(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
662		(3S)-N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 420 $(M+H)^+$
663		(3S)-N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
669		(3S)-N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
670		(3S)-N-{4-[1-(2-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
671		(3S)-N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
672		(3S)-N-{4-[1-(2,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
673		(3S)-N-[4-(1-heptanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-	(ESI(+))

		yl)pyrrolidine-3-carboxamide	m/e 464 $(M+H)^+$
674		(3S)-N-{4-[1-(2,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
675		(3S)-N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 488 $(M+H)^+$
676		(3S)-N-{4-[1-(2,3-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
677		(3S)-N-{4-[1-(3-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 470 $(M+H)^+$
678		(3S)-N-[4-(1-hexanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
679		(3S)-N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
680		(3S)-N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
681		(3S)-N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
682		(3S)-N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
683		(3S)-N-(4-{1-[(3,5-dimethylphenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 498 $(M+H)^+$
684		(3S)-N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
685		(3S)-N-{4-[1-(3-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 488 $(M+H)^+$
686		(3S)-N-(4-{1-[(4-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 504 $(M+H)^+$
687		(3S)-N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 446 $(M+H)^+$
688		(3S)-N-{4-[1-(3,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
689		(3S)-N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
690		(3S)-N-(4-{1-[2-chloro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 558 $(M+H)^+$
691		(3S)-N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-	(ESI(+))

		yl)pyrrolidine-3-carboxamide	m/e 394 $(M+H)^+$
692		(3S)-N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 492 $(M+H)^+$
693		(3S)-N-{4-[1-(3,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
694		(3S)-N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 452 $(M+H)^+$
695		(3S)-N-{4-[1-(2,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
696		(3S)-N-{4-[1-(2,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
697		(3S)-N-{4-[1-(5-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 488 $(M+H)^+$
698		(3S)-N-{4-[1-(diphenylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 546 $(M+H)^+$
699		(3S)-1-(pyridazin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
700		(3S)-N-{4-[1-(pent-4-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 434 $(M+H)^+$
701		(3S)-1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 540 $(M+H)^+$
702		(3S)-N-(4-{1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 496 $(M+H)^+$
703		(3S)-N-(4-{1-[2-fluoro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 542 $(M+H)^+$
704		(3S)-N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
705		(3S)-N-{4-[1-(4-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 486 $(M+H)^+$
706		(3S)-N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
707		(3S)-N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
708		(3S)-N-{4-[1-(4-tert-butylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 512 $(M+H)^+$
709		(3S)-N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-	(ESI(+))

		3-yl)pyrrolidine-3-carboxamide	m/e 490 $(M+H)^+$
710		(3S)-N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 488 $(M+H)^+$
711		(3S)-1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
712		(3S)-N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 434 $(M+H)^+$
713		(3S)-N-{4-[1-(pent-4-ynoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 432 $(M+H)^+$
714		(3S)-N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 488 $(M+H)^+$
715		(3S)-N-(4-{1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 454 $(M+H)^+$
716		(3S)-N-(4-{1-[(1-acetylpiperidin-4-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 505 $(M+H)^+$
717		(3S)-N-{4-[1-(but-3-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 420 $(M+H)^+$
718		(3S)-N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
719		(3S)-N-{4-[1-(3-fluoro-4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 488 $(M+H)^+$
720		(3S)-N-{4-[1-(3-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 486 $(M+H)^+$
721		(3S)-N-(4-{1-[(2-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 504 $(M+H)^+$
722		(3S)-N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 468 $(M+H)^+$
723		(3S)-N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
724		(3S)-N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 507 $(M+H)^+$
725		(3S)-N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
726		(3S)-N-{4-[1-(4-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 481 $(M+H)^+$
727		(3S)-N-{4-[1-(2-methoxybenzoyl)piperidin-4-yl]phenyl}-1-	(ESI(+))

		(pyridazin-3-yl)pyrrolidine-3-carboxamide	m/e 486 $(M+H)^+$
728		(3S)-N-{4-[1-(2,3-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
729		(3S)-N-(4-{1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 498 $(M+H)^+$
730		(3S)-N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
731		(3S)-1-(pyridazin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
732		(3S)-N-{4-[1-(4-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 472 $(M+H)^+$
733		(3S)-N-{4-[1-(3-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 481 $(M+H)^+$
734		(3S)-1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
735		(3S)-N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
736		(3S)-N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$

Example 314

tert-butyl 4-(4-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting 1-(pyridazin-3-yl)azetidin-3-amine for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 4-(1-(tert-butoxycarbonyl)piperidin-4-yl)benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) d 8.96 (d, J = 7.0 Hz, 1H), 8.56 (dd, J = 4.6, 1.3 Hz, 1H), 7.82 (d, J = 8.3 Hz, 2H), 7.41 – 7.31 (m, 3H), 6.83 (dd, J = 9.0, 1.3 Hz, 1H), 4.96 – 4.85 (m, 1H), 4.37 (t, J = 8.1 Hz, 2H), 4.16 – 3.97 (m, 4H), 2.88 – 2.65 (m, 3H), 1.80 – 1.70 (m, 2H), 1.60 – 1.43 (m, 2H), 1.41 (s, 9H); MS (ESI(+)) m/e 438 $(M+H)^+$.

Example 315

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide

Example 315A

5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-2-carboxylic acid

The title compound was prepared as described as described in Example 148A, substituting 5-bromothiophene-2-carboxylic acid for 4-bromoaniline.

Example 315B

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(pyridazin-3-yl)azetidin-3-amine for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-2-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.99 (d, J = 7.1 Hz, 1H), 8.57 (dd, J = 4.5, 1.3 Hz, 1H), 8.14 (d, J = 0.8 Hz, 1H), 7.81 – 7.79 (m, 1H), 7.72 (d, J = 3.9 Hz, 1H), 7.39 (dd, J = 8.9, 4.5 Hz, 1H), 7.21 (d, J = 3.8 Hz, 1H), 6.84 (dd, J = 9.0, 1.4 Hz, 1H), 4.92 – 4.81 (m, 1H), 4.37 (t, J = 8.1 Hz, 2H), 4.03 (dd, J = 8.6, 5.5 Hz, 2H), 3.92 (d, J = 7.1 Hz, 2H), 2.19 – 2.04 (m, 1H), 0.85 (d, J = 6.7 Hz, 6H); MS (ESI(+)) m/e 383 $(M+H)^+$.

Example 564

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 564A

tert-butyl 4-((4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)phenyl)thio)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(4-aminophenylthio)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 564B

tert-butyl 4-((4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)phenyl)sulfonyl)piperidine-1-carboxylate

To a 20 mL vial was added tert-butyl 4-((4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)phenyl)thio)piperidine-1-carboxylate (8.3 g, 15.79 mmol) in dichloromethane (79 ml). The reaction mixturewas cooled to ca -20°C in a methanol /dry ice bath treated with m-chloroperbenzoic acid (8.17 g, 47.4 mmol) and was allowed to warm slowly to room temperature. When complete, the reaction mixture was treated with 1N aqueous sodium hydroxide and extracted with dichloromethane. The combined organics were dried with sodium sulfate, filtered and concentrated by rotary evaporation. The residue was purified by regular phase chromatography to give the title compound.

Example 564C

tert-butyl 4-(4-(azetidine-3-carboxamido)phenylsulfonyl)piperidine-1-carboxylate

tert-Butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenylsulfonyl)piperidine-1-carboxylate (7.94 g, 14.24 mmol) and ethanol (160

ml) were added to 20% $Pd(OH)_2/C$, wet (1.5 g, 1.089 mmol) in a 250 mL SS pressure bottle and the mixture was stirred for 16 hours at 30 psi and room temperature. The mixture was filtered through a nylon membrane and concentrated to give the title compound.

Example 564D

tert-butyl 4-((4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)sulfonyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 147A, substituting tert-butyl 4-(4-(azetidine-3-carboxamido)phenylsulfonyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 564E

tert-butyl 4-((4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)sulfonyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 147B, substituting tert-butyl 4-((4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)sulfonyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 564F

N-(4-(piperidin-4-ylsulfonyl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-((4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)sulfonyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 564G

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-ylsulfonyl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 3-chlorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO/D_2O) δ ppm 8.53 (dd, J = 4.4, 1.2 Hz, 1H), 7.93 – 7.84 (m, 2H), 7.84 – 7.77 (m, 2H), 7.72 (dd, J = 9.3, 4.4 Hz, 1H), 7.58 – 7.38 (m, 2H), 7.40 – 7.21 (m, 3H), 4.58 – 4.37 (m, 5H), 4.02 (d, J = 31.5 Hz, 3H), 3.88 (tt, J = 8.8, 5.9 Hz, 1H), 3.48 (ddd, J = 11.6, 7.7, 3.9 Hz, 1H), 2.99 (t, J = 11.9 Hz, 2H), 1.92 (d, J = 10.6 Hz, 2H), 1.53 (qd, J = 12.2, 4.5 Hz, 3H); MS (ESI(+)) m/e 540 $(M+H)^+$.

Table 11.

The following Examples were prepared essentially as described in Example 564, substituting the appropriate carboxylic acid in Example 564F. Some products were purified

by flash chromatography while others were purified by reverse-phase HPLC. Accordingly, some Examples were isolated as trifluoroacetic acid salts.

Ex		Name	MS
565		N-(4-{[1-(4-tert-butylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 562 $(M+H)^+$
566		N-(4-{[1-(4-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 536 $(M+H)^+$
567		N-(4-{[1-(4-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 520 $(M+H)^+$
568		N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 512 $(M+H)^+$
569		N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
570		N-(4-{[1-(2-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 536 $(M+H)^+$
571		N-[4-({1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 548 $(M+H)^+$
572		N-[4-({1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 548 $(M+H)^+$
573		N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 540 $(M+H)^+$
574		N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 506 $(M+H)^+$
575		1-(pyridazin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]sulfonyl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 526 $(M+H)^+$
576		N-(4-{[1-(2,5-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 542 $(M+H)^+$
577		N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
578		N-(4-{[1-(2-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 520 $(M+H)^+$
579		N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 538 $(M+H)^+$
580		N-(4-{[1-(3-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 520 $(M+H)^+$
581		N-(4-{[1-(2,3-dimethylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 534

			$(M+H)^+$
582		N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 538 $(M+H)^+$
583		N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
584		1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 575 $(M+H)^+$
585		N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 556 $(M+H)^+$
586		N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 542 $(M+H)^+$
587		1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 574 $(M+H)^+$
588		N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 524 $(M+H)^+$
589		N-(4-{[1-(2,3-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 542 $(M+H)^+$
590		N-(4-{[1-(2,4-dichlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 574 $(M+H)^+$
591		N-(4-{[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 556 $(M+H)^+$
592		N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 470 $(M+H)^+$
593		N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 542 $(M+H)^+$
594		N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 486 $(M+H)^+$
595		N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 500 $(M+H)^+$
596		N-(4-{[1-(3-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 536 $(M+H)^+$
597		N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 486 $(M+H)^+$
598		N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 472 $(M+H)^+$
599		N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 498

			$(M+H)^+$
600		N-(4-{[1-(phenylacetyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 520 $(M+H)^+$
601		N-[4-({1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 546 $(M+H)^+$
611		N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 540 $(M+H)^+$
612		N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 500 $(M+H)^+$
613		N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 538 $(M+H)^+$

Example 602

N-{4-[1-(2-methylalanyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-methylalanine for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.14 (s, 1H), 8.18 – 8.11 (m, 4H), 8.07 (d, J = 2.5 Hz, 1H), 7.74 (dd, J = 8.6, 5.4 Hz, 1H), 7.55 (d, J = 8.5 Hz, 2H), 7.52 (dd, J = 8.7, 2.3 Hz, 1H), 7.21 (d, J = 8.5 Hz, 2H), 4.41 – 3.68 (m, 7H), 3.10 – 2.89 (m, 2H), 2.89 – 2.74 (m, 1H), 1.85 (d, J = 12.3 Hz, 2H), 1.58 (s, 6H), 1.52 – 1.37 (m, 2H); MS (ESI(+)) m/e 422 $(M+H)^+$.

Example 603

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide

Example 603A

(R)-tert-butyl 3-(5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-2-carboxamido)pyrrolidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting (R)-tert-butyl 3-aminopyrrolidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-2-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 603B

(R)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide

The title compound was prepared as described in Example 1D, substituting (R)-tert-butyl 3-(5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-2-carboxamido)pyrrolidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 603C

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide

The title compound was prepared as described in Example 1C, substituting (R)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 0.85 (d, J=6.78 Hz, 6 H) 1.90 - 2.38 (m, 3 H) 3.16 - 3.66 (m, 4 H) 3.92 (d, J=7.12 Hz, 2 H) 4.59 (d, J=5.76 Hz, 1 H) 6.92 (dd, J=8.48, 1.70 Hz, 1 H) 7.08 - 7.27 (m, 2 H) 7.72 (d, J=3.73 Hz, 1 H) 7.79 (s, 1 H) 7.85 (d, J=3.73 Hz, 1 H) 7.95 (d, J=2.71 Hz, 1 H) 8.13 (s, 1 H) 8.54 (d, J=7.12 Hz, 1 H); MS (ESI(+)) m/e 396 $(M+H)^+$.

Example 604

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-2-carboxamide

The title compound was prepared as described in Example 1C, substituting 4-bromopyridazine for 3-bromopyridine and (R)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO–d_6) δ ppm 0.85 (d, J=6.44 Hz, 6 H) 1.90 - 2.39 (m, 3 H) 3.38 - 3.75 (m, 4 H) 3.92 (d, J=7.12 Hz, 2 H) 4.43 - 4.71 (m, 1 H) 6.62 (dd, J=6.44, 3.05 Hz, 1 H) 7.19 (d, J=3.73 Hz, 1 H) 7.71 (d, J=4.07 Hz, 1 H) 7.79 (s, 1 H) 8.13 (s, 1 H) 8.55 (dd, J=8.99, 6.95 Hz, 2 H) 8.64 (d, J=2.71 Hz, 1 H); MS (ESI(+)) m/e 397 $(M+H)^+$.

Example 605

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide

Example 605A

(R)-N-(1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)-5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-2-carboxamide

The title compound was prepared as described in Example 147A, substituting (R)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 605B

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide

The title compound was prepared as described in Example 1B, substituting (R)-N-(1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)-5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-2-carboxamide for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-

carboxamido)phenoxy)piperidine-1-carboxylate. ^{1}H NMR (400 MHz, DMSO–d_6) δ ppm 0.85 (d, J=6.71 Hz, 6 H) 1.94 - 2.38 (m, 3 H) 3.39 - 3.84 (m, 4 H) 3.92 (d, J=7.32 Hz, 2 H) 4.45 - 4.66 (m, 1 H) 6.88 (d, J=8.24 Hz, 1 H) 7.19 (d, J=3.97 Hz, 1 H) 7.34 (dd, J=9.00, 4.43 Hz, 1 H) 7.73 (d, J=3.97 Hz, 1 H) 7.80 (s, 1 H) 8.14 (s, 1 H) 8.49 (d, J=3.66 Hz, 1 H) 8.56 (d, J=6.71 Hz, 1 H); MS (ESI(+)) m/e 397 $(M+H)^+$.

Example 606

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide

Example 606A

(S)-tert-butyl 3-(5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-2-carboxamido)pyrrolidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting (S)-tert-butyl 3-aminopyrrolidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-2-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 606B

(S)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl 3-(5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-2-carboxamido)pyrrolidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 606C

(S)-N-(1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)-5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-2-carboxamide

The title compound was prepared as described in Example 147A, substituting (S)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 606D

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide

The title compound was prepared as described in Example 1B, substituting (S)-N-(1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)-5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-2-carboxamide for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO–d_6) δ ppm 0.85 (d, J=6.78 Hz, 6 H) 1.91 - 2.42 (m, 3 H) 3.49 - 3.88 (m, 4 H) 3.87 - 4.07 (m, 2 H) 4.30 -

4.81 (m, 1 H) 7.20 (d, J=3.73 Hz, 1 H) 7.68 (d, J=8.82 Hz, 1 H) 7.74 - 7.94 (m, 3 H) 8.14 (s, 1 H) 8.58 (d, J=3.05 Hz, 1 H) 8.71 (d, J=6.44 Hz, 1 H); MS (ESI(+)) m/e 397 $(M+H)^+$.

Example 607

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-2-carboxamide

The title compound was prepared as described in Example 1C, substituting 4-bromopyridazine for 3-bromopyridine and (S)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO–d_6) δ ppm 0.75 - 0.98 (m, 6 H) 1.98 - 2.44 (m, 3 H) 3.67 - 4.18 (m, 6 H) 4.66 (s, 1 H) 7.15 (dd, J=7.12, 3.05 Hz, 1 H) 7.21 (d, J=3.73 Hz, 1 H) 7.54 - 7.91 (m, 2 H) 8.14 (s, 1 H) 8.56 - 8.95 (m, 3 H); MS (ESI(+)) m/e 397 $(M+H)^+$.

Example 608

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide

The title compound was prepared as described in Example 1C, substituting (S)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO–d_6) δ ppm 0.85 (d, J=6.78 Hz, 6 H) 1.88 - 2.38 (m, 3 H) 3.11 - 3.67 (m, 4 H) 3.92 (d, J=7.46 Hz, 2 H) 4.45 - 4.76 (m, 1 H) 6.75 - 7.01 (m, 1 H) 7.03 - 7.25 (m, 2 H) 7.73 (d, J=4.07 Hz, 1 H) 7.79 (s, 1 H) 7.81 - 7.93 (m, 1 H) 7.95 (d, J=2.71 Hz, 1 H) 8.13 (s, 1 H) 8.54 (d, J=7.12 Hz, 1 H); MS (ESI(+)) m/e 396 $(M+H)^+$.

Example 609

tert-butyl 4-(2-methyl-1-oxo-1-{4-[4-({[1-(pyridin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidin-1-yl}propan-2-yl)piperazine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-(4-(tert-butoxycarbonyl)piperazin-1-yl)-2-methylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. $_1$H NMR (300 MHz, DMSO-d_6) δ ppm 10.00 (s, 1H), 7.93 (dd, J = 4.6, 1.4 Hz, 1H), 7.85 (d, J = 2.5 Hz, 1H), 7.53 (d, J = 8.6 Hz, 2H), 7.23 – 7.13 (m, 3H), 6.86 (ddd, J = 8.3, 2.9, 1.4 Hz, 1H), 5.43 (bs, 1H), 4.59 (bs, 1H), 4.15 – 4.03 (m, 2H), 4.02 – 3.90 (m, 2H), 3.71 (tt, J = 8.3, 6.1 Hz, 1H), 3.42 – 3.32 (m, 4H), 3.04 (bs, 1H), 2.80 – 2.62 (m, 2H), 2.39 (bs, 4H), 1.78 (d, J = 11.1 Hz, 2H), 1.57 – 1.42 (m, 2H), 1.39 (s, 9H), 1.17 (s, 6H); MS (ESI(+)) m/e 591 $(M+H)^+$.

Example 610

N-(4-{1-[2-methyl-2-(piperazin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(2-methyl-1-oxo-1-{4-[4-({[1-(pyridin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidin-1-yl}propan-2-yl)piperazine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.08 (s, 1H), 8.52 (s, 1H), 8.14 (d, J = 5.2 Hz, 1H), 8.07 (d, J = 2.6 Hz, 1H), 7.76 (dd, J = 8.7, 5.4 Hz, 1H), 7.54 (d, J = 8.6 Hz, 2H), 7.20 (d, J = 8.6 Hz, 2H), 4.88 (bs, 4H), 4.23 (t, J = 8.4 Hz, 2H), 4.12 (dd, J = 7.9, 5.9 Hz, 2H), 3.87 – 3.66 (m, 1H), 3.10 (bs, 4H), 2.85 – 2.54 (m, 5H), 1.79 (d, J = 13.1 Hz, 2H), 1.61 – 1.32 (m, 2H), 1.21 (s, 6H); MS (ESI(+)) m/e 491 $(M+H)^+$.

Example 614

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide

Example 614A

tert-butyl 4-((4-(1-(5,6-dichloropyridazin-4-yl)azetidine-3 carboxamido)phenyl)sulfonyl)piperidine-1-carboxylate

To 3,4,5-trichloropyridazine (1.624 g, 8.85 mmol) and N-ethyl-N-isopropylpropan-2-amine (2.289 g, 17.71 mmol) in 50 mL N,N-dimethylformamide at 0°C was added tert-butyl 4-(4-(azetidine-3-carboxamido)phenylsulfonyl)piperidine-1-carboxylate (2.5 g, 5.90 mmol) in 10 ml N,N-dimethylformamide, dropwise. The reaction mixture was stirred from 0°C to room temperature overnight, diluted with water and extracted with ethyl acetate. The organic layer was dried with magnesium sulfate, filtered, concentrated and purified by flash chromatography to give the title compound.

Example 614B

tert-butyl 4-((4-(1-(pyridazin-4-yl)azetidine-3-carboxamido)phenyl)sulfonyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1B, substituting tert-butyl 4-((4-(1-(5,6-dichloropyridazin-4-yl)azetidine-3 carboxamido)phenyl)sulfonyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3 carboxamido)phenoxy)piperidine-1-carboxylate.

Example 614C

N-(4-(piperidin-4-ylsulfonyl)phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-((4-(1-(pyridazin-4-yl)azetidine-3-carboxamido)phenyl)sulfonyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 614D

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-ylsulfonyl)phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and isobutyric acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.70 (s, 1H), 8.79 (d, J = 7.2 Hz, 1H), 8.55 (d, J = 3.1 Hz, 1H), 7.93 – 7.86 (m, 2H), 7.85 – 7.78 (m, 2H), 7.00 (dd, J = 7.2, 3.1 Hz, 1H), 4.65 – 4.36 (m, 5H), 4.09 – 3.82 (m, 2H), 3.35 – 2.67 (m, 4H), 1.95 – 1.76 (m, 2H), 1.48 – 0.99 (m, 2H), 0.95 (d, J = 6.7 Hz, 6H); MS (ESI(+)) m/e 472 $(M+H)^+$.

Example 615

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-ylsulfonyl)phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.70 (s, 1H), 8.79 (d, J = 7.2 Hz, 1H), 8.55 (d, J = 3.3 Hz, 1H), 7.93 – 7.86 (m, 2H), 7.85 – 7.78 (m, 2H), 7.49 – 7.29 (m, 5H), 7.00 (dd, J = 7.2, 3.1 Hz, 1H), 4.65 – 4.35 (m, 4H), 3.99 – 3.83 (m, 1H), 3.73 – 3.50 (m, 1H), 3.28 – 2.65 (m, 4H), 2.37 – 1.59 (m, 2H), 1.56 – 1.06 (m, 2H); MS (ESI(+)) m/e 506 $(M+H)^+$.

Example 616

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-ylsulfonyl)phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 4-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.70 (s, 1H), 8.79 (d, J = 6.9 Hz, 1H), 8.55 (d, J = 3.1 Hz, 1H), 7.93 – 7.86 (m, 2H), 7.85 – 7.78 (m, 2H), 7.52 – 7.38 (m, 2H), 7.31 – 7.20 (m, 2H), 7.00 (dd, J = 7.2, 3.1 Hz, 1H), 4.63 – 4.19 (m, 4H), 3.99 – 3.83 (m, 1H), 3.73 – 3.46 (m, 2H), 3.23 – 2.65 (m, 3H), 2.37 – 1.60 (m, 2H), 1.56 – 1.06 (m, 2H); MS (ESI(+)) m/e 524 $(M+H)^+$.

Example 617

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-ylsulfonyl)phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide for tert-butyl 4-(4-

aminophenoxy)piperidine-1-carboxylate and cyclopentanecarboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.69 (s, 1H), 8.79 (d, J = 7.2 Hz, 1H), 8.55 (d, J = 3.1 Hz, 1H), 7.97 – 7.77(m, 4H), 7.00 (dd, J = 7.2, 3.1 Hz, 1H), 4.67 – 4.37 (m, 5H), 4.11 – 4.01 (m, 1H), 3.99 – 3.84 (m, 1H), 3.35 – 2.71 (m, 4H), 1.95 – 1.06 (m, 10H), 1.07 – 0.97 (m, 2H); MS (ESI(+)) m/e 498 $(M+H)^+$.

Example 618

N-[(3R)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide

3,4,5-Trichloropyridazine (269 mg, 1.464 mmol) was dissolved in 5 ml N,N-dimethylformamide and triethylamine (370 mg, 3.66 mmol) was added. The solution was cooled with an ice-bath when (R)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide bistrifluoroacetate (400 mg, 0.732 mmol) in N,N-dimethylformamide was added dropwise. The reaction mixture was stirred from 0°C to room temperature overnight, diluted with water and extracted with ethyl acetate. The organic layer was dried with magnesium sulfate, filtered, concentrated, and purified by flash chromatography to give the title compound. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.66 (s, 1H), 8.49 (d, J = 6.5 Hz, 1H), 8.14 (s, 1H), 7.79 (s, 1H), 7.70 (d, J = 3.9 Hz, 1H), 7.20 (d, J = 3.8 Hz, 1H), 4.59 – 4.45 (m, 1H), 4.05 (dd, J = 11.0, 6.4 Hz, 1H), 4.01 – 3.66 (m, 5H), 2.30 – 1.94 (m, 3H), 0.85 (d, J = 6.7 Hz, 6H); MS (ESI(+)) m/e 465 $(M+H)^+$.

Example 619

N-[(3R)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide

The title compound was prepared as described in Example 147A, substituting (R)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.55 (d, J = 6.6 Hz, 1H), 8.14 (s, 1H), 7.80 (s, 1H), 7.72 (d, J = 3.9 Hz, 1H), 7.49 (d, J = 9.4 Hz, 1H), 7.20 (d, J = 3.8 Hz, 1H), 7.03 (d, J = 9.4 Hz, 1H), 4.64 – 4.52 (m, 1H), 3.92 (d, J = 7.2 Hz, 2H), 3.76 (dd, J = 11.0, 6.6 Hz, 1H), 3.69 – 3.41 (m, 3H), 2.34 – 2.21 (m, 1H), 2.19 – 2.02 (m, 2H), 0.85 (d, J = 6.7 Hz, 6H); MS (ESI(+)) m/e 431 $(M+H)^+$.

Example 620

N-[(3S)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide

The title compound was prepared as described in Example 618, substituting (S)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide for (R)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.70 (s, 1H), 8.55 (d, J = 6.5 Hz, 1H), 8.19 (s, 1H), 7.85 (s, 1H), 7.75 (d, J = 3.9

Hz, 1H), 7.25 (d, J = 3.8 Hz, 1H), 4.64 – 4.47 (m, 1H), 4.10 (dd, J = 10.9, 6.4 Hz, 1H), 4.07 – 3.67 (m, 5H), 2.32 – 2.02 (m, 3H), 0.94 – 0.75 (m, 6H); MS (ESI(+)) m/e 465 $(M+H)^+$.

Example 621

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide

The title compound was prepared as described in Example 147A, substituting (S)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.54 (d, J = 6.7 Hz, 1H), 8.13 (d, J = 0.8 Hz, 1H), 7.79 (d, J = 0.8 Hz, 1H), 7.72 (d, J = 3.9 Hz, 1H), 7.49 (d, J = 9.4 Hz, 1H), 7.19 (d, J = 3.8 Hz, 1H), 7.03 (d, J = 9.4 Hz, 1H), 4.63 – 4.53 (m, 1H), 3.92 (d, J = 7.2 Hz, 2H), 3.76 (dd, J = 11.0, 6.6 Hz, 1H), 3.71 – 3.39 (m, 3H), 2.37 – 2.00 (m, 3H), 0.85 (d, J = 6.7 Hz, 6H); MS (ESI(+)) m/e 431 $(M+H)^+$.

Example 622

N-[(3R)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide

Example 622A

5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-3-carboxylic acid

The title compound was prepared as described as described in Example 148A, substituting 5-bromothiophene-3-carboxylic acid for 4-bromoaniline.

Example 622B

(R)-tert-butyl 3-(5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-3-carboxamido)pyrrolidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting (R)-tert-butyl 3-aminopyrrolidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 622B

(R)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-3-carboxamide

The title compound was prepared as described in Example 1D, substituting (R)-tert-butyl 3-(5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-3-carboxamido)pyrrolidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 622C

N-[(3R)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide

The title compound was prepared as described in Example 618, substituting (R)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-3-carboxamide for (R)-5-(1-isobutyl-

1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.66 (s, 1H), 8.37 (d, *J* = 6.5 Hz, 1H), 8.08 (d, *J* = 0.8 Hz, 1H), 7.94 (d, *J* = 1.4 Hz, 1H), 7.74 (d, *J* = 0.8 Hz, 1H), 7.51 (d, *J* = 1.4 Hz, 1H), 4.53 (q, *J* = 5.4 Hz, 1H), 4.06 (dd, *J* = 10.9, 6.4 Hz, 1H), 3.98 – 3.66 (m, 5H), 2.30 – 1.96 (m, 3H), 0.85 (d, *J* = 6.7 Hz, 6H); MS (ESI(+)) m/e 465 $(M+H)^+$.

Example 623

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-3-carboxamide

Example 623A

(R)-N-(1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)-5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-3-carboxamide

The title compound was prepared as described in Example 147A, substituting (R)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-3-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 623B

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-3-carboxamide

The title compound was prepared as described in Example 147B, substituting (R)-N-(1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)-5-(1-isobutyl-1H-pyrazol-4-yl)thiophene-3-carboxamide for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.49 (dd, *J* = 4.5, 1.3 Hz, 1H), 8.41 (d, *J* = 6.7 Hz, 1H), 8.08 (s, 1H), 7.96 (d, *J* = 1.4 Hz, 1H), 7.73 (s, 1H), 7.54 (d, *J* = 1.4 Hz, 1H), 7.37 (dd, *J* = 9.1, 4.4 Hz, 1H), 6.92 (d, *J* = 9.1 Hz, 1H), 4.67 – 4.55 (m, 1H), 3.92 (d, *J* = 7.2 Hz, 2H), 3.78 (dd, *J* = 10.9, 6.6 Hz, 1H), 3.72 – 3.41 (m, 3H), 2.40 – 1.98 (m, 3H), 0.85 (d, *J* = 6.7 Hz, 6H); MS (ESI(+)) m/e 397 $(M+H)^+$.

Example 624

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-3-carboxamide

The title compound was prepared as described in Example 1B, substituting N-[(3R)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.86 – 8.69 (m, 2H), 8.58 (d, *J* = 6.6 Hz, 1H), 8.08 (d, *J* = 0.8 Hz, 1H), 8.01 (d, *J* = 1.4 Hz, 1H), 7.74 (d, *J* = 0.8 Hz, 1H), 7.55 (d, *J* = 1.4 Hz, 1H), 7.15 (dd, *J* = 7.3, 3.1 Hz, 1H), 4.72 – 4.59 (m, 1H), 4.08 – 3.47 (m, 6H), 2.37 – 1.97 (m, 3H), 0.85 (d, *J* = 6.7 Hz, 6H); MS (ESI(+)) m/e 397 $(M+H)^+$.

Example 625

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide

Example 625A

benzyl 4-((4-(1-(tert-butoxycarbonyl)piperidin-4-yl)phenyl)carbamoyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(4-aminophenyl)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(benzyloxycarbonyl)piperidine-4-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 625B

tert-butyl 4-(4-(piperidine-4-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1B, substituting benzyl 4-((4-(1-(tert-butoxycarbonyl)piperidin-4-yl)phenyl)carbamoyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 625C

tert-butyl 4-(4-(1-(6-chloropyridazin-3-yl)piperidine-4-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 147A, substituting tert-butyl 4-(4-(piperidine-4-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 625D

tert-butyl 4-(4-(1-(pyridazin-3-yl)piperidine-4-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 147B, tert-butyl 4-(4-(1-(6-chloropyridazin-3-yl)piperidine-4-carboxamido)phenyl)piperidine-1-carboxylate for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 625E

N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)piperidine-4-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(4-(1-(pyridazin-3-yl)piperidine-4-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 625F

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)piperidine-4-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,2-dimethylpropanoic acid for 1-

(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.86 (s, 1H), 8.51 (d, J = 3.6 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.43 – 7.31 (m, 1H), 7.26 (d, J = 8.6 Hz, 1H), 7.17 – 7.11 (m, 2H), 4.45 – 4.34 (m, 4H), 2.94 (t, J = 11.6 Hz, 1H), 2.82 (t, J = 12.5 Hz, 1H), 2.66 (dddd, J = 33.0, 15.2, 8.0, 3.6 Hz, 1H), 1.89 – 1.81 (m, 2H), 1.80 – 1.71 (m, 2H), 1.70 – 1.53 (m, 2H), 1.51 – 1.33 (m, 2H), 1.20 (s, 9H), MS (ESI(+)) m/e 450 $(M+H)^+$.

Example 626

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)piperidine-4-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)piperidine-4-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.87 (s, 1H), 8.51 (d, J = 4.8 Hz, 1H), 7.54 – 7.48 (m, 2H), 7.47 – 7.36 (m, 5H), 7.35 (dd, J = 9.3, 4.4 Hz, 1H), 7.26 (d, J = 8.7 Hz, 1H), 7.21 – 7.15 (m, 2H), 4.60 (s, 1H), 4.46 – 4.37 (m, 2H), 3.63 (s, 1H), 3.24 – 2.56 (m, 6H), 1.89 – 1.80 (m, 2H), 1.80 – 1.46 (m, 5H), MS (ESI(+)) m/e 470 $(M+H)^+$.

Example 627

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)piperidine-4-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.87 (s, 1H), 8.51 (d, J = 4.4 Hz, 1H), 7.56 – 7.38 (m, 4H), 7.35 (dd, J = 9.3, 4.4 Hz, 1H), 7.32 – 7.21 (m, 3H), 7.16 (d, J = 8.5 Hz, 2H), 4.64 (d, J = 13.1 Hz, 1H), 4.41 (d, J = 13.3 Hz, 2H), 3.15 (t, J = 12.3 Hz, 1H), 2.93 (dd, J = 18.0, 7.3 Hz, 2H), 2.70 (dddd, J = 15.1, 11.4, 10.1, 7.0 Hz, 3H), 1.86 (t, J = 13.8 Hz, 3H), 1.76 – 1.39 (m, 5H); MS (ESI(+)) m/e 488 $(M+H)^+$.

Example 628

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}piperidine-4-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)piperidine-4-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 4,4,4-trifluorobutanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.86 (s, 1H), 8.51 (d, J = 4.3 Hz, 1H), 7.49 (t, J = 8.9 Hz, 2H), 7.41 – 7.30 (m, 1H), 7.25 (d, J = 9.3 Hz, 1H), 7.14 (d, J = 8.5 Hz, 2H), 4.51 (d, J = 13.0 Hz, 1H), 4.41 (d, J = 13.3 Hz, 2H), 3.94 (d, J = 13.4 Hz, 1H), 3.07 (t, J = 12.0 Hz, 1H), 2.94 (dd, J = 18.1, 7.3 Hz, 2H), 2.77 – 2.40 (m, 9H), 1.93 – 1.80 (m, 2H), 1.71 (d, J = 25.3 Hz, 2H), 1.58 (dqd, J = 29.0, 12.7, 4.0 Hz, 3H), 1.39 (qd, J = 12.7, 4.1 Hz, 1H); MS (ESI(+)) m/e 490 $(M+H)^+$.

Example 629

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide

The title compound was prepared as described in Example 147A, substituting (S)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-3-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 8.42 (d, J = 6.7 Hz, 1H), 8.08 (s, 1H), 7.96 (d, J = 1.3 Hz, 1H), 7.74 (d, J = 0.5 Hz, 1H), 7.54 (d, J = 1.3 Hz, 1H), 7.49 (d, J = 9.5 Hz, 1H), 7.02 (d, J = 9.5 Hz, 1H), 4.87 – 4.44 (m, 1H), 3.92 (d, 2H), 3.94 – 3.38 (m, 4H), 2.50 – 1.87 (m, 3H), 0.85 (d, J = 6.7 Hz, 6H); MS (ESI(+)) m/e 431 $(M+H)^+$.

Example 664

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-3-carboxamide

The title compound was prepared as described in Example 147B, substituting N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.58 (dd, J = 4.3, 1.2 Hz, 2H), 8.08 (d, J = 0.8 Hz, 1H), 8.02 (d, J = 1.4 Hz, 1H), 7.86 (dd, J = 9.5, 4.3 Hz, 1H), 7.77 – 7.66 (m, 2H), 7.57 (d, J = 1.4 Hz, 1H), 4.70 – 4.61 (m, 1H), 3.92 (d, J = 7.2 Hz, 2H), 3.67 – 2.93 (m, 4H), 2.41 – 2.00 (m, 3H), 0.88 – 0.81 (m, 6H); MS (ESI(+)) m/e 397 $(M+H)^+$.

Example 665

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-5-methylpyridin-3-yl)azetidine-3-carboxamide

Example 665A

benzyl 3-((4-(piperidin-4-yl)phenyl)carbamoyl)azetidine-1-carboxylate

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 665B

benzyl 3-((4-(1-benzoylpiperidin-4-yl)phenyl)carbamoyl)azetidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting benzyl 3-((4-(piperidin-4-yl)phenyl)carbamoyl)azetidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 665C

N-(4-(1-benzoylpiperidin-4-yl)phenyl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1B, substituting benzyl 3-((4-(1-benzoylpiperidin-4-yl)phenyl)carbamoyl)azetidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 665D

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-5-methylpyridin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1C, substituting 3-bromo-6-fluoro-5-methylpyridine for 3-bromopyridine and N-(4-(1-benzoylpiperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate. ^{1}H NMR (400 MHz, DMSO-d_6/D_2O) δ ppm 7.55 – 7.34 (m, 7H), 7.26 – 7.14 (m, 3H), 6.98 – 6.86 (m, 1H), 4.21 – 4.01 (m, 3H), 3.95 (dd, *J* = 8.8, 4.6 Hz, 2H), 3.69 (ddd, *J* = 8.5, 7.4, 4.3 Hz, 1H), 3.09 – 2.95 (m, 2H), 2.80 (d, *J* = 0.6 Hz, 1H), 2.23 – 2.14 (m, 3H), 1.87 – 1.75 (m, 2H), 1.58 (tt, *J* = 12.8, 6.1 Hz, 2H), 1.11 – 1.01 (m, 1H); MS (ESI(+)) m/e 473 $(M+H)^+$.

Table 12.

The following Examples were essentially prepared as described in Example 665, substituting an appropriate bromoheterocycle in Example 665D.

Ex		Name	MS
666		N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-fluoropyridin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 459 $(M+H)^+$
668		N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-fluoro-6-methylpyridin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 473 $(M+H)^+$
737		N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-cyanopyridin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 466 $(M+H)^+$
738		N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-cyanopyridin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 466 $(M+H)^+$
739		N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-4-methylpyridin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 473 $(M+H)^+$
740		N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-cyanopyridin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 466 $(M+H)^+$
741		N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-methylpyridin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 455 $(M+H)^+$

Example 667

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide

Example 667A

tert-butyl 4-(4-(1-(6-methylpyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1C, substituting 3-bromo-6-methylpyridazine for 3-bromopyridine and tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 667B

1-(6-methylpyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(4-(1-(6-methylpyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 667C

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(6-methylpyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d6) δ 10.02 (s, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.49 – 7.39 (m, 5H), 7.28 (d, J = 9.1 Hz, 1H), 7.22 (d, J = 8.5 Hz, 2H), 6.79 (d, J = 9.0 Hz, 1H), 4.72 – 4.51 (m, 1H), 4.19 (t, J = 8.2 Hz, 2H), 4.10 (dd, J = 7.8, 6.2 Hz, 2H), 3.71 (tt, J = 8.5, 6.1 Hz, 2H), 3.21 – 2.95 (m, 1H), 2.95 – 2.64 (m, 2H), 2.44 (s, 3H), 1.93 – 1.46 (m, 4H); (ESI(+)) m/e 456 $(M+H)^+$.

Table 13.

The following Examples were essentially prepared as described in Example 667, substituting the appropriate carboxylic acid in Example 667C.

Ex		Name	MS
851		N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
852		N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$

Example 742

2-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-1,3-thiazole-5-carboxamide

Example 742A

2-(1-isobutyl-1H-pyrazol-4-yl)thiazole-5-carboxylic acid

The title compound was prepared as described in Example 148A, substituting 2-bromothiazole-5-carboxylic acid for 4-bromoaniline.

Example 742B

(S)-tert-butyl 3-(2-(1-isobutyl-1H-pyrazol-4-yl)thiazole-5-carboxamido)pyrrolidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting (S)-tert-butyl 3-aminopyrrolidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-(1-isobutyl-1H-pyrazol-4-yl)thiazole-5-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 742C

(S)-2-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiazole-5-carboxamide

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl 3-(2-(1-isobutyl-1H-pyrazol-4-yl)thiazole-5-carboxamido)pyrrolidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 742D

(S)-N-(1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)-2-(1-isobutyl-1H-pyrazol-4-yl)thiazole-5-carboxamide

The title compound was prepared as described in Example 147A, substituting (S)-2-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiazole-5-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 742E

2-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-1,3-thiazole-5-carboxamide

The title compound was prepared as described in Example 147B, substituting (S)-N-(1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)-2-(1-isobutyl-1H-pyrazol-4-yl)thiazole-5-carboxamide for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.80(d, 1H), 8.41 (d, J = 0.8 Hz, 1H), 8.30(s, 1H), 8.28(s, 1H), 7.90(s, 1H), 7.34 (dd, J = 9.1, 4.5 Hz, 1H), 6.88 (dd, J = 9.1, 1.3 Hz, 1H), 4.67 – 4.52 (m, 1H), 4.03 – 3.93(m, 2H), 3.90 – 3.40 (m, 4H), 2.36 – 2.02 (m, 3H), 0.89 – 0.82 (m, 6H); MS (ESI(+)) m/e 398 $(M+H)^+$.

Example 743

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide

Example 743A

(S)-tert-butyl 4-(4-(1-((benzyloxy)carbonyl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(4-aminophenyl)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and (S)-1-((benzyloxy)carbonyl)pyrrolidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 743B

(S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1B, substituting (S)-tert-butyl 4-(4-(1-((benzyloxy)carbonyl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 743C

(S)-tert-butyl 4-(4-(1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1C, substituting 3-bromo-2-methylpyridine for 3-bromopyridine and (S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 743D

(S)-1-(2-methylpyridin-3-yl)-N-(4-(piperidin-4-yl)phenyl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl 4-(4-(1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 743E

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(2-methylpyridin-3-yl)-N-(4-(piperidin-4-yl)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.98 (s, 1H), 7.97 (ddd, J = 5.1, 2.2, 1.3 Hz, 2H), 7.69 (dt, J = 8.4, 0.9 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.47 – 7.41 (m, 5H), 7.24 – 7.18 (m, 3H), 7.09 (dd, J = 8.0, 4.7 Hz, 1H), 4.62 (s, 1H), 3.65 (s, 1H), 3.19 (ddd, J = 14.2, 10.1, 6.4 Hz, 4H), 2.76 (t, J = 11.9 Hz, 2H), 2.47 (s, 3H), 2.26 – 2.06 (m, 2H), 1.93 – 1.49 (m, 4H), 1.23 (s, 1H), MS (ESI(+)) m/e 469.3 $(M+H)^+$.

Example 744

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(2-methylpyridin-3-yl)-N-(4-(piperidin-4-yl)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.98

(s, 1H), 8.01 – 7.93 (m, 2H), 7.58 – 7.45 (m, 2H), 7.44 – 7.37 (m, 1H), 7.30 (tdd, J = 6.6, 3.7, 2.8 Hz, 2H), 7.20 (dd, J = 11.4, 4.7 Hz, 2H), 7.09 (dd, J = 8.1, 4.6 Hz, 1H), 4.66 (d, J = 13.1 Hz, 1H), 3.49 – 3.14 (m, 8H), 2.90 – 2.69 (m, 2H), 2.47 (s, 3H), 2.31 – 2.06 (m, 2H), 1.92 – 1.80 (m, 1H), 1.70 (s, 1H), 1.64 – 1.41 (m, 2H); MS (ESI(+)) m/e 487.3 $(M+H)^+$.

Example 745

(3S)-1-(2-methylpyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(2-methylpyridin-3-yl)-N-(4-(piperidin-4-yl)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 4,4,4-trifluorobutanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.97 (s, 1H), 7.97 (dd, J = 4.8, 3.6 Hz, 2H), 7.53 (d, J = 8.3 Hz, 3H), 7.24 – 7.13 (m, 3H), 4.53 (d, J = 12.9 Hz, 1H), 3.97 (d, J = 13.3 Hz, 1H), 3.39 (d, J = 7.5 Hz, 3H), 3.36 – 3.29 (m, 2H), 3.25 – 3.16 (m, 2H), 3.11 (dd, J = 24.4, 11.8 Hz, 1H), 2.70 (ddd, J = 15.1, 11.8, 8.3 Hz, 1H), 2.67 – 2.57 (m, 3H), 2.47 (s, 3H), 2.27 – 2.07 (m, 2H), 1.75 (s, 2H), 1.56 (dt, J = 12.5, 8.7 Hz, 1H), 1.41 (qd, J = 12.8, 4.3 Hz, 1H), MS (ESI(+)) m/e 489.3 $(M+H)^+$.

Example 746

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]furan-2-carboxamide

Example 746A

5-(1-isobutyl-1H-pyrazol-4-yl)furan-2-carboxylic acid

The title compound was prepared as described in Example 148A, substituting 5-bromofuran-2-carboxylic acid for 4-bromoaniline.

Example 746B

(S)-tert-butyl 3-(5-(1-isobutyl-1H-pyrazol-4-yl)furan-2-carboxamido)pyrrolidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting (S)-tert-butyl 3-aminopyrrolidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 5-(1-isobutyl-1H-pyrazol-4-yl)furan-2-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 746C

(S)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)furan-2-carboxamide

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl 3-(5-(1-isobutyl-1H-pyrazol-4-yl)furan-2-carboxamido)pyrrolidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 746D

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]furan-2-carboxamide

The title compound was prepared as described in Example 147A, substituting (S)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)furan-2-carboxamide for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.37 (d, J = 6.9 Hz, 1H), 8.14 (s, 1H), 7.87 (s, 1H), 7.49 (d, J = 9.4 Hz, 1H), 7.17 (d, J = 3.5 Hz, 1H), 7.03 (d, J = 9.4 Hz, 1H), 6.63 (d, J = 3.5 Hz, 1H), 4.69 – 4.54 (m, 1H), 3.95 (d, J = 7.2 Hz, 2H), 3.79 (dd, J = 11.0, 6.8 Hz, 1H), 3.72 – 3.58 (m, 1H), 3.60 – 3.39 (m, 2H), 2.36 – 2.19 (m, 1H), 2.22 – 2.03 (m, 2H), 0.85 (d, J = 6.7 Hz, 6H); MS (ESI(+)) m/e 415(M+H)$^+$.

Example 747

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]furan-2-carboxamide

The title compound was prepared as described in Example 147B, substituting N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]furan-2-carboxamide for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.49 (dd, J = 4.5, 1.2 Hz, 1H), 8.38 (d, J = 7.0 Hz, 1H), 8.15 (s, 1H), 7.87 (s, 1H), 7.34 (dd, J = 9.1, 4.4 Hz, 1H), 7.17 (d, J = 3.5 Hz, 1H), 6.88 (dd, J = 9.1, 1.3 Hz, 1H), 6.63 (d, J = 3.5 Hz, 1H), 4.70 – 4.54 (m, 1H), 3.95 (d, J = 7.2 Hz, 2H), 3.79 (dd, J = 10.8, 6.9 Hz, 1H), 3.75 – 3.61 (m, 1H), 3.61 – 3.39 (m, 2H), 2.37 – 2.01 (m, 3H), 0.85 (d, J = 6.7 Hz, 6H); MS (ESI(+)) m/e 381(M+H)$^+$.

Example 748

N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 748A

1-(6-chloropyridazin-3-yl)azetidine-3-carboxylic acid

The title compound was prepared as described in Example 147A, substituting azetidine-3-carboxylic acid for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 748B

1-(pyridazin-3-yl)azetidine-3-carboxylic acid

The title compound was prepared as described in Example 147B, substituting 1-(6-chloropyridazin-3-yl)azetidine-3-carboxylic acid for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 748C

N-(4-bromophenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 4-bromoaniline for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 748D

N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 148A, substituting 1-((4-methyltetrahydro-2H-pyran-4-yl)methyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole and N-(4-bromophenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for 4-bromoaniline. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.09 (s, 1H), 8.56 (dd, J = 4.5, 1.2 Hz, 1H), 8.06 (s, 1H), 7.82 (s, 1H), 7.61 (d, J = 8.7 Hz, 2H), 7.52 (d, J = 8.6 Hz, 2H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 6.83 (dd, J = 9.0, 1.2 Hz, 1H), 4.25 (t, J = 8.3 Hz, 2H), 4.16 (dd, J = 8.0, 6.0 Hz, 2H), 4.02 (s, 2H), 3.84 - 3.62 (m, 3H), 3.52 (ddd, J = 11.8, 9.2, 3.0 Hz, 2H), 1.51 (ddd, J = 13.3, 9.0, 4.2 Hz, 2H), 1.32 - 1.17 (m, 2H), 0.97 (s, 3H); MS (ESI(+)) m/e 433 $(M+H)^+$.

Example 749

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-4-[1-(2-methylpropanoyl)piperidin-4-yl]benzamide

Example 749A

(S)-tert-butyl (1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)carbamate

The title compound was prepared as described in Example 147A, substituting (S)-tert-butyl pyrrolidin-3-ylcarbamate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 749B

(S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-amine

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl (1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)carbamate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 749C

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-4-[1-(2-methylpropanoyl)piperidin-4-yl]benzamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-amine for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 4-(1-isobutyrylpiperidin-4-yl)benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.53 (d, J = 6.6 Hz, 1H), 7.83 – 7.76 (m, 2H), 7.48 (d, J = 9.4 Hz, 1H), 7.37 – 7.30 (m, 2H), 7.01 (d, J = 9.5 Hz, 1H), 4.68 – 4.49 (m, 2H), 4.12 – 4.00 (m, 1H), 3.77 (dd, J = 11.0, 6.6 Hz, 1H),

3.68 – 3.39 (m, 3H), 3.19 – 3.00 (m, 1H), 3.02 – 2.50 (m, 3H), 2.35 – 2.19 (m, 1H), 2.08 (dq, *J* = 12.5, 6.3 Hz, 1H), 1.91 – 1.70 (m, 2H), 1.65 – 1.07 (m, 2H). 1.05-0.88 (m, 6H); MS (ESI(+)) m/e 456 $(M+H)^+$.

Example 750

N-(4-{1-[2-(piperazin-1-yl)ethyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 750A

tert-butyl 4-(2-(4-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)-1H-pyrazol-1-yl)ethyl)piperazine-1-carboxylate

The title compound was prepared as described in Example 148A, substituting tert-butyl 4-(2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)ethyl)piperazine-1-carboxylate for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole and N-(4-bromophenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for 4-bromoaniline.

Example 750B

N-(4-{1-[2-(piperazin-1-yl)ethyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(2-(4-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)-1H-pyrazol-1-yl)ethyl)piperazine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.20 (s, 1H), 8.71 (s, 2H), 8.57 (dd, J = 4.3, 1.0 Hz, 1H), 8.14 (s, 1H), 7.86 (s, 1H), 7.80 (dd, J = 9.4, 4.4 Hz, 1H), 7.66 - 7.58 (m, 2H), 7.57 - 7.49 (m, 2H), 7.45 (d, J = 9.2 Hz, 1H), 4.56 - 4.36 (m, 4H), 4.31 (t, J = 6.3 Hz, 2H), 3.91 - 3.73 (m, 1H), 3.25 - 3.09 (m, 4H), 3.04 (t, J = 6.1 Hz, 2H), 2.83 (s, 4H); MS (ESI(+)) m/e 433 $(M+H)^+$.

Example 751

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 148A, substituting 1-neopentyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole and N-(4-bromophenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for 4-bromoaniline. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 10.14 (s, 1H), 8.57 (dd, J = 4.5, 1.2 Hz, 1H), 8.05 (s, 1H), 7.82 (s, 1H), 7.66 - 7.58 (m, 2H), 7.55 - 7.51 (m, 2H), 7.48 (dd, J = 9.1, 4.5 Hz, 1H), 6.98 (dd, J = 9.1, 1.1 Hz, 1H), 4.30 (t, J = 8.6 Hz, 2H), 4.22 (dd, J = 8.4, 6.0 Hz, 2H), 3.90 (s, 2H), 3.77 (tt, J = 8.6, 5.9 Hz, 1H), 0.92 (s, 9H); MS (ESI(+)) m/e 391 $(M+H)^+$.

Example 752

4-[1-(2-methylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]benzamide

The title compound was prepared as described in Example 147B, substituting N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-4-[1-(2-methylpropanoyl)piperidin-4-yl]benzamide for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.69 (d, *J* = 6.6 Hz, 1H), 8.57 (dd, *J* = 4.3, 1.2 Hz, 1H), 8.16 – 7.75 (m, 3H), 7.69 (dd, *J* = 9.5, 1.2 Hz, 1H), 7.37 – 7.31 (m, 2H), 4.90 – 4.41 (m, 2H), 4.33 – 3.60 (m, 5H), 3.20-2.50 (m, 4H), 2.37 – 2.14 (m, 2H), 1.87 – 1.74 (m, 2H), 1.63 – 1.20 (m, 2H), 1.02 (bs, *J* = 7.4 Hz, 6H); MS (ESI(+)) m/e 422 $(M+H)^+$.

Example 753

N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 148A, substituting 2-methyl-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)propan-2-ol for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole and N-(4-bromophenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for 4-bromoaniline. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.09 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 8.01 (s, 1H), 7.81 (s, 1H), 7.69 - 7.57 (m, 2H), 7.57 - 7.44 (m, 2H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 6.83 (dd, J = 9.0, 1.3 Hz, 1H), 4.70 (s, 1H), 4.25 (t, J = 8.4 Hz, 2H), 4.16 (dd, J = 8.0, 6.0 Hz, 2H), 4.01 (s, 2H), 3.74 (tt, J = 8.5, 6.0 Hz, 1H), 1.08 (s, 6H); MS (ESI(+)) m/e 393 $(M+H)^+$.

Example 754

5-[1-(3-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide

Example 754A

(S)-tert-butyl (1-(pyridazin-3-yl)pyrrolidin-3-yl)carbamate

The title compound was prepared as described in Example 147B, substituting (S)-tert-butyl (1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)carbamate for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 754B

(S)-1-(pyridazin-3-yl)pyrrolidin-3-amine

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl (1-(pyridazin-3-yl)pyrrolidin-3-yl)carbamate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 754C

5-(1-(tert-butoxycarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)thiophene-2-carboxylic acid

The title compound was prepared as described in Example 148A, substituting tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole and 5-bromothiophene-2-carboxylic acid for 4-bromoaniline.

Example 754D

5-(1-(tert-butoxycarbonyl)piperidin-4-yl)thiophene-2-carboxylic acid

The title compound was prepared as described in Example 1B, substituting 5-(1-(tert-butoxycarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)thiophene-2-carboxylic acid for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 754E

(S)-tert-butyl 4-(5-((1-(pyridazin-3-yl)pyrrolidin-3-yl)carbamoyl)thiophen-2-yl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting (S)-1-(pyridazin-3-yl)pyrrolidin-3-amine for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 5-(1-(tert-butoxycarbonyl)piperidin-4-yl)thiophene-2-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 754F

(S)-5-(piperidin-4-yl)-N-(1-(pyridazin-3-yl)pyrrolidin-3-yl)thiophene-2-carboxamide

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl 4-(5-((1-(pyridazin-3-yl)pyrrolidin-3-yl)carbamoyl)thiophen-2-yl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 754G

5-[1-(3-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-5-(piperidin-4-yl)-N-(1-(pyridazin-3-yl)pyrrolidin-3-yl)thiophene-2-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 3-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.63 – 8.44 (m, 2H), 7.66 (d, J = 3.8 Hz, 1H), 7.58 – 7.44 (m, 1H), 7.41 – 7.19 (m, 4H), 6.95 (d, J = 3.8 Hz, 1H), 6.87 (dd, J = 9.1, 1.4 Hz, 1H), 4.66 – 4.19 (m, 2H), 3.85 – 3.38 (m, 5H), 3.20 – 2.72 (m, 3H), 2.34 – 2.15 (m, 1H), 2.17 – 1.78 (m, 3H), 1.72 – 1.46 (m, 2H); MS (ESI(+)) m/e 480 $(M+H)^+$.

Table 14.

The following Examples were essentially prepared as described in Example 754, substituting an appropriate carboxylic acid in Example 754G.

Ex		Name	MS

755		5-[1-(4-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 480 $(M+H)^+$
758		N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide	(ESI(+)) m/e 470 $(M+H)^+$
760		5-[1-(2-methylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 428 $(M+H)^+$
761		5-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 498 $(M+H)^+$
762		5-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 440 $(M+H)^+$
763		5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 480 $(M+H)^+$
764		5-(1-benzoylpiperidin-4-yl)-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
765		N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide	(ESI(+)) m/e 456 $(M+H)^+$
766		N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-{1-[(2R)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}thiophene-2-carboxamide	(ESI(+)) m/e 456 $(M+H)^+$
767		5-{1-[(1-methylpiperidin-4-yl)acetyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 498 $(M+H)^+$
768		N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide	(ESI(+)) m/e 469 $(M+H)^+$
1013		5-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 442 $(M+H)^+$
1014		5-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 456 $(M+H)^+$
1015		5-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 456 $(M+H)^+$
1016		5-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 440 $(M+H)^+$
1017		N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]thiophene-2-carboxamide	(ESI(+)) m/e 468 $(M+H)^+$
1018		5-[1-(cyclopropylacetyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 440 $(M+H)^+$
1019		5-[1-(bicyclo[2.2.1]hept-2-ylacetyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$

Example 756

(3S)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

Example 756A

(S)-1-(6-chloropyridazin-3-yl)pyrrolidine-3-carboxylic acid

The title compound was prepared as described in Example 147A, substituting (S)-pyrrolidine-3-carboxylic acid for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 756B

(S)-1-(pyridazin-3-yl)pyrrolidine-3-carboxylic acid

The title compound was prepared as described in Example 147B, substituting (S)-1-(6-chloropyridazin-3-yl)pyrrolidine-3-carboxylic acid for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 756C

(S)-N-(4-bromophenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 4-bromoaniline for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and (S)-1-(pyridazin-3-yl)pyrrolidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 756D

(3S)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 148A, substituting 1-((4-methyltetrahydro-2H-pyran-4-yl)methyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole and (S)-N-(4-bromophenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide for 4-bromoaniline. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.11 (s, 1H), 8.48 (dd, J = 4.5, 1.2 Hz, 1H), 8.07 (s, 1H), 7.82 (s, 1H), 7.64 - 7.58 (m, 2H), 7.54 - 7.49 (m, 2H), 7.34 (dd, J = 9.1, 4.4 Hz, 1H), 6.88 (dd, J = 9.2, 1.3 Hz, 1H), 4.02 (s, 2H), 3.78 (dd, J = 10.5, 7.9 Hz, 1H), 3.72 - 3.58 (m, 4H), 3.56 - 3.45 (m, 3H), 3.37 - 3.32 (m, 1H), 2.42 - 2.09 (m, 2H), 1.51 (ddd, J = 13.4, 9.1, 4.2 Hz, 2H), 1.32 - 1.12 (m, 2H), 0.97 (s, 3H); MS (ESI(+)) m/e 447 $(M+H)^+$.

Table 15.

The following Examples were essentially prepared as described in Example 756, substituting an appropriate boronate in Example 756D.

Ex		Name	MS
757		(3S)-N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 407 $(M+H)^+$

759		(3S)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 405 $(M+H)^+$
769		(3S)-N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 391 $(M+H)^+$
770		(3S)-N-{4-[1-(propan-2-yl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 377 $(M+H)^+$
771		(3S)-N-{4-[1-(cyclopropylmethyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 389 $(M+H)^+$
772		(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-2-ylmethyl)-1H-pyrazol-4-yl]phenyl}pyrrolidine-3-carboxamide	(ESI(+)) m/e 433 $(M+H)^+$
773		(3S)-N-[4-(1-tert-butyl-1H-pyrazol-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 391 $(M+H)^+$

Example 774

(3S)-N-(4-{[(3R)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

Example 774A

(R)-tert-butyl 3-(4-((S)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamido)phenoxy)pyrrolidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting (R)-tert-butyl 3-(4-aminophenoxy)pyrrolidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and (S)-1-(pyridazin-3-yl)pyrrolidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 774B

(S)-1-(pyridazin-3-yl)-N-(4-((R)-pyrrolidin-3-yloxy)phenyl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting (R)-tert-butyl 3-(4-((S)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamido)phenoxy)pyrrolidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 774C

(3S)-N-(4-{[(3R)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(pyridazin-3-yl)-N-(4-((R)-pyrrolidin-3-yloxy)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.03 (d, J = 18.3 Hz, 1H), 8.51 (d, J = 4.2 Hz, 1H), 7.46 (tdt, J = 21.9, 19.2, 10.8 Hz, 8H),

7.13 – 7.02 (m, 1H), 6.96 (d, *J* = 8.9 Hz, 1H), 6.86 (d, *J* = 8.9 Hz, 1H), 5.00 (d, *J* = 34.1 Hz, 1H), 3.88 – 3.74 (m, 2H), 3.65 (dd, *J* = 12.1, 7.4 Hz, 4H), 3.51 (d, *J* = 7.3 Hz, 2H), 2.37 – 1.98 (m, 4H), MS (ESI(+)) m/e 458 $(M+H)^+$.

Table 16.

The following Examples were essentially prepared as described in Example 774, substituting an appropriate carboxylic acid in Example 774C.

Ex		Name	MS
775		(3S)-N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
776		(3S)-N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
777		(3S)-N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
778		(3S)-N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$
779		(3S)-N-(4-{[(3R)-1-(2-methylbenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 472 $(M+H)^+$
780		(3S)-N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
781		(3S)-N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 500 $(M+H)^+$
782		(3S)-1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(4,4,4-trifluorobutanoyl)pyrrolidin-3-yl]oxy}phenyl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
783		(3S)-N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 494 $(M+H)^+$

Example 784

N-[4-(5-propyl-1,2,4-oxadiazol-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 806, substituting butanoyl chloride for 3,3-dimethylbutanoyl chloride in Example 806A. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.39 (s, 1H), 8.57 (dd, J = 4.5, 1.3 Hz, 1H), 8.04 - 7.89 (m, 2H), 7.89 - 7.74 (m, 2H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 6.84 (dd, J = 8.9, 1.4 Hz, 1H), 4.26 (t, J = 8.4 Hz, 2H), 4.18 (dd, J = 8.2, 5.9 Hz, 2H), 3.79 (tt, J = 8.6, 5.9 Hz, 1H), 2.96 (t, J = 7.4 Hz, 2H), 1.81 (h, J = 7.4 Hz, 2H), 0.99 (t, J = 7.4 Hz, 3H); MS (ESI(+)) m/e 365 $(M+H)^+$.

Example 785

(3S)-N-{4-[1-(2-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

Example 785A

(S)-tert-butyl 3-(4-(1-(pyridazin-3-yl)pyrrolidine-3-carboxamido)phenyl)azetidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 3-(4-aminophenyl)azetidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and substituting (S)-1-(pyridazin-3-yl)pyrrolidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 785B

(S)-N-(4-(azetidin-3-yl)phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl 3-(4-(1-(pyridazin-3-yl)pyrrolidine-3-carboxamido)phenyl)azetidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 785C

(3S)-N-{4-[1-(2-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-N-(4-(azetidin-3-yl)phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 10.15 (bs, 1H), 8.51 – 8.46 (m, 1H), 7.67 – 7.40 (m, 4H), 7.40 – 7.24 (m, 5H), 6.90 – 6.85 (m, 1H), 4.50 – 4.42 (m, 1H), 4.41 – 4.34 (m, 1H), 4.02 – 3.96 (m, 2H), 3.93 – 3.83 (m, 1H), 3.81 – 3.73 (m, 1H), 3.67 – 3.58 (m, 2H), 3.53 – 3.44 (m, 1H), 3.40-3.30 (m, 1H), 2.43 – 2.12 (m, 2H); MS (ESI(+)) m/e 446 $(M+H)^+$.

Table 17.

The following Examples were essentially prepared as described in Example 785, substituting an appropriate carboxylic acid in Example 785C.

Ex		Name	MS
786		(3S)-N-{4-[1-(3-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 446 $(M+H)^+$
787		(3S)-N-{4-[1-(4-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 446 $(M+H)^+$
788		(3S)-N-[4-(1-benzoylazetidin-3-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 428 $(M+H)^+$
789		(3S)-N-{4-[1-(2,2-dimethylpropanoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 408 $(M+H)^+$
790		(3S)-N-{4-[1-(3,5-difluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 464 $(M+H)^+$
791		3S)-N-{4-[1-(2-methylbenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-	(ESI(+))

		3-yl)pyrrolidine-3-carboxamide	m/e 442 $(M+H)^+$
792		(3S)-N-{4-[1-(2,4-difluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 464 $(M+H)^+$

Example 793

(3R)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

Example 793A

(R)-1-(6-chloropyridazin-3-yl)pyrrolidine-3-carboxylic acid

The title compound was prepared as described in Example 147A, substituting (R)-pyrrolidine-3-carboxylic acid for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 793B

(R)-1-(pyridazin-3-yl)pyrrolidine-3-carboxylic acid

The title compound was prepared as described in Example 147B, substituting (R)-1-(6-chloropyridazin-3-yl)pyrrolidine-3-carboxylic acid for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 793C

(R)-tert-butyl 4-(4-(1-(pyridazin-3-yl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(4-aminophenyl)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and (R)-1-(pyridazin-3-yl)pyrrolidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 793D

(R)-N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting (R)-tert-butyl 4-(4-(1-(pyridazin-3-yl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 793E

(3R)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (R)-N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.06 (s, 1H), 8.48 (dd, J = 4.4, 0.9 Hz, 1H), 7.54 (t, J = 6.3 Hz, 2H), 7.47 – 7.40 (m, 5H), 7.35 (dd, J = 9.1, 4.5 Hz, 1H), 7.22 (d, J = 8.6 Hz, 2H), 6.89 (dd, J = 9.2, 1.1 Hz, 1H), 4.62 (s, 1H), 3.75 (dt, J = 25.9, 12.9 Hz, 1H), 3.62 (td, J = 10.2, 5.8 Hz, 3H), 3.55 – 3.41 (m, 1H),

3.13 (s, 1H), 2.98 – 2.69 (m, 2H), 2.39 – 2.11 (m, 2H), 1.90 – 1.48 (m, 4H), MS (ESI(+)) m/e 456 $(M+H)^+$.

Example 794

(3R)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (R)-N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.06 (s, 1H), 8.48 (dd, J = 4.5, 1.2 Hz, 1H), 7.59 – 7.40 (m, 4H), 7.41 – 7.23 (m, 3H), 7.19 (d, J = 8.5 Hz, 2H), 6.89 (dd, J = 9.2, 1.2 Hz, 1H), 4.66 (d, J = 13.1 Hz, 1H), 3.77 (dd, J = 10.5, 7.9 Hz, 1H), 3.73 – 3.56 (m, 2H), 3.48 (dt, J = 10.2, 7.4 Hz, 2H), 3.17 (t, J = 12.1 Hz, 1H), 2.82 (dt, J = 24.1, 11.3 Hz, 2H), 2.38 – 2.09 (m, 2H), 1.97 – 1.79 (m, 1H), 1.69 (t, J = 17.4 Hz, 1H), 1.52 (ddd, J = 20.9, 12.0, 6.1 Hz, 2H), MS (ESI(+)) m/e 474 $(M+H)^+$.

Example 795

(3R)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (R)-N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,2-dimethylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.04 (s, 1H), 8.48 (dd, J = 4.5, 1.3 Hz, 1H), 7.54 (t, J = 6.4 Hz, 1H), 7.34 (dd, J = 9.1, 4.5 Hz, 1H), 7.21 – 7.14 (m, 2H), 6.87 (dd, J = 9.1, 1.3 Hz, 1H), 4.46 – 4.35 (m, 2H), 3.76 (dd, J = 10.5, 7.9 Hz, 1H), 3.69 – 3.54 (m, 2H), 3.48 (dt, J = 10.2, 7.4 Hz, 1H), 2.94 – 2.63 (m, 3H), 2.39 – 2.07 (m, 2H), 1.83 – 1.73 (m, 2H), 1.50 (s, 1H), 1.22 (s, 9H), MS (ESI(+)) m/e 436 $(M+H)^+$.

Example 796

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

Example 796A

(S)-tert-butyl 4-(4-(1-(pyridazin-3-yl)pyrrolidine-3-carboxamido)phenoxy)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and (S)-1-(pyridazin-3-yl)pyrrolidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 796B

(S)-N-(4-(piperidin-4-yloxy)phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl 4-(4-(1-(pyridazin-3-yl)pyrrolidine-3-carboxamido)phenoxy)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 796C

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-N-(4-(piperidin-4-yloxy)phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and cyclohexanecarboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.97 (s, 1H), 8.48 (dd, J = 4.5, 1.3 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.34 (dd, J = 9.1, 4.4 Hz, 1H), 6.97 – 6.84 (m, 3H), 4.58 – 4.47 (m, 1H), 3.88 – 3.40 (m, 6H), 3.40 – 3.20 (m, 2H), 2.60-2.50 (m, 1H), 2.41 – 2.08 (m, 2H), 2.00 – 1.80 (m, 2H), 1.77 – 1.07 (m, 13H); MS (ESI(+)) m/e 478 $(M+H)^+$.

Table 18.

The following Examples were essentially prepared as described in Example 796, substituting an appropriate carboxylic acid in Example 796C.

Ex		Name	MS
797		(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
798		(3S)-N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
799		(3S)-N-{4-[(1-benzoylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 472 $(M+H)^+$
800		(3S)-N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 490 $(M+H)^+$
801		(3S)-N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 452 $(M+H)^+$
802		(3S)-N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$

Example 803

N-{4-[5-(2,2-dimethylpropyl)-1,3,4-oxadiazol-2-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 803A

N'-(3,3-dimethylbutanoyl)-4-nitrobenzohydrazide

A suspension of 4-nitrobenzohydrazide (0.500 g, 2.76 mmol), and 4-methylmorpholine (0.455 ml, 4.14 mmol) were stirred in dichloromethane (20 ml). 3,3–Dimethylbutanoyl chloride (0.422 ml, 3.04 mmol) was added and the reaction mixture was stirred for 2 hours. Normal phase chromatography of the crude reaction mixture gave the title compound.

Example 803B

2-neopentyl-5-(4-nitrophenyl)-1,3,4-oxadiazole

A mixture of N'-(3,3-dimethylbutanoyl)-4-nitrobenzohydrazide (0.556 g, 1.991 mmol) and methyl N-(triethylammoniumsulfonyl)carbamate (0.572 g, 2.389 mmol) in tetrahydrofuran (10 ml) was heated to 120°C in a microwave for 45 minutes. The crude reaction mixture was concentrated and purified by normal phase chromatography to give the title compound.

Example 803C

4-(5-neopentyl-1,3,4-oxadiazol-2-yl)aniline

The title compound was prepared as described in Example 1B, substituting 2-neopentyl-5-(4-nitrophenyl)-1,3,4-oxadiazole for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 803D

N-{4-[5-(2,2-dimethylpropyl)-1,3,4-oxadiazol-2-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 4-(5-neopentyl-1,3,4-oxadiazol-2-yl)aniline for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.45 (s, 1H), 8.57 (dd, J = 4.5, 1.3 Hz, 1H), 7.97 - 7.91 (m, 2H), 7.88 - 7.82 (m, 2H), 7.39 (dd, J = 9.0, 4.5 Hz, 1H), 6.84 (dd, J = 9.0, 1.4 Hz, 1H), 4.26 (t, J = 8.4 Hz, 2H), 4.18 (dd, J = 8.2, 5.9 Hz, 2H), 3.79 (tt, J = 8.6, 5.9 Hz, 1H), 2.82 (s, 2H), 1.03 (s, 9H); MS (ESI(+)) m/e 393 $(M+H)^+$.

Example 804

N-{4-[1-(2,2-dimethylpropyl)-1H-imidazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 804A

1-neopentyl-4-(4-nitrophenyl)-1H-imidazole

To a solution of 4-(4-nitrophenyl)-1H-imidazole (0.500 g, 2.64 mmol) in N,N-dimethylformamide (10 ml) was added cesium carbonate (1.292 g, 3.96 mmol) followed by 1-bromo-2,2-dimethylpropane (0.366 ml, 2.91 mmol). After heating at 85° overnight, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, washed with

water and brine, dried over magnesium sulfate, filtered and concentrated. Normal phase chromatography provided the title compound.

Example 804B

4-(1-neopentyl-1H-imidazol-4-yl)aniline

The title compound was prepared as described in Example 1B, substituting 1-neopentyl-4-(4-nitrophenyl)-1H-imidazole for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 804C

N-{4-[1-(2,2-dimethylpropyl)-1H-imidazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 4-(1-neopentyl-1H-imidazol-4-yl)aniline for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.08 (s, 1H), 8.56 (dd, J = 4.6, 1.3 Hz, 1H), 7.73 - 7.66 (m, 2H), 7.64 - 7.58 (m, 2H), 7.57 (d, J = 1.2 Hz, 1H), 7.49 (d, J = 1.1 Hz, 1H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 6.83 (dd, J = 9.0, 1.4 Hz, 1H), 4.25 (t, J = 8.3 Hz, 2H), 4.16 (dd, J = 8.1, 6.0 Hz, 2H), 3.77 (s, 2H), 3.77 - 3.69 (m, 1H), 0.91 (s, 9H); MS (ESI(+)) m/e 391 $(M+H)^+$.

Example 805

N-[4-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 805A

3-cyclopropyl-1-(4-nitrophenyl)prop-2-yn-1-one

A 250-mL round bottom flask was charged with bis(triphenylphosphine)palladium bischloride (151 mg, 0.216 mmol) and copper iodide (82 mg, 0.431 mmol), and the flask was degassed with nitrogen. Tetrahydrofuran (40 mL) was added through a septum, and nitrogen was bubbled through the mixture for 30 minutes. To this was added dropwise a nitrogen-degassed solution of 4-nitrobenzoyl chloride (2 g, 10.8 mmol), ethynylcyclopropane (784 mg, 11.9 mmol) and triethylamine (1.31 g, 12.9 mmol) in tetrahydrofuran (15 mL). The reaction mixture was stirred at room temperature for 2 hours and then concentrated to dryness. The residue was purified by normal phase chromatography to give the title compound.

Example 805B

3-cyclopropyl-1-methyl-5-(4-nitrophenyl)-1H-pyrazole

3-Cyclopropyl-1-(4-nitrophenyl)prop-2-yn-1-one (500 mg, 2.323 mmol) was dissolved in N,N-dimethylformamide (7.75 mL), and the solution was chilled to 0 °C. Methylhydrazine (118 mg, 2.56 mmol) was added dropwise. The mixture was stirred

overnight at room temperature then diluted with water (25 mL) and stirred for 45 minutes. The resulting precipitate was collected by filtration to give the title compound.

Example 805C

4-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)aniline

The title compound was prepared as described in Example 1B, substituting 3-cyclopropyl-1-methyl-5-(4-nitrophenyl)-1H-pyrazole for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 805D

N-[4-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 4-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)aniline for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) d 10.11 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.69 – 7.58 (m, 4H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 6.83 (dd, J = 9.0, 1.3 Hz, 1H), 6.28 (s, 1H), 4.25 (t, J = 8.3 Hz, 2H), 4.16 (dd, J = 8.1, 6.0 Hz, 2H), 3.84 (s, 3H), 3.75 (dq, J = 8.3, 5.9 Hz, 1H), 1.95 – 1.82 (m, 1H), 1.02 – 0.92 (m, 2H), 0.71 – 0.62 (m, 2H); MS (ESI(+)) m/e 375 $(M+H)^+$.

Example 806

N-{4-[5-(2,2-dimethylpropyl)-1,2,4-oxadiazol-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 806A

5-neopentyl-3-(4-nitrophenyl)-1,2,4-oxadiazole

To a suspension of (Z)-N'-hydroxy-4-nitrobenzimidamide (0.500 g, 2.76 mmol) in dichloromethane (6 ml) was added 4-methylmorpholine (0.455 ml, 4.14 mmol) followed by 3,3-dimethylbutanoyl chloride (0.422 ml, 3.04 mmol). After 1 hour, the crude reaction mixture was purified by normal phase chromatography and the collected intermediate was dissolved in dichloromethane (8 ml) and treated with tetrabutylammonium fluoride (1.0M in THF) (8.28 ml, 8.28 mmol). After 3 hours at room temperature, the mixture was diluted with ethyl acetate, washed with water, dried over magnesium sulfate, filtered, and concentrated. Normal phase chromatography provided the title compound.

Example 806B

4-(5-neopentyl-1,2,4-oxadiazol-3-yl)aniline

The title compound was prepared as described in Example 1B, substituting 5-neopentyl-3-(4-nitrophenyl)-1,2,4-oxadiazole for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 806C

N-{4-[5-(2,2-dimethylpropyl)-1,2,4-oxadiazol-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 4-(5-neopentyl-1,2,4-oxadiazol-3-yl)aniline for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.40 (s, 1H), 8.57 (dd, J = 4.6, 1.3 Hz, 1H), 8.05 - 7.89 (m, 2H), 7.89 - 7.75 (m, 2H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 6.84 (dd, J = 9.0, 1.3 Hz, 1H), 4.26 (t, J = 8.4 Hz, 2H), 4.18 (dd, J = 8.1, 5.9 Hz, 2H), 3.79 (tt, J = 8.5, 5.9 Hz, 1H), 2.90 (s, 2H), 1.04 (s, 9H); MS (ESI(+)) m/e 393 $(M+H)^+$.

Example 807

N-{4-[3-cyclopropyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 805, substituting (2-methoxyethyl)hydrazine for methylhydrazine in Example 805B. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.20 (s, 1H), 8.56 (d, J = 4.5 Hz, 1H), 7.72 – 7.57 (m, 4H), 7.55 – 7.48 (m, 1H), 7.07 – 6.99 (m, 1H), 6.28 (s, 1H), 4.38 – 4.18 (m, 6H), 3.83 – 3.69 (m, 3H), 3.25 (s, 3H), 1.98 – 1.87 (m, 1H), 1.00 – 0.91 (m, 2H), 0.67 (d, J = 2.3 Hz, 2H); MS (ESI(+)) m/e 419 $(M+H)^+$.

Example 808

tert-butyl 4-(5-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}thiophen-2-yl)piperidine-1-carboxylate

Example 808A

tert-butyl (1-(6-chloropyridazin-3-yl)azetidin-3-yl)carbamate

The title compound was prepared as described in Example 147A, substituting tert-butyl azetidin-3-ylcarbamate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 808B

tert-butyl (1-(pyridazin-3-yl)azetidin-3-yl)carbamate

The title compound was prepared as described in Example 147B, substituting tert-butyl (1-(6-chloropyridazin-3-yl)azetidin-3-yl)carbamate for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 808C

1-(pyridazin-3-yl)azetidin-3-amine

The title compound was prepared as described in Example 1D, substituting tert-butyl (1-(pyridazin-3-yl)azetidin-3-yl)carbamate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 808D

tert-butyl 4-(5-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}thiophen-2-yl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting 1-(pyridazin-3-yl)azetidin-3-amine for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 5-(1-(tert-butoxycarbonyl)piperidin-4-yl)thiophene-2-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.95 (d, J = 7.2 Hz, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.65 (d, J = 3.8 Hz, 1H), 7.38 (dd, J = 8.9, 4.5 Hz, 1H), 6.95 (dd, J = 3.8, 0.8 Hz, 1H), 6.83 (dd, J = 9.0, 1.4 Hz, 1H), 4.92 – 4.77 (m, 1H), 4.36 (t, J = 8.1 Hz, 2H), 4.05 – 3.97 (m, 4H), 3.09 – 2.66 (m, 3H), 1.98 – 1.88 (m, 2H), 1.40 (s, 11H); MS (ESI(+)) m/e 444 $(M+H)^+$.

Example 809

tert-butyl 4-fluoro-4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidine-1-carboxylate

Example 809A

tert-butyl 4-(4-aminophenyl)-4-hydroxypiperidine-1-carboxylate

N-(4-Bromophenyl)-1,1,1-trimethyl-N-(trimethylsilyl)silanamine (7 g, 22.12 mmol) in tetrahydrofuran (100 mL) was treated with a solution of n-BuLi (1M, 22 mL) at -78°C. The reaction mixture was stirred an additional hour at -78°C and then treated with a solution of tert-butyl 4-oxopiperidine-1-carboxylate (3.97 g, 19.91 mmol) in tetrahydrofuran (20 mL). The reaction mixture was stirred at -78°C for 30 minutes and then warmed to room temperature. The reaction was quenched by addition of saturated ammonium chloride solution (100 mL) and then was extracted with ethyl acetate. The combined organics were washed with water, brine, dried with magnesium sulfate, filtered and concentrated. The crude tert-butyl 4-(4-(bis(trimethylsilyl)amino)phenyl)-4-hydroxypiperidine-1-carboxylate was treated with a solution of tetrabutylammonium fluoride (1M THF, 40 mL) at room temperature for 1 hour. The reaction mixture was diluted with water and extracted with ethyl acetate. The organics were washed with water and brine, dried with magnesium sulfate, filtered and concentrated. Purification by normal phase chromatography provided the title compund.

Example 809B

tert-butyl 4-(4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)phenyl)-4-hydroxypiperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(4-aminophenyl)-4-hydroxypiperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-((benzyloxy)carbonyl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 809C

tert-butyl 4-(4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)phenyl)-4-fluoropiperidine-1-carboxylate

tert-Butyl 4-(4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)phenyl)-4-hydroxypiperidine-1-carboxylate (2.5 g, 4.91 mmol) in 50 mL dichloromethane was cooled to -78°C and diethylaminosulfur trifluoride was added dropwise via a syringe. The reaction solution was stirred at -78 °C for an additional 1 hour and then warmed to 0° C. The reaction was allowed to stir at 0 °C for 1 hour and was cooled back down to -78 °C. The reaction mixture was diluted with 50 mL of dichloromethane followed by quenching with 10 mL methanol. The solution was washed with saturated sodium bicarbonate and brine, dried with magnesium sulfate and filtered. Concentration and normal phase chromatography provided the title compound.

Example 809D

tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)-4-fluoropiperidine-1-carboxylate

The title compound was prepared as described in Example 1B, substituting tert-butyl 4-(4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)phenyl)-4-fluoropiperidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 809E

tert-butyl 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)-4-fluoropiperidine-1-carboxylate

The title compound was prepared as described in Example 147A, substituting tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)-4-fluoropiperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 809F

tert-butyl 4-fluoro-4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidine-1-carboxylate

The title compound was prepared as described in Example 147B, substituting tert-butyl 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)-4-fluoropiperidine-1-carboxylate for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.18 – 10.08 (m, 1H), 8.55 (dd, J = 4.5, 1.4 Hz, 1H), 7.65 – 7.56 (m, 2H), 7.40 – 7.33 (m, 3H), 6.82 (dd, J = 8.9, 1.4 Hz, 1H), 4.23 (t, J = 8.3 Hz, 2H), 4.14 (dd, J = 8.2, 5.7 Hz, 2H), 4.08 – 3.91 (m, 2H), 3.81 – 3.68 (m, 1H), 3.17 – 2.70 (m, 2H), 2.07 – 1.82 (m, 3H), 1.42-1.35 (s, 10H); MS (ESI(+)) m/e 456 $(M+H)^+$.

Example 810

5-(1-benzoylpiperidin-4-yl)-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide

Example 810A

5-(piperidin-4-yl)-N-(1-(pyridazin-3-yl)azetidin-3-yl)thiophene-2-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(5-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}thiophen-2-yl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 810B

5-(1-benzoylpiperidin-4-yl)-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide

The title compound was prepared as described in Example 1A, substituting 5-(piperidin-4-yl)-N-(1-(pyridazin-3-yl)azetidin-3-yl)thiophene-2-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.96 (d, J = 7.2 Hz, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.66 (d, J = 3.8 Hz, 1H), 7.51 – 7.34 (m, 6H), 6.98 (dd, J = 3.8, 0.8 Hz, 1H), 6.84 (dd, J = 9.0, 1.4 Hz, 1H), 4.92 – 4.77 (m, 1H), 4.6 (bs, 1H),4.36 (t, J = 8.1 Hz, 2H), 4.01 (dd, J = 8.6, 5.6 Hz, 2H), 3.64 (bs, 1H), 3.23 – 2.83 (m, 3H), 2.10 – 1.84 (m, 2H), 1.67 – 1.48 (m, 2H); MS (ESI(+)) m/e 448 $(M+H)^+$.

Table 19.

The following Examples were essentially prepared as described in Example 810, substituting an appropriate carboxylic acid in Example 810B.

Ex		Name	MS
811		5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 466 $(M+H)^+$
812		5-[1-(2-methylbenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
813		5-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
814		5-[1-(3-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 466 $(M+H)^+$
815		5-[1-(4-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 466 $(M+H)^+$
816		5-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 484 $(M+H)^+$
847		5-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 428 $(M+H)^+$
848		5-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 426 $(M+H)^+$
849		N-[1-(pyridazin-3-yl)azetidin-3-yl]-5-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]thiophene-2-carboxamide	(ESI(+)) m/e 454

			$(M+H)^+$
850		5-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 442 $(M+H)^+$
855		N-[1-(pyridazin-3-yl)azetidin-3-yl]-5-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]thiophene-2-carboxamide	(ESI(+)) m/e 468 $(M+H)^+$
856		5-[1-(cyclopropylcarbonyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide	(ESI(+)) m/e 412 $(M+H)^+$

Example 817

N-{4-[3-cyclopropyl-1-(2-hydroxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 805, substituting 2-hydrazinylethanol for methylhydrazine in 805B. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.14 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.72 – 7.58 (m, 4H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 6.83 (dd, J = 9.0, 1.4 Hz, 1H), 6.27 (s, 1H), 4.90 (br s, 1H), 4.31 – 4.08 (m, 6H), 3.84 – 3.69 (m, 3H), 2.01 – 1.88 (m, 1H), 1.01 – 0.89 (m, 2H), 0.72 – 0.62 (m, 2H); MS (ESI(+)) m/e 405 $(M+H)^+$.

Example 818

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide

Example 818A

tert-butyl 4-(4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(4-aminophenyl)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-((benzyloxy)carbonyl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 818B

tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1B, substituting tert-butyl 4-(4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 818C

tert-butyl 4-(4-(1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 147A, substituting tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-

(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate and 3,6-difluoropyridazine for 3,6-dichloropyridazine.

Example 818D

1-(6-fluoropyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(4-(1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 818E

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(6-fluoropyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.03 (s, 1H), 7.54 (d, J = 8.6 Hz, 2H), 7.49 – 7.38 (m, 6H), 7.22 (d, J = 8.6 Hz, 2H), 7.12 (dd, J = 9.5, 6.8 Hz, 1H), 4.23 (t, J = 8.3 Hz, 2H), 4.14 (dd, J = 8.0, 6.0 Hz, 2H), 3.71 (ddd, J = 14.4, 8.4, 5.9 Hz, 2H), 2.86 (dd, J = 67.9, 55.9 Hz, 3H), 2.04 – 1.43 (m, 4H); MS (ESI(+)) m/e 460 $(M+H)^+$.

Example 819

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(6-fluoropyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.04 (s, 1H), 7.58 – 7.34 (m, 5H), 7.35 – 7.25 (m, 2H), 7.23 – 7.17 (m, 2H), 7.12 (dd, J = 9.4, 6.7 Hz, 1H), 4.70 – 4.61 (m, 1H), 4.23 (t, J = 8.3 Hz, 2H), 4.14 (d, J = 13.9 Hz, 2H), 3.77 – 3.66 (m, 1H), 3.50 – 3.41 (m, 1H), 3.23 – 3.09 (m, 1H), 2.95 – 2.72 (m, 2H), 1.91 – 1.82 (m, 1H), 1.79 – 1.42 (m, 3H); MS (ESI(+)) m/e 478 $(M+H)^+$.

Example 820

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(6-fluoropyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,2-dimethylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.03 (s, 1H), 7.57 – 7.50 (m, 2H), 7.41 (dd, J = 9.4, 1.9 Hz, 1H), 7.22 – 7.15 (m, 2H), 7.12 (dd, J = 9.4, 6.7 Hz, 1H), 4.45 – 4.36 (m, 2H), 4.23 (t, J = 8.3 Hz, 2H), 4.14 (dd, J = 8.0, 5.9

Hz, 2H), 3.77 – 3.66 (m, 1H), 2.93 – 2.66 (m, 3H), 1.82 – 1.74 (m, 2H), 1.52 – 1.35 (m, 2H), 1.22 (s, 9H); MS (ESI(+)) m/e 440 $(M+H)^+$.

Example 821

1-(6-fluoropyridazin-3-yl)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(6-fluoropyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and isobutyric acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.03 (s, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.41 (dd, J = 9.5, 1.9 Hz, 1H), 7.18 (d, J = 8.5 Hz, 2H), 7.12 (dd, J = 9.5, 6.8 Hz, 1H), 4.62 – 4.45 (m, 1H), 4.23 (t, J = 8.3 Hz, 2H), 4.14 (dd, J = 7.9, 6.1 Hz, 2H), 4.10 – 3.97 (m, 1H), 3.72 (ddd, J = 8.4, 7.2, 4.2 Hz, 1H), 3.10 (s, 1H), 2.89 (dt, J = 13.4, 6.7 Hz, 1H), 2.81 – 2.64 (m, 1H), 2.57 (s, 1H), 1.79 (ddd, J = 16.4, 10.0, 2.9 Hz, 2H), 1.58 – 1.25 (m, 2H), 1.12 – 0.92 (m, 6H); MS (ESI(+)) m/e 426 $(M+H)^+$.

Example 822

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(6-fluoropyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-ethylbutanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.03 (s, 1H), 7.57 – 7.51 (m, 2H), 7.41 (dd, J = 9.4, 1.9 Hz, 1H), 7.21 – 7.08 (m, 3H), 4.68 – 4.59 (m, 1H), 4.31 – 4.06 (m, 1H), 3.77 – 3.66 (m, 1H), 3.15 – 3.04 (m, 1H), 2.66 (ddt, J = 25.3, 20.0, 12.2 Hz, 1H), 1.87 – 1.74 (m, 2H), 1.64 – 1.27 (m, 6H), 0.87 – 0.76 (m, 6H); MS (ESI(+)) m/e 454 $(M+H)^+$.

Example 823

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(6-fluoropyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 4-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.04 (s, 1H), 7.59 – 7.46 (m, 4H), 7.41 (dd, J = 9.4, 1.9 Hz, 1H), 7.32 – 7.17 (m, 4H), 7.13 (dd, J = 9.4, 6.7 Hz, 1H), 4.70 – 4.48 (m, 1H), 4.24 (t, J = 8.3 Hz, 2H), 4.14 (dd, J = 8.0, 5.9 Hz, 2H), 4.06 – 3.53 (m, 2H), 3.22 – 2.68 (m, 3H), 2.04 – 1.50 (m, 4H); MS (ESI(+)) m/e 478 $(M+H)^+$.

Example 824

(3S)-N-(4-{[(3S)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

Example 824A

(S)-tert-butyl 3-(4-((S)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamido)phenoxy)pyrrolidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting (R)-tert-butyl 3-(4-aminophenoxy)pyrrolidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and (S)-1-(pyridazin-3-yl)pyrrolidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 824B

(S)-1-(pyridazin-3-yl)-N-(4-((S)-pyrrolidin-3-yloxy)phenyl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl 3-(4-((S)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamido)phenoxy)pyrrolidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 774C

(3S)-N-(4-{[(3S)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(pyridazin-3-yl)-N-(4-((S)-pyrrolidin-3-yloxy)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.04 – 9.95 (m, 1H), 8.51 – 8.45 (m, 1H), 7.61 – 7.37 (m, 7H), 7.37 – 7.30 (m, 1H), 6.99 – 6.92 (m, 1H), 6.90 – 6.83 (m, 2H), 5.07 – 4.92 (m, 1H), 3.88 – 3.70 (m, 2H), 3.71 – 3.38 (m, 6H), 2.37 – 1.97 (m, 4H); MS (ESI(+)) m/e 458 $(M+H)^+$.

Example 825

(3S)-N-(4-{[(3S)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(pyridazin-3-yl)-N-(4-((S)-pyrrolidin-3-yloxy)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.04 – 9.96 (m, 1H), 8.48 (d, J = 4.5 Hz, 1H), 7.59 – 7.37 (m, 4H), 7.37 – 7.22 (m, 3H), 6.94 (d, J = 8.7 Hz, 1H), 6.87 (dd, J = 8.9, 4.4 Hz, 2H), 3.86 – 3.52 (m, 5H), 3.54 – 3.37 (m, 2H), 2.37 – 1.97 (m, 4H); MS (ESI(+)) m/e 476$(M+H)^+$.

Example 826

(3S)-N-(4-{[(3S)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(pyridazin-3-yl)-N-(4-((S)-pyrrolidin-3-yloxy)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,4-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.07 – 9.93 (m, 1H), 8.47 (t, J = 4.6 Hz, 1H), 7.54 (dt, J = 12.8, 10.3 Hz, 2H), 7.44 – 7.18 (m, 4H), 7.02 – 6.80 (m, 3H), 5.16 – 4.85 (m, 1H), 3.91 – 3.70 (m, 2H), 3.70 – 3.35 (m, 7H), 2.43 – 1.97 (m, 4H); MS (ESI(+)) m/e 494$(M+H)^+$.

Example 827

(3S)-N-(4-{[(3S)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(pyridazin-3-yl)-N-(4-((S)-pyrrolidin-3-yloxy)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,2-dimethylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.99 (s, 1H), 8.48 (dd, J = 4.5, 1.3 Hz, 1H), 7.57 – 7.50 (m, 2H), 7.33 (dd, J = 9.1, 4.5 Hz, 1H), 6.95 – 6.83 (m, 4H), 4.95 (bs, 1H), 3.86 – 3.39 (m, 8H), 2.39 – 1.92 (m, 4H), 1.15 (s, 9H); MS (ESI(+)) m/e 438. $(M+H)^+$.

Example 828

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 828A

tert-butyl 4-(4-amino-3-fluorophenyl)-5,6-dihydropyridine-1(2H)-carboxylate

The title compound was prepared as described in Example 148A, substituting tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole and 4-bromo-2-fluoroaniline for 4-bromoaniline.

Example 828B

tert-butyl 4-(4-amino-3-fluorophenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1B, substituting tert-butyl 4-(4-amino-3-fluorophenyl)-5,6-dihydropyridine-1(2H)-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 828C

tert-butyl 4-(4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)-3-fluorophenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(4-amino-3-fluorophenyl)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-((benzyloxy)carbonyl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 828D

tert-butyl 4-(4-(azetidine-3-carboxamido)-3-fluorophenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1B, substituting tert-butyl 4-(4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)-3-fluorophenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 828E

tert-butyl 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)-3-fluorophenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 147A, substituting tert-butyl 4-(4-(azetidine-3-carboxamido)-3-fluorophenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 828F

tert-butyl 4-(3-fluoro-4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 147B, substituting tert-butyl 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)-3-fluorophenyl)piperidine-1-carboxylate for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 828G

N-(2-fluoro-4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(3-fluoro-4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 828H

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(2-fluoro-4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.86 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.79 (t, J = 8.3 Hz, 1H), 7.58 – 7.41 (m, 2H), 7.42 –

7.25 (m, 3H), 7.23 – 7.14 (m, 1H), 7.11 – 7.03 (m, 1H), 6.83 (dd, J = 9.0, 1.4 Hz, 1H), 4.70 – 4.61 (m, 1H), 4.24 (t, J = 8.3 Hz, 2H), 4.14 (dd, J = 8.1, 5.8 Hz, 2H), 3.92 – 3.81 (m, 1H), 3.51 – 3.42 (m, 1H), 3.23 – 3.10 (m, 1H), 2.92 – 2.76 (m, 2H), 1.94 – 1.81 (m, 1H), 1.83 – 1.44 (m, 3H); MS (ESI(+)) m/e 478 $(M+H)^+$.

Table 20.

The following Examples were essentially prepared as described in Example 828, substituting the appropriate carboxylic acid in Example 828H.

Ex		Name	MS
829		N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 460 $(M+H)^+$
830		N-{2-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
831		N-{2-fluoro-4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
832		N-{2-fluoro-4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
833		N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 496 $(M+H)^+$
834		N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 460 $(M+H)^+$
835		N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 454 $(M+H)^+$
858		N-{2-fluoro-4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 426 $(M+H)^+$
859		N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 440 $(M+H)^+$
860		N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 424 $(M+H)^+$
861		N-(2-fluoro-4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
862		N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$

Example 836

(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide

Example 836A

(S)-tert-butyl 4-(4-(1-((benzyloxy)carbonyl)pyrrolidine-3-carboxamido)phenoxy)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting (S)-1-benzyl 3-tert-butyl pyrrolidine-1,3-dicarboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 836B

(S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenoxy)piperidine-1-carboxylate

The title compound was prepared as described in Example 1B, substituting (S)-tert-butyl 4-(4-(1-((benzyloxy)carbonyl)pyrrolidine-3-carboxamido)phenoxy)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 836C

(S)-tert-butyl 4-(4-(1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamido)phenoxy)piperidine-1-carboxylate

The title compound was prepared as described in Example 1C, substituting 3-bromo-6-methylpyridazine for 3-bromopyridine and (S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenoxy)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 836D

(S)-1-(6-methylpyridazin-3-yl)-N-(4-(piperidin-4-yloxy)phenyl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl 4-(4-(1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamido)phenoxy)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 836E

(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(6-methylpyridazin-3-yl)-N-(4-(piperidin-4-yloxy)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.98 (s, 1H), 7.57 – 7.45 (m, 3H), 7.42 (td, J = 7.2, 1.8 Hz, 1H), 7.35 – 7.20 (m, 3H), 6.98 – 6.91 (m, 2H), 6.83 (d, J = 9.1 Hz, 1H), 4.63 – 4.54 (m, 1H), 4.05 – 3.95 (m, 1H), 3.74 (dd, J = 10.3, 7.9 Hz, 1H), 3.64 – 3.42 (m, 3H), 3.31 – 3.03 (m, 3H), 2.40(s, 3H), 2.36 – 2.08 (m, 2H), 2.07 – 1.76 (m, 2H), 1.78 – 1.19 (m, 4H); MS (ESI(+)) m/e 504 $(M+H)^+$.

Example 837

(3S)-N-{4-[(1-benzoylpiperidin-4-yl)oxy]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(6-methylpyridazin-3-yl)-N-(4-(piperidin-4-yloxy)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.98 (s, 1H), 7.55 – 7.48 (m, 2H), 7.48 – 7.37 (m, 5H), 7.23 (d, J = 9.1 Hz, 1H), 6.97 – 6.91 (m, 2H), 6.83 (d, J = 9.1 Hz, 1H), 4.57 (dq, J = 7.7, 3.8 Hz, 1H), 4.04 – 3.42 (m, 8H), 3.26 (p, J = 7.4 Hz, 1H), 2.41 (s, 3H), 2.35 – 2.08 (m, 2H), 2.09 – 1.84 (m, 2H), 1.68 – 1.51 (m, 2H); MS (ESI(+)) m/e 486 $(M+H)^+$.

Example 838

(3S)-N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(6-methylpyridazin-3-yl)-N-(4-(piperidin-4-yloxy)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,2-dimethylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.98 (s, 1H), 7.55 – 7.48 (m, 2H), 7.24 (d, J = 9.1 Hz, 1H), 6.96 – 6.90 (m, 2H), 6.83 (d, J = 9.1 Hz, 1H), 4.59 – 4.50 (m, 1H), 3.94 – 3.80 (m, 2H), 3.74 (dd, J = 10.3, 7.9 Hz, 1H), 3.65 – 3.52 (m, 2H), 3.32 – 3.18 (m, 4H), 2.40(s, 3H), 2.34 – 2.08 (m, 2H), 1.97 – 1.83 (m, 2H), 1.58 – 1.43 (m, 2H), 1.20 (s, 9H); MS (ESI(+)) m/e 466 $(M+H)^+$.

Example 839

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(6-methylpyridazin-3-yl)-N-(4-(piperidin-4-yloxy)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and cyclohexanecarboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.98 (s, 1H), 7.55 – 7.48 (m, 2H), 7.24 (d, J = 9.1 Hz, 1H), 6.97 – 6.90 (m, 2H), 6.83 (d, J = 9.2 Hz, 1H), 4.52 (dq, J = 7.8, 3.9 Hz, 1H), 3.89 – 3.66 (m, 3H), 3.68 – 3.49 (m, 2H), 3.45 – 3.13 (m, 3H), 2.61-2.55 (m, 1H), 2.40(s, 3H), 2.36 – 2.11 (m, 2H), 2.04 – 1.80 (m, 2H), 1.74 – 1.08 (m, 13H); MS (ESI(+)) m/e 492 $(M+H)^+$.

Example 840

N-{4-[8-(2-methylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 840A

tert-butyl 3-(4-nitrophenyl)-8-azabicyclo[3.2.1]oct-2-ene-8-carboxylate

The title compound was prepared as described in Example 148A, substituting 2,2-dimethyl-1-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-8-azabicyclo[3.2.1]oct-3-en-8-yl)propan-1-one for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole and 1-bromo-4-nitrobenzene for 4-bromoaniline.

Example 840B

tert-butyl 3-(4-aminophenyl)-8-azabicyclo[3.2.1]octane-8-carboxylate

The title compound was prepared as described in Example 1B, substituting tert-butyl 3-(4-nitrophenyl)-8-azabicyclo[3.2.1]oct-2-ene-8-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 840C

tert-butyl 3-(4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)phenyl)-8-azabicyclo[3.2.1]octane-8-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 3-(4-aminophenyl)-8-azabicyclo[3.2.1]octane-8-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-((benzyloxy)carbonyl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 840D

tert-butyl 3-(4-(azetidine-3-carboxamido)phenyl)-8-azabicyclo[3.2.1]octane-8-carboxylate

The title compound was prepared as described in Example 1B, substituting tert-butyl 3-(4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)phenyl)-8-azabicyclo[3.2.1]octane-8-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 840F

tert-butyl 3-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)-8-azabicyclo[3.2.1]octane-8-carboxylate

The title compound was prepared as described in Example 147A, substituting tert-butyl 3-(4-(azetidine-3-carboxamido)phenyl)-8-azabicyclo[3.2.1]octane-8-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 840G

tert-butyl 3-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)-8-azabicyclo[3.2.1]octane-8-carboxylate

The title compound was prepared as described in Example 147B, substituting tert-butyl 3-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)-8-azabicyclo[3.2.1]octane-8-carboxylate for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 840H

N-(4-(8-azabicyclo[3.2.1]octan-3-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 3-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)-8-azabicyclo[3.2.1]octane-8-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 840I

N-{4-[8-(2-methylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(8-azabicyclo[3.2.1]octan-3-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and isobutyric acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.03 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.52 (dd, J = 7.4, 3.4 Hz, 2H), 7.37 (dd, J = 9.0, 4.5 Hz, 1H), 7.18 (dd, J = 17.7, 8.6 Hz, 2H), 6.82 (dd, J = 9.0, 1.3 Hz, 1H), 4.51 (ddd, J = 15.0, 5.1, 4.4 Hz, 1H), 4.43 – 4.29 (m, 1H), 4.18 (dt, J = 14.0, 8.1 Hz, 4H), 3.72 (ddd, J = 8.4, 5.9, 2.5 Hz, 1H), 2.77 (dt, J = 13.4, 6.7 Hz, 1H), 2.48 – 2.14 (m, 3H), 2.04 – 1.37 (m, 7H), 1.15 – 0.94 (m, 6H); MS (ESI(+)) m/e 434 $(M+H)^+$.

Example 841

1-(pyridazin-3-yl)-N-{4-[8-(4,4,4-trifluorobutanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(8-azabicyclo[3.2.1]octan-3-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 4,4,4-trifluorobutanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.03 (d, J = 3.6 Hz, 1H), 8.56 (dd, J = 4.5, 1.1 Hz, 1H), 7.53 (dd, J = 8.6, 2.7 Hz, 2H), 7.37 (dt, J = 14.0, 7.0 Hz, 1H), 7.21 (dd, J = 23.0, 8.6 Hz, 2H), 6.80 (dd, J = 19.3, 8.9 Hz, 1H), 4.61 – 4.47 (m, 1H), 4.32 (dd, J = 16.5, 8.6 Hz, 1H), 4.23 (t, J = 8.3 Hz, 2H), 4.14 (t, J = 7.0 Hz, 2H), 3.82 – 3.62 (m, 1H), 3.22 – 3.04 (m, 1H), 3.04 – 2.90 (m, 1H), 2.78 – 2.50 (m, 6H), 2.41 – 2.12 (m, 1H), 2.05 – 1.38 (m, 8H); MS (ESI(+)) m/e 488 $(M+H)^+$.

Example 842

N-[4-(8-benzoyl-8-azabicyclo[3.2.1]oct-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(8-azabicyclo[3.2.1]octan-3-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.04 (d, J = 2.4 Hz, 1H), 8.56 (dt, J = 9.1, 4.5 Hz, 1H), 7.63 – 7.42 (m, 7H), 7.37 (dt, J = 14.0, 7.0 Hz, 1H), 7.29 (d, J = 8.5 Hz, 1H), 7.23 (d, J = 8.5 Hz, 1H), 6.91 – 6.70 (m, 1H), 4.69

(d, J = 6.1 Hz, 1H), 4.24 (t, J = 8.3 Hz, 2H), 4.19 – 4.11 (m, 2H), 4.01 (d, J = 14.9 Hz, 1H), 3.85 – 3.61 (m, 1H), 2.47 – 2.22 (m, 1H), 2.02 – 1.53 (m, 7H); MS (ESI(+)) m/e 468 $(M+H)^+$.

Example 843

N-{4-[8-(2-fluorobenzoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(8-azabicyclo[3.2.1]octan-3-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.04 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.59 – 7.44 (m, 4H), 7.46 – 7.16 (m, 5H), 6.82 (dd, J = 9.0, 1.4 Hz, 1H), 4.73 – 4.65 (m, 1H), 4.24 (t, J = 8.3 Hz, 2H), 4.14 (dd, J = 8.0, 5.9 Hz, 2H), 3.81 – 3.67 (m, 2H), 2.10 (s, 1H), 2.05 – 1.35 (m, 8H); MS (ESI(+)) m/e 486 $(M+H)^+$.

Example 844

N-{4-[8-(2,2-dimethylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(8-azabicyclo[3.2.1]octan-3-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,2-dimethylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.02 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.56 – 7.49 (m, 2H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 7.24 – 7.14 (m, 2H), 6.82 (dd, J = 9.0, 1.4 Hz, 1H), 4.66 – 4.51 (m, 2H), 4.23 (t, J = 8.3 Hz, 2H), 4.14 (dd, J = 8.1, 5.9 Hz, 2H), 3.72 (tt, J = 8.5, 5.9 Hz, 1H), 2.43 – 2.07 (m, 3H), 1.92 – 1.39 (m, 8H), 1.23 – 1.17 (m, 9H); MS (ESI(+)) m/e 448 $(M+H)^+$.

Example 845

N-(4-{8-[(1-methylcyclopropyl)carbonyl]-8-azabicyclo[3.2.1]oct-3-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(8-azabicyclo[3.2.1]octan-3-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-methylcyclopropylacetic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.03 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.56 – 7.49 (m, 2H), 7.38 (dd, J = 8.9, 4.5 Hz, 1H), 7.26 – 7.15 (m, 2H), 6.82 (dd, J = 8.9, 1.4 Hz, 1H), 4.62 – 4.38 (m, 2H), 4.23 (t, J = 8.3 Hz, 2H), 4.14 (dd, J = 8.1, 5.9 Hz, 2H), 3.72 (tt, J = 8.5, 5.9 Hz, 1H), 2.37 – 2.21 (m, 1H), 1.93 – 1.45 (m, 8H), 1.28 (d, J = 5.7 Hz, 3H), 1.02 – 0.72 (m, 2H), 0.51 (dd, J = 6.2, 2.1 Hz, 2H); MS (ESI(+)) m/e 446 $(M+H)^+$.

Example 846

N-{4-[1-(2-methoxyethyl)-3-(2-methylpropyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 805, substituting 4-methylpent-1-yne for ethynylcyclopropane in Example 805A and (2-methoxyethyl)hydrazine for methylhydrazine in 805B. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.21 (s, 1H), 8.56 (dd, J = 4.4, 1.2 Hz, 1H), 7.78 – 7.58 (m, 4H), 7.24 (d, J = 8.5 Hz, 1H), 6.42 (s, 1H), 4.45 – 4.25 (m, 3H), 4.18 (t, J = 5.5 Hz, 2H), 3.87 – 3.73 (m, 1H), 3.69 (t, J = 5.5 Hz, 2H), 3.46 – 3.30 (m, 4H), 3.22 (s, 3H), 2.01 – 1.84 (m, 1H), 0.95 (d, J = 6.6 Hz, 6H); MS (ESI(+)) m/e 435 $(M+H)^+$.

Example 853

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-fluoropiperidine-1-carboxylate

The title compound was prepared as described in Example 809C, substituting benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-hydroxypiperidine-1-carboxylate for tert-butyl 4-(4-(1-((benzyloxy)carbonyl)azetidine-3-carboxamido)phenyl)-4-hydroxypiperidine-1-carboxylate. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.18 – 10.11 (m, 1H), 7.67 – 7.57 (m, 2H), 7.53 (d, *J* = 9.3 Hz, 1H), 7.47 – 7.23 (m, 7H), 6.96 (d, *J* = 9.3 Hz, 1H), 5.14 – 5.08 (m, 2H), 4.26 (t, *J* = 8.4 Hz, 2H), 4.17 (dd, *J* = 8.3, 5.8 Hz, 2H), 4.09 – 3.98 (m, 2H). 3.80-3.60 (m, 2H), 3.30-3.20 (m, 2H), 2.2-1.8 (m, 3H); MS (ESI(+)) m/e 524 $(M+H)^+$.

Example 854

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-hydroxypiperidine-1-carboxylate

Example 854A

benzyl 4-(4-aminophenyl)-4-hydroxypiperidine-1-carboxylate

The title compound was prepared as described in Example 809A, substituting benzyl 4-oxopiperidine-1-carboxylate for tert-butyl 4-oxopiperidine-1-carboxylate.

Example 854B

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-hydroxypiperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting benzyl 4-(4-aminophenyl)-4-hydroxypiperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(6-chloropyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.06 (s, 1H), 7.59 – 7.49 (m, 3H), 7.41 – 7.28 (m, 7H), 6.96 (d, *J* = 9.3 Hz, 1H), 5.09 (s, 2H), 5.04 (s, 1H), 4.26 (t, *J* = 8.4 Hz, 2H), 4.16 (dd, *J* = 8.3, 5.8 Hz, 2H), 3.97 – 3.86 (m, 2H),

3.73 (tt, J = 8.5, 5.8 Hz, 1H), 3.3-3.0 (m, 2H), 1.91 – 1.70 (m, 2H), 1.63 – 1.54 (m, 2H); MS (ESI(+)) m/e 522.0 $(M+H)^+$.

Example 857

N-{4-[4-fluoro-1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 857A

N-(4-(4-fluoropiperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-fluoro-4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 857B

N-{4-[4-fluoro-1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(4-fluoropiperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.06 (s, 1H), 7.59 – 7.49 (m, 3H), 7.41 – 7.28 (m, 7H), 6.96 (d, J = 9.3 Hz, 1H), 5.09 (s, 2H), 5.04 (s, 1H), 4.26 (t, J = 8.4 Hz, 2H), 4.16 (dd, J = 8.3, 5.8 Hz, 2H), 3.97 – 3.86 (m, 2H), 3.73 (tt, J = 8.5, 5.8 Hz, 1H), 3.3-3.0 (m, 2H), 1.91 – 1.70 (m, 2H), 1.63 – 1.54 (m, 2H); MS (ESI(+)) m/e 478 $(M+H)^+$.

Example 863

N-[4-(1-benzoyl-4-fluoropiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(4-fluoropiperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.20 – 10.03 (m, 1H), 8.57 (d, J = 4.5 Hz, 1H), 7.68 – 7.59 (m, 2H), 7.60 – 7.30 (m, 8H), 6.87 – 6.80 (m, 1H), 4.78 – 4.09 (m, 5H), 4.10 – 3.44 (m, 3H), 3.14 – 3.01 (m, 1H), 2.25 – 1.51 (m, 4H); MS (ESI(+)) m/e 460 $(M+H)^+$.

Example 864

N-{4-[1-(2,2-dimethylpropanoyl)-4-fluoropiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(4-fluoropiperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,2-dimethypropanoic acid for 1-

(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.20 – 10.02 (m, 1H), 8.56 (dd, *J* = 4.5, 1.3 Hz, 1H), 7.67 – 7.58 (m, 2H), 7.47 – 7.30 (m, 3H), 6.83 (dd, *J* = 8.9, 1.4 Hz, 1H), 4.48 – 4.10 (m, 6H), 3.80 – 3.69 (m, 1H), 3.23 – 2.96 (m, 2H), 2.07 – 1.60 (m, 4H), 1.23 (s, 9H); MS (ESI(+)) m/e 440 $(M+H)^+$.

Example 865

N-{4-[3-tert-butyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 805, substituting 3,3-dimethylbut-1-yne for ethynylcyclopropane in Example 805A and (2-methoxyethyl)hydrazine for methylhydrazine in Example 805B. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.14 (s, 1H), 8.57 (dd, J = 4.5, 1.3 Hz, 1H), 7.70 (d, J = 8.7 Hz, 2H), 7.64 (d, J = 8.7 Hz, 2H), 7.39 (dd, J = 8.9, 4.5 Hz, 1H), 6.84 (d, J = 8.9 Hz, 1H), 6.40 (s, 1H), 4.31 (t, J = 6.0 Hz, 2H), 4.25 (t, J = 8.3 Hz, 2H), 4.17 (dd, J = 8.0, 6.0 Hz, 2H), 3.83 (t, J = 6.0 Hz, 2H), 3.75 (tt, J = 8.7, 6.1 Hz, 1H), 3.25 (s, 3H), 1.37 (s, 9H); MS (ESI(+)) m/e 435 $(M+H)^+$.

Example 866

N-[4-(1-butyl-3-tert-butyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 805, substituting 3,3-dimethylbut-1-yne for ethynylcyclopropane in Example 805A and butylhydrazine for methylhydrazine in 805B. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.14 (s, 1H), 8.57 (dd, J = 4.5, 1.3 Hz, 1H), 7.69 (d, J = 8.7 Hz, 2H), 7.63 (d, J = 8.8 Hz, 2H), 7.39 (dd, J = 8.9, 4.5 Hz, 1H), 6.84 (dd, J = 8.9, 1.3 Hz, 1H), 6.38 (s, 1H), 4.25 (t, J = 8.3 Hz, 2H), 4.21 – 4.09 (m, 4H), 3.81 – 3.70 (m, 1H), 1.92 – 1.77 (m, 2H), 1.46 – 1.37 (m, 2H), 1.36 (s, 9H), 0.94 (t, J = 7.3 Hz, 3H); MS (ESI(+)) m/e 433 $(M+H)^+$.

Example 867

N-{4-[3-tert-butyl-1-(tetrahydro-2H-pyran-4-ylmethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 805, substituting 3,3-dimethylbut-1-yne for ethynylcyclopropane in Example 805A and (tetrahydro-2H-pyran-4-ylmethyl)hydrazine for methylhydrazine in Example 805B. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.14 (s, 1H), 8.57 (dd, J = 4.5, 1.3 Hz, 1H), 7.70 (d, J = 8.7 Hz, 2H), 7.63 (d, J = 8.8 Hz, 2H), 7.39 (dd, J = 8.9, 4.5 Hz, 1H), 6.83 (dd, J = 8.9, 1.4 Hz, 1H), 6.41 (s, 1H), 4.25 (t, J = 8.3 Hz, 2H), 4.16 (dd, J = 8.1, 5.9 Hz, 2H), 4.03 (d, J = 7.0 Hz, 2H), 3.85 (dd, J = 11.3, 3.0 Hz, 2H), 3.80 – 3.71 (m, 1H), 3.32 – 3.22 (m, 2H), 2.39 – 2.25 (m, 1H), 1.55 (dd, J = 12.8, 1.9 Hz, 2H), 1.37 (s, 9H), 1.42 – 1.30 (m, 2H); MS (ESI(+)) m/e 475 $(M+H)^+$.

Example 868

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide

Example 868A

tert-butyl 4-(4-(1-(5,6-dichloropyridazin-4-yl)azetidine-3-carboxamido)-3-fluorophenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 618, substituting tert-butyl 4-(4-(azetidine-3-carboxamido)-3-fluorophenyl)piperidine-1-carboxylate for (R)-5-(1-isobutyl-1H-pyrazol-4-yl)-N-(pyrrolidin-3-yl)thiophene-2-carboxamide.

Example 868B

tert-butyl 4-(3-fluoro-4-(1-(pyridazin-4-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 147B, substituting tert-butyl 4-(4-(1-(5,6-dichloropyridazin-4-yl)azetidine-3-carboxamido)-3-fluorophenyl)piperidine-1-carboxylate for 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate.

Example 868C

N-(2-fluoro-4-(piperidin-4-yl)phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(3-fluoro-4-(1-(pyridazin-4-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 868D

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(2-fluoro-4-(piperidin-4-yl)phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.39 (s, 1H), 8.66 (d, J = 6.3 Hz, 1H), 8.52 (d, J = 3.0 Hz, 1H), 7.66 – 7.37 (m, 4H), 7.35 – 7.27 (m, 3H), 6.68 (dd, J = 6.3, 3.2 Hz, 1H), 4.71 – 4.62 (m, 1H), 4.37 – 3.92 (m, 4H), 3.94 – 2.70 (m, 5H), 1.88 – 12 (m, 4H); MS (ESI(+)) m/e 478 $(M+H)^+$.

Example 869

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(2-fluoro-4-(piperidin-4-yl)phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm

10.27 (s, 1H), 8.61 (dd, J = 6.0, 0.9 Hz, 1H), 8.51 (dd, J = 3.0, 0.9 Hz, 1H), 7.57 (dd, J = 12.9, 2.0 Hz, 1H), 7.51 – 7.38 (m, 5H), 7.34 (t, J = 8.4 Hz, 1H), 7.28 (dd, J = 8.4, 2.0 Hz, 1H), 6.55 (dd, J = 6.0, 3.0 Hz, 1H), 4.71 – 4.51 (m, 1H), 4.22 (t, J = 8.4 Hz, 2H), 4.12 (dd, J = 8.2, 5.7 Hz, 2H), 4.04 – 3.45 (m, 2H), 3.22 – 2.76 (m, 3H), 2.08 – 1.33 (m, 4H); MS (ESI(+)) m/e 460 $(M+H)^+$.

Example 870

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(2-fluoro-4-(piperidin-4-yl)phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,2-dimethylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 10.28 (s, 1H), 8.61 (dd, J = 6.0, 0.9 Hz, 1H), 8.51 (d, J = 3.4 Hz, 1H), 7.68 – 7.24 (m, 3H), 6.57 (dd, J = 6.1, 3.0 Hz, 1H), 4.5 (d, 2H), 4.30- 4.13 (m, 4H), 3.90– 2.78 (m, 4H), 1.79 – 1.71 (m, 2H), 1.72 – 1.44 (m, 2H), 1.21 (s, 9H); MS (ESI(+)) m/e 440 $(M+H)^+$.

Example 871

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(2-fluoro-4-(piperidin-4-yl)phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 3,3,-dimethylbutanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 10.28 (s, 1H), 8.62 (d, J = 6.1 Hz, 1H), 8.51 (d, J = 3.4 Hz, 1H), 7.60 – 7.23 (m, 3H), 6.57 (dd, J = 6.1, 3.0 Hz, 1H), 4.65 – 4.58 (m, 1H), 4.30 – 4.00 (m, 5H), 3.85 – 2.83 (m, 3H), 2.60-2.50 (m, 1H), 2.30 (d, J = 14.0 Hz, 1H), 2.21 (d, J = 14.0 Hz, 1H), 1.79 – 1.40 (m, 4H), 1.00 (s, 9H); MS (ESI(+)) m/e 454 $(M+H)^+$.

Example 872

N-{2-fluoro-4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(2-fluoro-4-(piperidin-4-yl)phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 4,4,4-trifluorobutanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 10.3(s, 1H), 8.70-8.50(m, 2H), 7.90 – 7.20 (m, 3H), 6.55-6.65(m, 1H) , 4.6(, d, 1H), 4.30-3.90(m, 5H), 3.80-2.90(m, 3H), 2.80-2.50 (m, 5H), 1.80-1.40 (m, 4H); MS (ESI(+)) m/e 480 $(M+H)^+$.

Example 873

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described as described in Example 148A, substituting N-(4-bromophenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for 4-bromoaniline and tert-butyl 4-methyl-4-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)methyl)piperidine-1-carboxylate for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole followed by TFA deprotection as described in Example 1D to give the title compound as a TFA salt. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.24 (s, 1H), 8.57 (d, J = 4.0 Hz, 1H), 8.52 (s, 1H), 8.40 (s, 1H), 8.11 (s, 1H), 7.87 (s, 1H), 7.80 (dd, J = 9.3, 4.3 Hz, 1H), 7.63 (d, J = 8.6 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 9.3 Hz, 1H), 4.47 (t, J = 9.1 Hz, 2H), 4.43 - 4.34 (m, 2H), 4.08 (s, 2H), 3.81 (ddd, J = 14.5, 8.7, 6.0 Hz, 1H), 3.27 - 3.13 (m, 2H), 3.13 - 2.97 (m, 2H), 1.73 - 1.58 (m, 2H), 1.57 - 1.42 (m, 2H), 0.98 (s, 3H); MS (ESI(+)) m/e 432 $(M+H)^+$.

Example 874

N-{4-[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 805, substituting 3,3,3-trifluoroprop-1-yne for ethynylcyclopropane in Example 805A. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 10.47 (s, 1H), 8.57 (d, J = 3.8 Hz, 1H), 7.80 (d, J = 8.4 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H), 7.56 – 7.49 (m, 1H), 7.06 (d, J = 8.6 Hz, 1H), 6.87 (s, 1H), 4.34 (t, J = 8.4 Hz, 2H), 4.29 – 4.22 (m, 2H), 3.92 (s, 3H), 3.86 – 3.78 (m, 1H); MS (ESI(+)) m/e 403 $(M+H)^+$.

Example 875

1-(6-chloropyridazin-3-yl)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}azetidine-3-carboxamide

Example 875A

4-(1-neopentyl-1H-pyrazol-4-yl)aniline

The title compound was prepared as described as described in Example 148A, substituting 1-neopentyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole.

Example 875B

1-(6-chloropyridazin-3-yl)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 4-(1-neopentyl-1H-pyrazol-4-yl)aniline for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(6-chloropyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.10 (s, 1H), 8.04 (s, 1H), 7.82 (s, 1H), 7.61 (d, J = 8.7 Hz, 2H), 7.56 - 7.50 (m, 3H), 6.98 (d,

J = 9.3 Hz, 1H), 4.27 (t, J = 8.5 Hz, 2H), 4.19 (dd, J = 8.3, 5.9 Hz, 2H), 3.90 (s, 2H), 3.74 (tt, J = 8.6, 5.9 Hz, 1H), 0.92 (s, 9H); MS (ESI(+)) m/e 425 $(M+H)^+$.

Example 876

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridin-3-yl)azetidine-3-carboxamide

Example 876A

tert-butyl 4-(4-(1-(6-methylpyridin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1C, substituting 5-bromo-2-methylpyridine for 3-bromopyridine and tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 876B

1-(6-methylpyridin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(4-(1-(6-methylpyridin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 876C

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(6-methylpyridin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.99 (s, 1H), 7.73 (d, *J* = 2.8 Hz, 1H), 7.53 (d, *J* = 8.5 Hz, 2H), 7.48 – 7.39 (m, 5H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.04 (d, *J* = 8.3 Hz, 1H), 6.80 (dd, *J* = 8.3, 2.9 Hz, 1H), 4.62 (s, 1H), 4.05 (t, *J* = 7.7 Hz, 2H), 3.90 (t, *J* = 6.7 Hz, 2H), 3.69 (ddd, *J* = 14.5, 8.1, 6.3 Hz, 2H), 3.13 (s, 1H), 2.99 – 2.69 (m, 2H), 2.34 (s, 3H), 1.89 – 1.47 (m, 4H), MS (ESI(+)) m/e 455 $(M+H)^+$.

Example 877

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide

Example 877A

tert-butyl 1-(pyridin-3-yl)azetidine-3-carboxylate

The title compound was prepared as described in Example 1C, substituting tert-butyl azetidine-3-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 877B

1-(pyridin-3-yl)azetidine-3-carboxylic acid

The title compound was prepared as described in Example 1D, substituting tert-butyl 1-(pyridin-3-yl)azetidine-3-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 877C

N-(4-bromophenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 4-bromoaniline for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 877D

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide

The title compound as described as described in Example 148A, substituting N-(4-bromophenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide for 4-bromoaniline and tert-butyl 4-methyl-4-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)methyl)piperidine-1-carboxylate for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole followed by TFA deprotection as described in Example 1D to give the title compound as a TFA salt. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.21 (s, 1H), 8.58 (s, 1H), 8.45 (s, 1H), 8.15 (d, J = 5.3 Hz, 1H), 8.10 (s, 1H), 8.08 (d, J = 2.6 Hz, 1H), 7.86 (s, 1H), 7.77 (dd, J = 8.6, 5.4 Hz, 1H), 7.62 (d, J = 8.7 Hz, 2H), 7.58 - 7.51 (m, 3H), 4.24 (t, J = 8.3 Hz, 2H), 4.15 (dd, J = 7.9, 6.0 Hz, 2H), 4.08 (s, 2H), 3.79 (dq, J = 8.6, 5.9 Hz, 1H), 3.28 - 3.12 (m, 2H), 3.12 - 2.95 (m, 2H), 1.65 (ddd, J = 13.4, 9.3, 3.8 Hz, 2H), 1.56 - 1.40 (m, 2H), 0.97 (s, 3H); MS (ESI(+)) m/e 431 $(M+H)^+$.

Example 878

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide

To 1-(6-chloropyridazin-3-yl)-N-(4-(1-neopentyl-1H-pyrazol-4-yl)phenyl)azetidine-3-carboxamide (0.076 g, 0.179 mmol) was added methylzinc(II) chloride (2.0M in THF) (0.179 ml, 0.358 mmol) and 5 mg of palladium catalyst. The reaction mixture was heated to 60°C and a thick precipitate developed. N-methylpyrrolidine (0.2 ml) was added and the mixture was heated to 85°C for 2 hours. The mixture was diluted with dichloromethane and purified by normal phase chromatography to give the title compound. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.11 (s, 1H), 8.04 (s, 1H), 7.82 (s, 1H), 7.61 (d, J = 8.7 Hz, 2H), 7.53 (d, J = 8.7 Hz, 2H), 7.43 (d, J = 9.2 Hz, 1H), 6.99 (d, J = 9.1 Hz, 1H), 4.27 (t, J = 8.5 Hz, 2H), 4.19 (dd, J = 8.2, 6.1 Hz, 2H), 3.90 (s, 2H), 3.75 (ddd, J = 17.0, 8.5, 6.0 Hz, 1H), 2.45 (s, 3H), 0.92 (s, 9H); MS (ESI(+)) m/e 405 $(M+H)^+$.

Example 879

N-{3-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 879A

tert-butyl 4-(4-amino-2-fluorophenyl)-5,6-dihydropyridine-1(2H)-carboxylate

The title compound was prepared as described as described in Example 148A, substituting 4-bromo-3-fluoroaniline for 4-bromoaniline and tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole.

Example 879B

tert-butyl 4-(4-amino-2-fluorophenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1B, substituting tert-butyl 4-(4-amino-2-fluorophenyl)-5,6-dihydropyridine-1(2H)-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 879C

tert-butyl 4-(2-fluoro-4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(4-amino-2-fluorophenyl)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 879D

N-(3-fluoro-4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(2-fluoro-4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 879E

N-{3-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(3-fluoro-4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 3-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.86 (s, 1H), 8.56 (dd, J = 4.5, 1.1 Hz, 1H), 7.79 (t, J = 8.3 Hz, 1H), 7.56 – 7.45 (m, 1H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 7.25 (ddd, J = 20.2, 14.3, 8.7 Hz, 4H), 7.10 (d, J = 8.2 Hz, 1H), 6.83 (dd, J = 8.9, 1.0 Hz, 1H), 4.60 (s, 1H), 4.19 (dt, J = 14.0, 8.2 Hz, 4H), 3.99 – 3.74 (m, 1H), 3.59 (s,

1H), 3.07 (d, J = 59.7 Hz, 1H), 2.85 (dd, J = 39.3, 27.7 Hz, 2H), 2.08 – 1.43 (m, 4H); MS (ESI(+)) m/e 478.3 $(M+H)^+$.

Table 21.

The following Examples were essentially prepared as described in Example 879, substituting an appropriate carboxylic acid in Example 879E.

Ex		Name	MS
880		N-{3-fluoro-4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 426 $(M+H)^+$
881		N-{3-fluoro-4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 466 $(M+H)^+$
882		N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 454 $(M+H)^+$
883		N-{3-fluoro-4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 480 $(M+H)^+$
884		N-[4-(1-benzoylpiperidin-4-yl)-3-fluorophenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 460 $(M+H)^+$
885		N-{3-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 478 $(M+H)^+$
886		N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 440 $(M+H)^+$
887		N-{3-fluoro-4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 440 $(M+H)^+$
888		N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$

Example 889

N-{4-[1-(2-fluorobenzoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 889A

benzyl 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)-4-hydroxypiperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting benzyl 4-(4-aminophenyl)-4-hydroxypiperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(6-chloropyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 889B

N-(4-(4-hydroxypiperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1B, substituting benzyl 4-(4-(1-(6-chloropyridazin-3-yl)azetidine-3-carboxamido)phenyl)-4-hydroxypiperidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 889C

N-{4-[1-(2-fluorobenzoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(4-hydroxypiperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.08 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.61 – 7.54 (m, 2H), 7.55 – 7.33 (m, 5H), 7.35 – 7.22 (m, 2H), 6.83 (dd, J = 8.9, 1.3 Hz, 1H), 5.16 (s, 1H), 4.50 – 4.42 (m, 1H), 4.24 (t, J = 8.3 Hz, 2H), 4.15 (dd, J = 8.1, 5.9 Hz, 2H), 3.79 – 3.68 (m, 1H), 3.52 – 3.41 (m, 1H), 3.27 – 3.13 (m, 2H), 2.07 – 1.65 (m, 3H), 1.66 – 1.40 (m, 1H); MS (ESI(+)) m/e 476.1$(M+H)^+$.

Example 890

N-{4-[1-(2,2-dimethylpropanoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(4-hydroxypiperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,2-dimethylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.06 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.46 – 7.33 (m, 3H), 6.83 (dd, J = 8.9, 1.3 Hz, 1H), 5.06 (s, 1H), 4.30 – 4.08 (m, 6H), 3.79 – 3.68 (m, 1H), 3.25 – 3.13 (m, 2H), 1.83 – 1.68 (m, 2H), 1.66 – 1.58 (m, 2H), 1.22 (s, 9H); MS (ESI(+)) m/e 438.2$(M+H)^+$.

Example 891

1-(6-methylpyridazin-3-yl)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)azetidine-3-carboxamide

Example 891A

tert-butyl 1-(6-methylpyridazin-3-yl)azetidine-3-carboxylate

The title compound was prepared as described in Example 1C, substituting 3-chloro-6-methylpyridazine for 3-bromopyridine and tert-butyl azetidine-3-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 891B

1-(6-methylpyridazin-3-yl)azetidine-3-carboxylic acid

The title compound was prepared as described in Example 1D, substituting tert-butyl 1-(6-methylpyridazin-3-yl)azetidine-3-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 891C

N-(4-bromophenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 4-bromoaniline for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(6-methylpyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 891D

1-(6-methylpyridazin-3-yl)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)azetidine-3-carboxamide

The title compound was prepared as described as described in Example 148A, substituting N-(4-bromophenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide for 4-bromoaniline and 1-((4-methyltetrahydro-2H-pyran-4-yl)methyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.08 (s, 1H), 8.06 (s, 1H), 7.82 (s, 1H), 7.61 (d, J = 8.7 Hz, 2H), 7.52 (d, J = 8.6 Hz, 2H), 7.29 (d, J = 9.1 Hz, 1H), 6.79 (d, J = 9.0 Hz, 1H), 4.20 (t, J = 8.2 Hz, 2H), 4.12 (dd, J = 7.8, 6.2 Hz, 2H), 4.02 (s, 2H), 3.78 - 3.64 (m, 3H), 3.52 (ddd, J = 11.8, 9.3, 2.9 Hz, 2H), 2.44 (s, 3H), 1.51 (ddd, J = 13.3, 9.1, 4.1 Hz, 2H), 1.30 - 1.19 (m, 2H), 0.97 (s, 3H); MS (ESI(+)) m/e 447 $(M+H)^+$.

Example 892

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide

Example 892A

(S)-tert-butyl 4-(4-(1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1C, substituting 3-bromo-6-methylpyridazine for 3-bromopyridine and (S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 892B

(S)-1-(6-methylpyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl 4-(4-(1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 892C

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(6-methylpyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.25 – 9.59 (m, 1H), 7.63 – 7.39 (m, 4H), 7.38 – 7.11 (m, 5H), 6.84 (dd, *J* = 10.8, 7.3 Hz, 1H), 4.79 – 4.47 (m, 1H), 3.85 – 3.39 (m, 6H), 3.25 – 3.07 (m, 1H), 3.00 – 2.68 (m, 2H), 2.42 (s, 3H), 2.37 – 2.09 (m, 2H), 1.97 – 1.37 (m, 4H); MS (ESI(+)) m/e 488.3$(M+H)^+$.

(S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate

Example 893

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(6-methylpyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.25 – 9.84 (m, 1H), 7.62 – 7.51 (m, 2H), 7.50 – 7.36 (m, 5H), 7.31 – 7.12 (m, 3H), 6.91 – 6.76 (m, 1H), 4.77 – 4.30 (m, 1H), 3.98 – 3.37 (m, 7H), 3.02 – 2.62 (m, 2H), 2.42 (s, 3H), 2.38 – 2.01 (m, 2H), 1.97 – 1.43 (m, 4H); MS (ESI(+)) m/e 470.2$(M+H)^+$.

Example 894

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(6-methylpyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,2-dimethylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.04 (s, 1H), 7.56 – 7.50 (m, 2H), 7.23 (d, *J* = 9.1 Hz, 1H), 7.21 – 7.14 (m, 2H), 6.83 (d, *J* = 9.1 Hz, 1H), 4.45 – 4.36 (m, 2H), 3.74 (dd, *J* = 10.3, 7.9 Hz, 1H), 3.64 – 3.52 (m, 2H), 3.50 – 3.39 (m, 1H), 3.35-3.25(m, 1H), 2.93 – 2.66 (m, 3H), 2.40(s, 3H), 2.37 – 2.11 (m, 2H), 1.82 – 1.74 (m, 2H), 1.53 – 1.35 (m, 2H), 1.22 (s, 9H); MS (ESI(+)) m/e 450.3$(M+H)^+$.

Example 895

N-{4-[(1-benzoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 895A

4-(pyridin-4-ylmethyl)aniline

The title compound was prepared as described in Example 1B, substituting 4-(4-nitrobenzyl)pyridine for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 348B

2,2,2-trifluoro-N-(4-(pyridin-4-ylmethyl)phenyl)acetamide

A solution of 4-(pyridin-4-ylmethyl)aniline (21.6 g, 117 mmol) and triethylamine (19.61 ml, 141 mmol) in dichloromethane (586 ml) was cooled to 0 °C. Trifluoroacetic anhydride (19.87 ml, 141 mmol) was added dropwise via additional funnel over a period of 20 minutes. The mixture was stirred at 0 °C for 1 hour and then at room temperature for 2 hours. The reaction mixture was then concentrated in vacuo and the resulting residue was purified by regular phase column chromatography to give the title compound.

Example 895C

2,2,2-trifluoro-N-(4-(piperidin-4-ylmethyl)phenyl)acetamide

2,2,2-Trifluoro-N-(4-(pyridin-4-ylmethyl)phenyl)acetamide (28.5 g, 102 mmol) and acetic acid (205 ml) were added to platinum(IV) oxide (3.42 g, 15.06 mmol) in a 500 mL stainless steel pressure bottle and the mixture was stirred for 16 hours at 40 psi. The mixture was filtered through a nylon membrane and concentrated in vacuo; and the resulting residue was taken up in methanol (100 mL) and poured into diethyl ether (600 mL). The precipitate was filtered, washed with ether and dried with sodium sulfate to afford the title compound.

Example 895D

tert-butyl 4-(4-aminobenzyl)piperidine-1-carboxylate

A solution of 2,2,2-trifluoro-N-(4-(piperidin-4-ylmethyl)phenyl)acetamide (26.4 g, 92 mmol) in dichloromethane (369 ml) was cooled to 0°C and triethylamine (19.28 ml, 138 mmol) was added slowly. To the resulting solution was added di-tert-butyl dicarbonate (22.14 g, 101 mmol) in dichloromethane (75 ml) via addition funnel over 10 minutes. The 0°C mixture was stirred for 2 hours and warmed slowly overnight. The reaction mixture was recooled to 0°C, treated with 1 N aqueous sodium hydroxide (100 ml), warmed to room temperature and stirred for 1 hour. The bilayer was separated and the organics were washed with water and brine, dried with magnesium sulfate, filtered and concentrated in vacuo. The residue was purified by normal phase chromatography to give the title compound.

Example 895E

tert-butyl 4-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)benzyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(4-aminobenzyl)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 895F

N-(4-(piperidin-4-ylmethyl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)benzyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 895G

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-ylmethyl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.03 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.52 (d, J = 8.5 Hz, 2H), 7.47 – 7.28 (m, 6H), 7.11 (d, J = 8.5 Hz, 2H), 6.83 (dd, J = 9.0, 1.3 Hz, 1H), 4.58 – 4.34 (m, 1H), 4.23 (t, J = 8.3 Hz, 2H), 4.14 (dd, J = 8.1, 6.0 Hz, 2H), 3.72 (tt, J = 8.6, 6.0 Hz, 1H), 3.66 – 3.47 (m, 1H), 3.08 – 2.83 (m, 1H), 2.83 – 2.59 (m, 1H), 1.87 – 1.69 (m, 1H), 1.69 – 1.57 (m, 1H), 1.57 – 1.41 (m, 1H), 1.31 – 0.90 (m, 2H); MS (ESI(+)) m/e 456 $(M+H)^+$.

Table 22.

The following Examples were essentially prepared as described in Example 895, substituting an appropriate carboxylic acid in Example 895G. Some products were purified by flash chromatography while others were purified by reverse-phase HPLC. Accordingly, some Examples were isolated as trifluoroacetic acid salts.

Ex		Name	MS
896		N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 474 $(M+H)^+$
897		N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
898		N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
899		N-(4-{[1-(2-ethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
900		1-(pyridazin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
901		N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
902		N-{4-[(1-acetylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 394 $(M+H)^+$
903		N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
904		N-[4-({1-[(1-methylcyclopropyl)carbonyl]piperidin-4-	(ESI(+))

		yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	m/e 434 $(M+H)^+$
927		1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 463 $(M+H)^+$
928		N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 448 $(M+H)^+$
929		N-(4-{[1-(1H-pyrazol-4-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 446 $(M+H)^+$
930		N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
931		N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 434 $(M+H)^+$
932		N-[4-({1-[(methylsulfanyl)acetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 440 $(M+H)^+$
933		N-[4-({1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 488 $(M+H)^+$
934		N-(4-{[1-(2-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
935		N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
936		N-[4-({1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 454 $(M+H)^+$
937		1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 463 $(M+H)^+$
938		N-(4-{[1-(1H-pyrazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 446 $(M+H)^+$
939		N-[4-({1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 471 $(M+H)^+$
940		N-[4-({1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 476 $(M+H)^+$
941		N-(4-{[1-(pent-4-ynoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 432 $(M+H)^+$
942		1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
943		N-(4-{[1-(methoxyacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e XXX $(M+H)^+$
944		1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-	(ESI(+))

		4-yl]methyl}phenyl)azetidine-3-carboxamide	m/e 424 $(M+H)^+$
945		N-[4-({1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 468 $(M+H)^+$
946		N-(4-{[1-(ethoxyacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 438 $(M+H)^+$
947		1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
948		N-{4-[(1-hexanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
949		N-[4-({1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 459 $(M+H)^+$
950		N-(4-{[1-(but-3-enoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 420 $(M+H)^+$
951		1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 463 $(M+H)^+$
952		N-(4-{[1-(furan-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 446 $(M+H)^+$
953		N-(4-{[1-(1,2-oxazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 447 $(M+H)^+$
954		1-(pyridazin-3-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 457 $(M+H)^+$
955		N-(4-{[1-(furan-3-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 446 $(M+H)^+$
956		N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 434 $(M+H)^+$
957		N-(4-{[1-(2-methylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
958		N-{4-[(1-propanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 408 $(M+H)^+$
959		N-{4-[(1-butanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 422 $(M+H)^+$
960		N-(4-{[1-(cyclobutylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 434 $(M+H)^+$
961		N-{4-[(1-pentanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
962		N-(4-{[1-(cyclopentylacetyl)piperidin-4-yl]methyl}phenyl)-1-	(ESI(+))

		(pyridazin-3-yl)azetidine-3-carboxamide	m/e 462 $(M+H)^+$
963		N-(4-{[1-(2-methylbenzoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 470 $(M+H)^+$
964		N-(4-{[1-(3-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 450 $(M+H)^+$
965		N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$
966		N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 436 $(M+H)^+$
967		N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 420(M+H)$^+$
968		1-(pyridazin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 462 $(M+H)^+$

Example 905

N-[4-(1-{[4-methyl-1-(oxetan-3-yl)piperidin-4-yl]methyl}-1H-pyrazol-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide

Example 905A

tert-butyl 4-methyl-4-((4-(4-(1-(6-methylpyridazin-3-yl)azetidine-3-carboxamido)phenyl)-1H-pyrazol-1-yl)methyl)piperidine-1-carboxylate

The title compound was prepared as described as described in Example 148A, substituting N-(4-bromophenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide for 4-bromoaniline and tert-butyl 4-methyl-4-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)methyl)piperidine-1-carboxylate for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole.

Example 905B

N-(4-(1-((4-methylpiperidin-4-yl)methyl)-1H-pyrazol-4-yl)phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-methyl-4-((4-(4-(1-(6-methylpyridazin-3-yl)azetidine-3-carboxamido)phenyl)-1H-pyrazol-1-yl)methyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 905C

N-[4-(1-{[4-methyl-1-(oxetan-3-yl)piperidin-4-yl]methyl}-1H-pyrazol-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide

N-(4-(1-((4-Methylpiperidin-4-yl)methyl)-1H-pyrazol-4-yl)phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide was dissolved in methanol (3 ml) and treated with oxetan-3-one (0.022 ml, 0.338 mmol) and sodium cyanoborohydride (0.021 g, 0.338 mmol) and stirred overnight. The mixture was was concentrated, purified by normal phase chromatography, triturated with ether and concentrated to give the title compound. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.09 (s, 1H), 8.05 (s, 1H), 7.82 (s, 1H), 7.64 - 7.58 (m, 2H), 7.56 - 7.49 (m, 2H), 7.29 (d, J = 9.1 Hz, 1H), 6.80 (d, J = 9.0 Hz, 1H), 4.51 (t, J = 6.4 Hz, 2H), 4.40 (t, J = 5.8 Hz, 2H), 4.20 (t, J = 8.3 Hz, 2H), 4.12 (dd, J = 7.9, 6.1 Hz, 2H), 3.98 (s, 2H), 3.73 (tt, J = 8.5, 6.1 Hz, 1H), 3.48 - 3.39 (m, 1H), 2.44 (s, 3H), 2.42 - 2.33 (m, 2H), 2.16 - 1.99 (m, 2H), 1.58 - 1.46 (m, 2H), 1.30 (d, J = 12.6 Hz, 2H), 0.89 (s, 3H); MS (ESI(+)) m/e 502 $(M+H)^+$.

Example 906

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide

Example 906A

tert-butyl 4-(4-(1-(4-methylpyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1C, substituting 3-chloro-4-methylpyridazine for 3-bromopyridine and tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 906B

1-(4-methylpyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(4-(1-(4-methylpyridazin-3-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 906C

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(4-methylpyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.03 (s, 1H), 8.49 (d, *J* = 4.6 Hz, 1H), 7.58 – 7.52 (m, 2H), 7.53 – 7.37 (m, 5H), 7.25 – 7.17 (m, 3H), 4.81 – 4.37 (m, 1H), 4.39 – 4.25 (m, 4H), 4.26 – 3.38 (m, 2H), 3.24 – 2.58 (m, 3H), 2.19 (s, 3H), 2.10 – 1.11 (m, 4H); MS (ESI(+)) m/e 456.2$(M+H)^+$

Example 907

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]furan-2-carboxamide

Example 907A

5-(1-(tert-butoxycarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)furan-2-carboxylic acid

The title compound was prepared as described as described in Example 148A, substituting 5-bromofuran-2-carboxylic acid for 4-bromoaniline and tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole.

Example 907B

5-(1-(tert-butoxycarbonyl)piperidin-4-yl)furan-2-carboxylic acid

The title compound was prepared as described in Example 1B, substituting 5-(1-(tert-butoxycarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)furan-2-carboxylic acid for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 907C

(S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-amine

The title compound was prepared as described in Example 1C, substituting 3,6-dichloropyridazine for 3-bromopyridine and (S)-tert-butyl pyrrolidin-3-ylcarbamate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate followed by TFA deprotection as described in Example 1D.

Example 907D

(S)-tert-butyl 4-(5-((1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)carbamoyl)furan-2-yl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting (S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-amine for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 5-(1-(tert-butoxycarbonyl)piperidin-4-yl)furan-2-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 907E

(S)-tert-butyl 4-(5-((1-(pyridazin-3-yl)pyrrolidin-3-yl)carbamoyl)furan-2-yl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1B, substituting (S)-tert-butyl 4-(5-((1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl)carbamoyl)furan-2-yl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 907F

(S)-5-(piperidin-4-yl)-N-(1-(pyridazin-3-yl)pyrrolidin-3-yl)furan-2-carboxamide

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl 4-(5-((1-(pyridazin-3-yl)pyrrolidin-3-yl)carbamoyl)furan-2-yl)piperidine-1-carboxylate

for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 907G

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]furan-2-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-5-(piperidin-4-yl)-N-(1-(pyridazin-3-yl)pyrrolidin-3-yl)furan-2-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.48 (dd, J = 4.4, 0.9 Hz, 1H), 8.40 (d, J = 7.0 Hz, 1H), 7.55 - 7.46 (m, 1H), 7.41 (t, J = 6.9 Hz, 1H), 7.37 - 7.24 (m, 3H), 7.06 (d, J = 3.4 Hz, 1H), 6.86 (dd, J = 9.1, 0.8 Hz, 1H), 6.31 (d, J = 3.4 Hz, 1H), 4.67 - 4.47 (m, 2H), 3.76 (dd, J = 10.8, 6.9 Hz, 1H), 3.70 - 3.59 (m, 1H), 3.59 - 3.48 (m, 1H), 3.48 - 3.39 (m, 2H), 3.19 (t, J = 12.1 Hz, 1H), 3.08 - 2.89 (m, 2H), 2.33 - 2.19 (m, 1H), 2.13 - 2.02 (m, 2H), 1.99 - 1.88 (m, 1H), 1.67 - 1.41 (m, 2H); MS (ESI(+)) m/e 464 $(M+H)^+$.

Example 908

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide

Example 908A

tert-butyl 4-(4-(1-(3-methylpyridazin-4-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1C, substituting 4-chloro-3-methylpyridazine for 3-bromopyridine and tert-butyl 4-(4-(azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 908B

1-(3-methylpyridazin-4-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(4-(1-(3-methylpyridazin-4-yl)azetidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 908C

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(3-methylpyridazin-4-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.05 (s, 1H), 8.55 (d, *J* = 5.8 Hz, 1H), 7.57 – 7.51 (m, 2H), 7.49 – 7.33 (m, 5H), 7.26 – 7.19

(m, 2H), 6.45 (d, J = 5.8 Hz, 1H), 4.62 (s, 1H), 4.31 (t, J = 8.4 Hz, 2H), 4.24 (dd, J = 20.4, 14.1 Hz, 3H), 3.66 (ddd, J = 14.6, 8.5, 6.1 Hz, 2H), 2.76 (t, J = 11.9 Hz, 2H), 2.52 (s, 3H), 2.13 – 1.45 (m, 5H); MS (ESI(+)) m/e 456.3$(M+H)^+$.

Example 909

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(3-methylpyridazin-4-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.08 (s, 1H), 8.55 (d, J = 5.8 Hz, 1H), 7.76 – 7.24 (m, 8H), 6.45 (d, J = 5.8 Hz, 1H), 4.50 – 4.45 (m, 1H), 4.32 (t, J = 8.3 Hz, 2H), 4.23 (d, J = 13.9 Hz, 2H), 3.73 – 3.62 (m, 1H), 3.50 – 3.41 (m, 1H), 3.26 – 3.07 (m, 2H), 2.94 – 2.56 (m, 3H), 2.45 – 1.03 (m, 5H),; MS (ESI(+)) m/e 474.2$(M+H)^+$.

Example 910

N-(4-{1-[(2-aminopyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-aminonicotinic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.04 (s, 1H), 8.56 (dd, J = 4.5, 1.1 Hz, 1H), 8.00 (dd, J = 4.9, 1.8 Hz, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.46 - 7.32 (m, 2H), 7.21 (d, J = 8.5 Hz, 2H), 6.83 (dd, J = 9.0, 1.2 Hz, 1H), 6.59 (dd, J = 7.3, 4.9 Hz, 1H), 5.92 (s, 2H), 4.24 (t, J = 8.3 Hz, 2H), 4.14 (dd, J = 8.0, 6.0 Hz, 2H), 4.09 - 3.84 (m, 2H), 3.73 (tt, J = 8.5, 6.0 Hz, 1H), 2.99 (bs, 2H), 2.74 (tt, J = 11.7, 3.2 Hz, 1H), 1.76 (d, J = 11.8 Hz, 2H), 1.70 - 1.52 (m, 2H); MS (ESI(+)) m/e 458 $(M+H)^+$.

Example 911

1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylic acid

Ethyl 1-methyl-5-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)-1H-pyrazole-3-carboxylate (368 mg, 0.905 mmol) was taken up in tetrahydrofuran (3.38 mL), and methanol (3.38 mL) then 1N aqueous lithium hydroxide (1.35 mL, 1.350 mmol) was added. The mixture was heated at 60°C for 2 hours. The mixture was concentrated to dryness, suspended in water and treated with 1N aqueous HCl to pH 2. The solution was extracted with ethyl acetate and the organic layers were dried with sodium sulfate, filtered, and concentrated to give a colorless syrup that solidified upon standing. This solid was triturated with ether and collected by filtration to give the title compound. ^{1}H NMR (400 MHz, DMSO-

d_6) δ ppm 12.67 (s, 1H), 10.32 (bs, 1H), 8.60 – 8.55 (m, 1H), 7.77 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H), 7.42 (dd, J = 9.0, 4.5 Hz, 1H), 6.89 (d, J = 8.9 Hz, 1H), 6.80 (s, 1H), 4.34 – 4.13 (m, 4H), 3.91 (s, 3H), 3.83 – 3.74 (m, 1H); MS (ESI(+)) m/e 379 $(M+H)^+$.

Example 912

ethyl 1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate

Example 912A

ethyl 4-(4-nitrophenyl)-2,4-dioxobutanoate

1-(4-Nitrophenyl)ethanone (2 g, 12.11 mmol) was dissolved in tetrahydrofuran (20 mL) and chilled to 0°C. Sodium ethanolate (21% in ethanol) (7.85 g, 24.22 mmol) was added dropwise and the resulting solution was stirred for 15 minutes at 0°C. Diethyl oxylate (1.947 g, 13.32 mmol) was added dropwise and the ice bath was removed. The mixture was stirred at room temperature for 3 hours and diluted with 1N aqueous HCl (125 mL). The resulting suspension was stirred for 30 minutes and collected by filtration to give the title compound.

Example 912B

ethyl 1-methyl-5-(4-nitrophenyl)-1H-pyrazole-3-carboxylate

Ethyl 4-(4-nitrophenyl)-2,4-dioxobutanoate (500 mg, 1.885 mmol) was dissolved in hexafluoroisopropanol (4 ml) and methylhydrazine (87 mg, 1.885 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 3 hours, concentrated to dryness, triturated with ether; and filtered to provide the title compound.

Example 912C

ethyl 5-(4-aminophenyl)-1-methyl-1H-pyrazole-3-carboxylate

The title compound was prepared as described in Example 1B, substituting ethyl 1-methyl-5-(4-nitrophenyl)-1H-pyrazole-3-carboxylate for tert-butyl 4-(4-(1-(benzyloxycarbonyl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 912D

ethyl 1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate

The title compound was prepared as described in Example 1A, substituting ethyl 5-(4-aminophenyl)-1-methyl-1H-pyrazole-3-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.31 (s, 1H), 8.57 (dd, J = 4.5, 1.3 Hz, 1H), 7.77 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 8.6 Hz, 2H), 7.39 (dd, J = 8.9, 4.5 Hz, 1H), 6.84 (s, 1H), 6.84 (dd, J = 9.0, 1.4 Hz, 1H), 4.32 – 4.22 (m, 4H), 4.18 (dd, J = 8.1, 5.8 Hz, 2H), 3.92 (s, 3H), 3.84 – 3.72 (m, 1H), 1.30 (t, J = 7.1 Hz, 3H); MS (ESI(+)) m/e 407 $(M+H)^+$.

Example 913

ethyl 1-phenyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate

The title compound was preapred as described in Example 912, substituting phenylhydrazine for methylhydrazine in Example 912B. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 10.24 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.60 (d, J = 8.7 Hz, 2H), 7.51 – 7.41 (m, 3H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 7.34 – 7.30 (m, 2H), 7.20 (d, J = 8.7 Hz, 2H), 7.08 (s, 1H), 6.82 (dd, J = 9.0, 1.3 Hz, 1H), 4.33 (q, J = 7.1 Hz, 2H), 4.24 (t, J = 8.4 Hz, 2H), 4.14 (dd, J = 8.0, 6.0 Hz, 2H), 3.77 – 3.69 (m, 1H), 1.32 (t, J = 7.1 Hz, 3H); MS (ESI(+)) m/e 469 $(M+H)^+$.

Example 914

N-{6-[1-(2-fluorobenzoyl)piperidin-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 914A

tert-butyl 4-(5-(1-(pyridazin-3-yl)azetidine-3-carboxamido)pyridin-2-yl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(5-aminopyridin-2-yl)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 914B

N-(6-(piperidin-4-yl)pyridin-3-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(5-(1-(pyridazin-3-yl)azetidine-3-carboxamido)pyridin-2-yl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 914C

N-{6-[1-(2-fluorobenzoyl)piperidin-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(6-(piperidin-4-yl)pyridin-3-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.27 (s, 1H), 8.67 (d, J = 2.5 Hz, 1H), 8.57 (dd, J = 4.5, 1.2 Hz, 1H), 8.01 (dd, J = 8.5, 2.5 Hz, 1H), 7.56 - 7.46 (m, 1H), 7.46 - 7.35 (m, 2H), 7.35 - 7.23 (m, 3H), 6.83 (dd, J = 9.0, 1.2 Hz, 1H), 4.64 (d, J = 13.0 Hz, 1H), 4.26 (t, J = 8.4 Hz, 2H), 4.16 (dd, J = 8.0, 6.0 Hz, 2H), 3.76 (tt, J = 8.5, 5.9 Hz, 1H), 3.47 (d, J = 12.6 Hz, 1H), 3.19 (t, J = 12.3 Hz, 1H), 3.01 - 2.85 (m, 2H), 1.94 (d, J = 13.0 Hz, 1H), 1.79 (d, J = 12.1 Hz, 1H), 1.73 - 1.53 (m, 2H); MS (ESI(+)) m/e 461 $(M+H)^+$.

Example 915

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide

Example 915A

(R)-tert-butyl 3-(4-(1-(6-methylpyridazin-3-yl)azetidine-3-carboxamido)phenoxy)pyrrolidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting (R)-tert-butyl 3-(4-aminophenoxy)pyrrolidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(6-methylpyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 915B

(R)-1-(6-methylpyridazin-3-yl)-N-(4-(pyrrolidin-3-yloxy)phenyl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting (R)-tert-butyl 3-(4-(1-(6-methylpyridazin-3-yl)azetidine-3-carboxamido)phenoxy)pyrrolidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 915C

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (R)-1-(6-methylpyridazin-3-yl)-N-(4-(pyrrolidin-3-yloxy)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 3-methylbutanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6, T = 90°C) δ ppm 9.63 (s, 1H), 7.49 (d, J = 8.9 Hz, 2H), 7.21 (d, J = 9.0 Hz, 1H), 6.88 (d, J = 8.7 Hz, 2H), 6.71 (d, J = 9.0 Hz, 1H), 5.03 – 4.85 (m, 1H), 4.16 (dt, J = 14.0, 8.0 Hz, 4H), 3.69 (tt, J = 8.5, 6.1 Hz, 1H), 3.62 – 3.34 (m, 3H), 2.43 (s, 3H), 2.23 – 1.98 (m, 6H), 0.91 (d, J = 6.2 Hz, 6H); MS (ESI(+)) m/e 438 $(M+H)^+$.

Example 916

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (R)-1-(6-methylpyridazin-3-yl)-N-(4-(pyrrolidin-3-yloxy)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and isobutyric acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6, T = 90°C) δ ppm 9.63 (s, 1H), 7.50 (d, J = 9.0 Hz, 2H), 7.21 (d, J = 9.0 Hz, 1H), 6.88 (d, J = 8.9 Hz, 2H), 6.71 (d, J = 9.0 Hz, 1H), 5.01 – 4.86 (m, 1H), 4.23 – 4.10 (m, 4H), 3.74 – 3.64 (m, 1H), 3.64 – 3.40 (m, 4H), 2.72 – 2.58 (m, 1H), 2.43 (s, 3H), 2.26 – 1.98 (m, 2H), 1.03 (dd, J = 9.7, 4.0 Hz, 6H); MS (ESI(+)) m/e 424 $(M+H)^+$.

Example 917

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (R)-1-(6-methylpyridazin-3-yl)-N-(4-(pyrrolidin-3-yloxy)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,4-difluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6, T = 90°C) δ ppm 9.63 (bs, 1H), 7.53 – 7.44 (m, 3H), 7.25 – 7.18 (m, 2H), 7.14 – 7.03 (m, 1H), 6.95 – 6.80 (m, 2H), 6.71 (d, J = 8.9 Hz, 1H), 5.05 – 4.92 (m, 1H), 4.19 (t, J = 8.2 Hz, 2H), 4.13 (t, J = 7.0 Hz, 2H), 3.68 (tdd, J = 10.3, 5.0, 1.7 Hz, 1H), 3.82 – 3.22 (m, 4H), 2.43 (s, 3H), 2.32 – 2.05 (m, 2H); MS (ESI(+)) m/e 494 $(M+H)^+$.

Example 918

1-(6-methylpyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (R)-1-(6-methylpyridazin-3-yl)-N-(4-(pyrrolidin-3-yloxy)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and thiazole-4-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6, T = 90°C) δ ppm 9.63 (s, 1H), 9.09 (d, J = 1.6 Hz, 1H), 8.19 (d, J = 2.0 Hz, 1H), 7.49 (d, J = 8.7 Hz, 2H), 7.21 (d, J = 9.0 Hz, 1H), 6.89 (d, J = 8.6 Hz, 2H), 6.71 (d, J = 9.0 Hz, 1H), 5.00 (dt, J = 4.5, 2.2 Hz, 1H), 4.16 (dt, J = 14.0, 8.0 Hz, 4H), 4.09 – 3.57 (m, 4H), 3.69 (tt, J = 8.4, 6.1 Hz, 1H), 2.43 (s, 3H), 2.20 (dd, J = 33.6, 24.3 Hz, 2H); MS (ESI(+)) m/e 465.2 $(M+H)^+$.

Example 919

1-(pyridazin-3-yl)-N-{6-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]pyridin-3-yl}azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(6-(piperidin-4-yl)pyridin-3-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 4,4,4-trifluorobutanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.27 (s, 1H), 8.67 (d, J = 2.6 Hz, 1H), 8.57 (dd, J = 4.5, 1.3 Hz, 1H), 8.00 (dd, J = 8.5, 2.6 Hz, 1H), 7.40 (dd, J = 9.0, 4.5 Hz, 1H), 7.26 (d, J = 8.5 Hz, 1H), 6.86 (dd, J = 9.0, 1.3 Hz, 1H), 4.50 (d, J = 13.0 Hz, 1H), 4.26 (t, J = 8.4 Hz, 2H), 4.17 (dd, J = 8.2, 5.9 Hz, 2H), 3.97 (d, J = 13.6 Hz, 1H), 3.76 (tt, J = 8.6, 5.9 Hz, 1H), 3.11 (dd, J = 18.5, 7.6 Hz, 1H), 2.90 (tt, J = 11.7, 3.6 Hz, 1H), 2.76 - 2.59 (m, 2H), 2.59 - 2.43 (m, 2H), 1.91 - 1.77 (m, 2H), 1.66 (qd, J = 12.6, 4.0 Hz, 1H), 1.51 (qd, J = 12.7, 4.1 Hz, 1H); MS (ESI(+)) m/e 463 $(M+H)^+$.

Example 920

N-{6-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(6-(piperidin-4-yl)pyridin-3-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 3,3-dimethylbutanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.26 (s, 1H), 8.66 (d, J = 2.5 Hz, 1H), 8.57 (dd, J = 4.5, 1.1 Hz, 1H), 8.00 (dd, J = 8.5, 2.6 Hz, 1H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 7.25 (d, J = 8.5 Hz, 1H), 6.83 (dd, J = 9.0, 1.2 Hz, 1H), 4.58 (d, J = 12.9 Hz, 1H), 4.26 (t, J = 8.4 Hz, 2H), 4.16 (dd, J = 8.0, 6.0 Hz, 2H), 4.07 (d, J = 13.4 Hz, 1H), 3.76 (tt, J = 8.5, 5.9 Hz, 1H), 3.10 (t, J = 12.1 Hz, 1H), 2.88 (tt, J = 11.7, 3.6 Hz, 1H), 2.59 (t, J = 11.8 Hz, 1H), 2.29 (d, J = 14.0 Hz, 1H), 2.22 (d, J = 14.0 Hz, 1H), 1.84 (t, J = 10.8 Hz, 2H), 1.60 (qd, J = 12.7, 3.8 Hz, 1H), 1.48 (qd, J = 12.7, 4.0 Hz, 1H), 1.00 (s, 9H); MS (ESI(+)) m/e 437 $(M+H)^+$.

Example 921

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide

Example 921A

(S)-tert-butyl 4-(4-(1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1C, substituting 3-chloro-4-methylpyridazine for 3-bromopyridine and (S)-tert-butyl 4-(4-(pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 921B

(S)-1-(4-methylpyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting (S)-tert-butyl 4-(4-(1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamido)phenyl)piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 921C

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(4-methylpyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.03 (s, 1H), 8.46 (d, *J* = 4.6 Hz, 1H), 7.58 – 7.52 (m, 2H), 7.50 – 7.37 (m, 5H), 7.28 – 7.15

(m, 3H), 4.71 – 4.55 (m, 1H), 3.89 – 3.38 (m, 5H), 3.28 – 2.58 (m, 4H), 2.34 (s, 3H), 2.32 – 1.98 (m, 2H), 2.00 – 1.49 (m, 4H); MS (ESI(+)) m/e 470.2$(M+H)^+$.

Example 922

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting (S)-1-(4-methylpyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)pyrrolidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2,2-dimethylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.02 (s, 1H), 8.46 (d, J = 4.6 Hz, 1H), 7.57 – 7.51 (m, 2H), 7.22 – 7.13 (m, 3H), 4.45 – 4.36 (m, 2H), 3.85 – 3.72 (m, 2H), 3.68 (dd, J = 7.9, 5.7 Hz, 2H), 3.21 (p, J = 7.7 Hz, 1H), 2.93 – 2.66 (m, 3H), 2.34 (s, 3H), 2.31 – 2.05 (m, 2H), 1.82 – 1.74 (m, 2H), 1.53 – 1.34 (m, 2H), 1.22 (s, 9H); MS (ESI(+)) m/e 450.3$(M+H)^+$.

Example 923

N-{4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 805, substituting 3,3,3-trifluoroprop-1-yne for ethynylcyclopropane in Example 805A and phenylhydrazine for methylhydrazine in Example 805B. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.26 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.61 (d, J = 8.7 Hz, 2H), 7.50 – 7.44 (m, 3H), 7.41 – 7.31 (m, 3H), 7.23 (d, J = 8.7 Hz, 2H), 7.14 (s, 1H), 6.83 (dd, J = 8.9, 1.4 Hz, 1H), 4.24 (t, J = 8.3 Hz, 2H), 4.14 (dd, J = 8.1, 5.8 Hz, 2H), 3.74 (tt, J = 8.5, 5.8 Hz, 1H); MS (ESI(+)) m/e 465.1 $(M+H)^+$.

Example 924

N-{6-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 924A

N-(6-chloropyridin-3-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 6-chloropyridin-3-amine for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 924B

N-{6-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described as described in Example 148A, substituting N-(6-chloropyridin-3-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for 4-

bromoaniline and 1-neopentyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.31 (s, 1H), 8.69 (d, J = 2.6 Hz, 1H), 8.57 (dd, J = 4.5, 1.3 Hz, 1H), 8.18 (s, 1H), 8.06 (dd, J = 8.6, 2.6 Hz, 1H), 7.95 (d, J = 0.4 Hz, 1H), 7.63 (dd, J = 8.6, 0.4 Hz, 1H), 7.39 (dd, J = 8.9, 4.5 Hz, 1H), 6.84 (dd, J = 9.0, 1.4 Hz, 1H), 4.27 (t, J = 8.4 Hz, 2H), 4.18 (dd, J = 8.2, 5.9 Hz, 2H), 3.94 (s, 2H), 3.78 (tt, J = 8.6, 5.9 Hz, 1H), 0.93 (s, 9H); MS (ESI(+)) m/e 392 $(M+H)^+$.

Example 925

tert-butyl 4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)-1H-pyrazol-1-yl]piperidine-1-carboxylate

The title compound was prepared as described in Example 1A, substituting tert-butyl 4-(4-amino-1H-pyrazol-1-yl)piperidine-1-carboxylate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.15 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.98 - 7.90 (m, 1H), 7.47 (d, J = 0.5 Hz, 1H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 6.82 (dd, J = 9.0, 1.4 Hz, 1H), 4.31 (tt, J = 11.3, 3.9 Hz, 1H), 4.22 (t, J = 8.3 Hz, 2H), 4.12 (dd, J = 8.1, 6.0 Hz, 2H), 4.02 (d, J = 12.3 Hz, 2H), 3.67 (tt, J = 8.6, 6.0 Hz, 1H), 2.88 (bs, 2H), 1.95 (dd, J = 12.4, 2.4 Hz, 2H), 1.74 (qd, J = 12.4, 4.4 Hz, 2H), 1.41 (s, 9H); MS (ESI(+)) m/e 428 $(M+H)^+$.

Example 926

N-(6-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}pyridin-3-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described as described in Example 148A, substituting N-(6-chloropyridin-3-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for 4-bromoaniline and tert-butyl 4-methyl-4-((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)methyl)piperidine-1-carboxylate for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole followed by TFA deprotection as described in Example 1D to give the title compound as a TFA salt. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.63 (s, 1H), 8.79 (d, J = 2.5 Hz, 1H), 8.67 - 8.54 (m, 2H), 8.52 - 8.39 (m, 1H), 8.31 (s, 1H), 8.13 (dd, J = 8.7, 2.5 Hz, 1H), 8.05 (s, 1H), 7.84 (dd, J = 9.4, 4.4 Hz, 1H), 7.76 (d, J = 8.7 Hz, 1H), 7.51 (dd, J = 9.4, 0.9 Hz, 1H), 4.51 (t, J = 9.3 Hz, 2H), 4.44 (dd, J = 9.5, 5.9 Hz, 2H), 4.14 (s, 2H), 3.87 (tt, J = 8.8, 5.9 Hz, 1H), 3.29 - 3.14 (m, 2H), 3.14 - 2.96 (m, 2H), 1.74 - 1.58 (m, 2H), 1.56 - 1.42 (m, 2H), 0.98 (s, 3H); MS (ESI(+)) m/e 433 $(M+H)^+$.

Example 969

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting 1-(4-methylpyridazin-3-yl)-N-(4-(piperidin-4-yl)phenyl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 3,3-dimethylbutanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.02 (s, 1H), 8.49 (d, *J* = 4.6 Hz, 1H), 7.57 – 7.51 (m, 2H), 7.22 – 7.14 (m, 3H), 4.65 – 4.57 (m, 1H), 4.39 – 4.24 (m, 4H), 4.12 – 4.03 (m, 1H), 3.68 (p, *J* = 7.4 Hz, 1H), 3.07 (t, *J* = 12.0 Hz, 1H), 2.77 – 2.64 (m, 1H), 2.34 – 2.26 (m, 1H), 2.25 – 2.16 (m, 4H), 2.12 – 1.56 (m, 2H), 1.58 – 1.07 (m, 3H), 1.09 – 0.87 (m, 9H); MS (ESI(+)) m/e 450.3$(M+H)^+$.

Example 970

N-{1-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-1H-pyrazol-4-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 970A

N-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)-1H-pyrazol-1-yl]piperidine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate.

Example 970B

N-{1-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-1H-pyrazol-4-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 3,3-dimethylbutanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 10.16 (s, 1H), 8.56 (dd, J = 4.5, 1.1 Hz, 1H), 7.95 (s, 1H), 7.46 (s, 1H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 6.83 (dd, J = 9.0, 1.2 Hz, 1H), 4.53 (d, J = 13.3 Hz, 1H), 4.38 (tt, J = 11.3, 4.0 Hz, 1H), 4.23 (t, J = 8.3 Hz, 2H), 4.12 (dd, J = 8.0, 6.1 Hz, 2H), 4.07 (d, J = 13.6 Hz, 1H), 3.67 (tt, J = 8.5, 6.0 Hz, 1H), 3.15 (t, J = 12.1 Hz, 1H), 2.66 (t, J = 11.9 Hz, 1H), 2.30 (d, J = 14.1 Hz, 1H), 2.23 (d, J = 14.1 Hz, 1H), 1.98 (t, J = 10.7 Hz, 2H), 1.80 (qd, J = 12.3, 4.1 Hz, 1H), 1.68 (qd, J = 12.3, 4.2 Hz, 1H), 1.00 (s, 9H); MS (ESI(+)) m/e 426 $(M+H)^+$.

Example 971

N-{1-[1-(2-fluorobenzoyl)piperidin-4-yl]-1H-pyrazol-4-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(1-(piperidin-4-yl)-1H-pyrazol-4-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-fluorobenzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm

10.15 (s, 1H), 8.56 (dd, J = 4.5, 1.3 Hz, 1H), 7.98 (s, 1H), 7.54 - 7.42 (m, 3H), 7.38 (dd, J = 9.0, 4.5 Hz, 1H), 7.34 - 7.26 (m, 2H), 6.82 (dd, J = 9.0, 1.3 Hz, 1H), 4.59 (d, J = 13.3 Hz, 1H), 4.45 (tt, J = 11.2, 3.9 Hz, 1H), 4.23 (t, J = 8.3 Hz, 2H), 4.12 (dd, J = 8.0, 6.0 Hz, 2H), 3.67 (tt, J = 8.5, 6.0 Hz, 1H), 3.47 (d, J = 13.3 Hz, 1H), 3.22 (t, J = 12.2 Hz, 1H), 2.98 (td, J = 13.0, 2.7 Hz, 1H), 2.09 (d, J = 11.2 Hz, 1H), 2.00 - 1.91 (m, 1H), 1.90 - 1.74 (m, 2H); MS (ESI(+)) m/e 450 $(M+H)^+$.

Example 972

N-[4-(phenylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 972A

methyl 4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)benzoate

The title compound was prepared as described in Example 1A, substituting methyl 4-aminobenzoate for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 1-(pyridazin-3-yl)azetidine-3-carboxylic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid.

Example 972B

4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)benzoic acid

The procedure was followed as described in Example 911, substituting methyl 4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)benzoate for ethyl 1-methyl-5-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)-1H-pyrazole-3-carboxylate.

Example 972C

N-[4-(phenylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting aniline for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)benzoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid. ^{1}H NMR (400 MHz, DMSO-d_6/D_2O) δ ppm 8.53 (dd, *J* = 4.4, 1.3 Hz, 1H), 7.98 – 7.92 (m, 2H), 7.77 – 7.65 (m, 5H), 7.38 – 7.24 (m, 3H), 7.15 – 7.07 (m, 1H), 4.49 (t, *J* = 9.0 Hz, 2H), 4.46 – 4.38 (m, 2H), 4.00 – 3.81 (m, 1H); MS (ESI(+)) m/e 374 $(M+H)^+$.

Table 23.

The following Examples were essentially prepared as described in Example 972, substituting an appropriate amine in Example 972C. Some products were purified by flash chromatography while others were purified by reverse-phase HPLC. Accordingly, some Examples were isolated as trifluoroacetic acid salts.

Ex		Name	MS
973		N-{4-[(2,2-dimethylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 368 $(M+H)^+$
974		N-{4-[(3-methoxy-2,2-dimethylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 398 $(M+H)^+$
975		N-{4-[(2-cyclopropylethyl)carbamoyl]phenyl}-1-(pyridazin-3-	(ESI(+))

		yl)azetidine-3-carboxamide	m/e XXX $(M+H)^+$
976		N-(4-{[2-(2-ethylpiperidin-1-yl)ethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 366 $(M+H)^+$
977		N-{4-[(cyclobutylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 366 $(M+H)^+$
978		N-{4-[(2S)-butan-2-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 354 $(M+H)^+$
979		N-[4-(butylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 354 $(M+H)^+$
980		N-{4-[(2,2-dimethyltetrahydro-2H-pyran-4-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 410 $(M+H)^+$
981		N-(4-{[(1S)-1-cyclopropylethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 366 $(M+H)^+$
982		N-[4-({2-[methyl(phenyl)amino]ethyl}carbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 430 $(M+H)^+$
983		N-{4-[1,1'-bi(cyclopropyl)-1-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 378 $(M+H)^+$
984		1-(pyridazin-3-yl)-N-[4-(thiophen-3-ylcarbamoyl)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 366 $(M+H)^+$
985		N-(4-{[(1R)-1-cyclopropylethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 366 $(M+H)^+$
986		N-{4-[(1-methylpiperidin-4-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 395 $(M+H)^+$
987		N-{4-[(2R)-butan-2-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 354 $(M+H)^+$
988		N-[4-(1-azabicyclo[2.2.2]oct-3-ylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 407 $(M+H)^+$
989		1-(pyridazin-3-yl)-N-{4-[(tetrahydrofuran-3-ylmethyl)carbamoyl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 382 $(M+H)^+$
990		N-{4-[(oxetan-3-ylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 368 $(M+H)^+$
991		N-{4-[(2-methylcyclopropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 352 $(M+H)^+$
992		N-[4-(cyclobutylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 352 $(M+H)^+$
993		N-{4-[(1-methylcyclopropyl)carbamoyl]phenyl}-1-(pyridazin-3-	(ESI(+))

		yl)azetidine-3-carboxamide	m/e 352 $(M+H)^+$
994		N-{4-[(2-methoxy-2-methylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 384 $(M+H)^+$
995		N-{4-[(cyclopropylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 352 $(M+H)^+$
996		1-(pyridazin-3-yl)-N-(4-{[(2R)-tetrahydrofuran-2-ylmethyl]carbamoyl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 382 $(M+H)^+$
997		1-(pyridazin-3-yl)-N-{4-[(3,3,3-trifluoropropyl)carbamoyl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 394 $(M+H)^+$
998		N-{4-[(1-methylpiperidin-3-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 395 $(M+H)^+$
999		N-(4-{[(3-methyloxetan-3-yl)methyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 382 $(M+H)^+$
1000		1-(pyridazin-3-yl)-N-(4-{[(2S)-tetrahydrofuran-2-ylmethyl]carbamoyl}phenyl)azetidine-3-carboxamide	(ESI(+)) m/e 382 $(M+H)^+$
1001		1-(pyridazin-3-yl)-N-{4-[(tetrahydro-2H-pyran-4-ylmethyl)carbamoyl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 396 $(M+H)^+$
1002		1-(pyridazin-3-yl)-N-[4-(tetrahydro-2H-pyran-4-ylcarbamoyl)phenyl]azetidine-3-carboxamide	(ESI(+)) m/e 382 $(M+H)^+$
1003		N-(4-{[(1-methylpiperidin-3-yl)methyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 409 $(M+H)^+$
1004		N-[4-(cyclopropylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 338 $(M+H)^+$
1005		N-[4-(cyclopentylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 366 $(M+H)^+$
1006		N-[4-(benzylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 388 $(M+H)^+$
1007		N-{4-[(3-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 392 $(M+H)^+$
1008		N-[4-(propylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 340 $(M+H)^+$
1009		N-{4-[(4-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 392 $(M+H)^+$
1010		N-{4-[(2-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 392 $(M+H)^+$
1011		N-{4-[(1-methylcyclobutyl)carbamoyl]phenyl}-1-(pyridazin-3-	(ESI(+))

		yl)azetidine-3-carboxamide	m/e 366 $(M+H)^+$
1012		N-[4-(prop-2-en-1-ylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 338 $(M+H)^+$
1020		1-(pyridazin-3-yl)-N-{4-[(3S)-tetrahydrofuran-3-ylcarbamoyl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 368 $(M+H)^+$
1021		N-[4-({4-[2-(dimethylamino)ethyl]phenyl}carbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 445 $(M+H)^+$
1022		1-(pyridazin-3-yl)-N-{4-[(3R)-tetrahydrofuran-3-ylcarbamoyl]phenyl}azetidine-3-carboxamide	(ESI(+)) m/e 368 $(M+H)^+$
1023		N-{4-[(2-methoxyethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide	(ESI(+)) m/e 356 $(M+H)^+$

Example 1024

N-{4-[1-(3-amino-2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 1024A

tert-butyl (2,2-dimethyl-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)propyl)carbamate

A solution of tert-butyl (3-hydroxy-2,2-dimethylpropyl)carbamate (1.000 g, 4.92 mmol), 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (1.145 g, 5.90 mmol) and 2-(tributylphosphoranylidene)acetonitrile (1.425 g, 5.90 mmol) were stirred together in toluene (20 ml) at 90°C overnight. The reaction mixture was concentrated and purified by normal phase chromatography to give the title compound.

Example 1024B

tert-butyl (2,2-dimethyl-3-(4-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)-1H-pyrazol-1-yl)propyl)carbamate

The title compound was prepared as described as described in Example 148A, substituting N-(4-bromophenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for 4-bromoaniline and tert-butyl (2,2-dimethyl-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)propyl)carbamate for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole.

Example 1024C

N-{4-[1-(3-amino-2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl (2,2-dimethyl-3-(4-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)-1H-pyrazol-1-yl)propyl)carbamate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-

carboxamido)phenoxy)piperidine-1-carboxylate to give the title compound as a TFA salt. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 10.26 (s, 1H), 8.57 (dd, J = 4.4, 1.1 Hz, 1H), 8.12 (s, 1H), 7.95 (bs, 3H), 7.92 (s, 1H), 7.74 (dd, J = 9.3, 4.4 Hz, 1H), 7.64 (d, J = 8.7 Hz, 2H), 7.55 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 9.2 Hz, 1H), 4.44 (t, J = 9.1 Hz, 2H), 4.37 (dd, J = 9.2, 5.9 Hz, 2H), 4.10 (s, 2H), 3.81 (tt, J = 8.8, 5.9 Hz, 1H), 2.83 - 2.70 (m, 2H), 0.96 (s, 6H); MS (ESI(+)) m/e 406 $(M+H)^+$.

Example 1025

N-(4-{1-[2,2-dimethyl-3-(piperazin-1-yl)propyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

Example 1025A

tert-butyl 4-(2,2-dimethyl-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)propyl)piperidine-1-carboxylate

The title compound was prepared as described in Example 1024A, substituting tert-butyl 4-(3-hydroxy-2,2-dimethylpropyl)piperidine-1-carboxylate for tert-butyl (3-hydroxy-2,2-dimethylpropyl)carbamate.

Example 1025B

tert-butyl 4-(2,2-dimethyl-3-(4-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)-1H-pyrazol-1-yl)propyl)piperazine-1-carboxylate

The title compound was prepared as described as described in Example 148A, substituting N-(4-bromophenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for 4-bromoaniline and tert-butyl 4-(2,2-dimethyl-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazol-1-yl)propyl)piperidine-1-carboxylate for 1-isobutyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole.

Example 1025C

N-(4-{1-[2,2-dimethyl-3-(piperazin-1-yl)propyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1D, substituting tert-butyl 4-(2,2-dimethyl-3-(4-(4-(1-(pyridazin-3-yl)azetidine-3-carboxamido)phenyl)-1H-pyrazol-1-yl)propyl)piperazine-1-carboxylate for tert-butyl 4-(4-(1-(pyridin-3-yl)azetidine-3-carboxamido)phenoxy)piperidine-1-carboxylate to give the title compound as a TFA salt. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 10.25 (s, 1H), 8.81 (s, 2H), 8.57 (dd, J = 4.3, 1.0 Hz, 1H), 8.07 (s, 1H), 7.86 (s, 1H), 7.80 (dd, J = 9.3, 4.4 Hz, 1H), 7.62 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 8.6 Hz, 2H), 7.45 (d, J = 8.9 Hz, 1H), 4.47 (t, J = 9.2 Hz, 2H), 4.40 (dd, J = 9.3, 5.9 Hz, 2H), 4.03 (s, 2H), 3.87 - 3.74 (m, 1H), 3.19 (s, 4H), 2.92 (s, 4H), 2.45 (s, 2H), 0.89 (s, 6H); MS (ESI(+)) m/e 475 $(M+H)^+$.

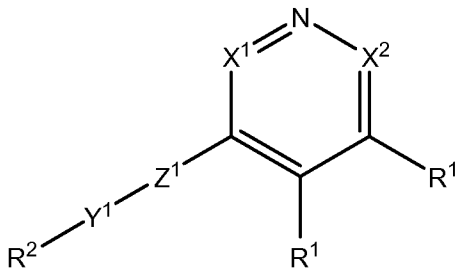
Example 1026

N-(4-{1-[2-methyl-2-(piperazin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide

The title compound was prepared as described in Example 1A, substituting N-(4-(piperidin-4-yl)phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide for tert-butyl 4-(4-aminophenoxy)piperidine-1-carboxylate and 2-(4-(tert-butoxycarbonyl)piperazin-1-yl)-2-methylpropanoic acid for 1-(benzyloxycarbonyl)azetidine-3-carboxylic acid, followed by TFA deprotection as described in Example 1D to give the title compound as a TFA salt. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.17 (s, 1H), 8.67 (s, 2H), 8.56 (d, J = 4.3 Hz, 1H), 7.77 (dd, J = 9.3, 4.4 Hz, 1H), 7.55 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 9.3 Hz, 1H), 7.21 (d, J = 8.5 Hz, 2H), 5.27 (s, 1H), 4.59 (s, 1H), 4.45 (t, J = 9.1 Hz, 2H), 4.37 (dd, J = 9.2, 5.9 Hz, 2H), 3.91 - 3.71 (m, 1H), 3.11 (s, 5H), 2.81 - 2.53 (m, 6H), 1.80 (d, J = 12.0 Hz, 2H), 1.45 (td, J = 12.3, 9.1 Hz, 2H), 1.21 (s, 6H); MS (ESI(+)) m/e 492 $(M+H)^+$.

WHAT IS CLAIMED IS:

1. A compound of formula (IC), or a therapeutically acceptable salt thereof,



Formula (IC);

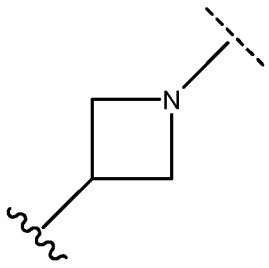
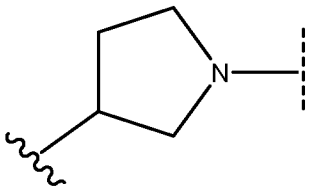
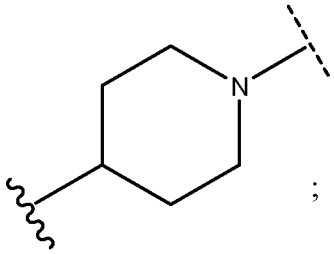
X^1 is N and X^2 is CR^1; or

X^1 is CR^1 and X^2 is N; or

X^1 is CR^1 and X^2 is CR^1;

Y^1 is C(O)NH, or NHC(O);

Z^1 is


, 
, or 
;

wherein  indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl;

R^1, at each occurrence, is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydoxyalkyl, alkoxy, OH, NH_2, CN, NO_2, F, Cl, Br and I;

R^2 is independently selected from the group consisting of C_4-C_6-alkyl, C_4-C_6-alkenyl, C_4-C_6-alkynyl, aryl, and 5-6 membered heteroaryl; wherein each R^2 C_4-C_6-alkyl, C_4-C_6-alkenyl, and C_4-C_6-alkynyl is substituted with one or more substituents independently selected from the group consisting of R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^2 aryl and 5-6 membered heteroaryl is optionally substituted with one or more substituents independently selected from the group consisting of R^4, OR^4, SR^4, $S(O)R^4$,

SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, and I;

R^3, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, and heterocyclyl; wherein each R^3 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, C(O)NHOH, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^3 aryl, cycloalkyl, cycloalkenyl, and heterocyclyl is optionally substituted with one or more substituents independently selected from the group consisting of R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^6)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, C(O)NHOH, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^4, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^4 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I;

R^5, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^5 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$,

$C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), C(O)OH, N_3, CN, NH_2, F, Cl, Br and I;

R^6, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^6 alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br and I;

R^7, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^8, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

R^9, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

wherein the cyclic moieties represented by R^4, R^5, R^6, R^7, R^8, and R^9 are independently optionally substituted with one or more substituents independently selected from the group consisting of R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br and I;

R^{10}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{10} alkyl, alkenyl, and alkynyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br and I; wherein each R^{10} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$,

$OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, C(O)NHOH, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br and I;

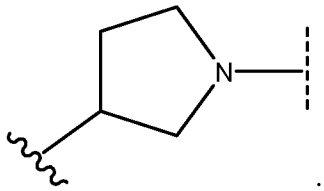
R^{11}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein each R^{11} alkyl, alkenyl, and alkynyl is optionally substituted with alkoxy or aryl; wherein each R^{11} aryl, heterocyclyl, cycloalkyl, and cycloalkenyl is optionally substituted with one or more substituents independently selected from the group consisting of R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br and I;

R^{12}, at each occurrence, is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; and

R^{13}, at each occurrence, is independently selected from the group consisting of alkyl, haloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;

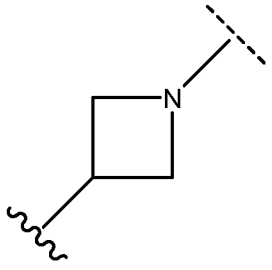
with the proviso that

when X^1 is CR^1 and X^2 is CR^1; R^1 is hydrogen; Y^1 is NHC(O); Z^1 is



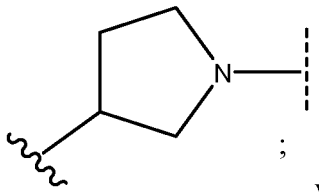
; and R^2 is pyrrolyl; the R^2 pyrrolyl is not substituted with two alkyl groups.

2. The compound of claim 1, or a therapeutically acceptable salt thereof, wherein Z^1 is



; wherein  indicates the point of attachment to Y^1 and  indicates the point of attachment to the nitrogen containing heteroaryl.

3. The compound of claim 1, or a therapeutically acceptable salt thereof, wherein Z^1 is



; wherein ~ indicates the point of attachment to Y^1 and ⁄ indicates the point of attachment to the nitrogen containing heteroaryl.

4. The compound of claim 2, or a therapeutically acceptable salt thereof, wherein Y^1 is C(O)NH.

5. The compound of claim 3, or a therapeutically acceptable salt thereof, wherein Y^1 is C(O)NH.

6. The compound of claim 4, or a therapeutically acceptable salt thereof, wherein X^1 is N and X^2 is CR^1.

7. The compound of claim 5, or a therapeutically acceptable salt thereof, wherein X^1 is N and X^2 is CR^1.

8. The compound of claim 6, or a therapeutically acceptable salt thereof, wherein R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

9. The compound of claim 7, or a therapeutically acceptable salt thereof, wherein R^2 is phenyl; wherein each R^2 phenyl is substituted with one substituent independently selected from the group consisting of R^4, OR^4, and SO_2R^4.

10. The compound of claim 8, or a therapeutically acceptable salt thereof, wherein R^1, at each occurrence, is hydrogen.

11. The compound of claim 9, or a therapeutically acceptable salt thereof, wherein R^1, at each occurrence, is hydrogen.

12. The compound of claim 10, or a therapeutically acceptable salt thereof, wherein R^4, at each occurrence, is heterocyclyl.

13. The compound of claim 11, or a therapeutically acceptable salt thereof, wherein R^4, at each occurrence, is heterocyclyl.

14. The compound of claim 1, selected from the group consisting of

1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(2-cyanopyridin-3-yl)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-[2-(trifluoromethyl)pyridin-3-yl]azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(4-methylpyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(4-fluoropyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-[4-(trifluoromethyl)pyridin-3-yl]azetidine-3-carboxamide;

tert-butyl 4-[4-({[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate;

tert-butyl 4-[4-({[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbonyl}amino)phenoxy]piperidine-1-carboxylate;

1-(pyridin-3-yl)-N-(4-{1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-[4-({1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-[4-({1-[(2R)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[1-(pyridin-3-yl)azetidin-3-yl]-4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]oxy}benzamide;

N-(4-{1-[(2S)-2-methylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)-N-[1-(pyridin-3-yl)azetidin-3-yl]benzamide;

4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}-N-[1-(pyridin-3-yl)azetidin-3-yl]benzamide;

1-(pyridin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-(4-{[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbamoyl}phenoxy)piperidine-1-carboxylate;

tert-butyl 4-(4-{[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]carbamoyl}phenoxy)piperidine-1-carboxylate;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-[4-({1-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-{4-[(1-pentanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylpentanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-ethoxypropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-butanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(ethoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(N-acetyl-L-leucyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(morpholin-4-ylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(furan-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propanoylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methoxypyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylmethyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpentyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-ethylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propylpiperidin-4-yl)oxy]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-cyclopropylethyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylmethyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutyl)piperidin-4-yl]oxy}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylmethyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylmethyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpentyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methoxypyridin-3-yl)azetidine-3-carboxamide;

1-(4-cyanopyridin-3-yl)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-pentanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(morpholin-4-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(pyrrolidin-1-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(5-oxo-D-prolyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperazin-1-yl)acetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(5-oxo-L-prolyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(morpholin-4-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

1-(pyridin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(piperidin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-hydroxy-2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)pyrrolidine-3-carboxamide;

N-(4-{1-[(2S)-2-methylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(pyridazin-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-[4-(1-pentanoylpiperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(morpholin-4-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(pyrrolidin-1-ylacetyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(5-oxo-D-prolyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(N,N-dimethyl-beta-alanyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperazin-1-yl)acetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(5-oxo-L-prolyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[3-(morpholin-4-yl)propanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

1-(2-methylpyridin-3-yl)-N-(4-{1-[3-(piperidin-1-yl)propanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)pyrrolidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]azetidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-{4-[(1-benzoylazetidin-3-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-hydroxy-2-methylpropanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-pentanoylazetidin-3-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylacetyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclobutylcarbonyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)azetidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)azetidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]azetidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[difluoro(phenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-(4-{[1-(3,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)oxy]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]furan-2-carboxamide;

(3S)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-4-ylacetyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

tert-butyl 4-(4-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}phenyl)piperidine-1-carboxylate;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-pentanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-hexanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-heptanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(but-3-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(pent-4-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(methylsulfanyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-nitropropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(pent-4-ynoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,3-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{1-[(3,5-dimethylphenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(5-methylpyrazin-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[(pyrimidin-2-ylsulfanyl)acetyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-(4-{1-[(1-acetylpiperidin-4-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(diphenylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(5-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-fluoro-4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,3-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-tert-butylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-fluoro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-chloro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylphenoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{1-[(3-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2R)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[N-(furan-2-ylcarbonyl)glycyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(benzyloxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-1-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(N-benzoylglycyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{1-[4-(thiophen-2-yl)butanoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(2,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclobutylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-{N-[(4-methylphenyl)sulfonyl]glycyl}piperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,3-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2S)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(naphthalen-2-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-phenylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(2,6-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[3-(phenylsulfonyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(2,5-dimethylfuran-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-oxopropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(1,3-thiazol-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2S)-2-methylbutanoyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydro-2H-pyran-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethoxy)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(thiophen-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3,5-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[3-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2,4-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(5-methylthiophen-2-yl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[3-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(pyridin-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methyl-2-phenylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(methoxyacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(thiophen-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-{[3-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[4-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-({(3R)-1-[4-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{[(3R)-1-(3,3,3-trifluoropropanoyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[difluoro(phenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2S)-2-methylbutanoyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydro-2H-pyran-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethoxy)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(thiophen-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3,5-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(3-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[3-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2,4-difluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[4-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(5-methylthiophen-2-yl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(2-fluorophenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(cyclopropylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(tetrahydrofuran-3-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[3-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(pyridin-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(4-chlorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methyl-2-phenylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(methoxyacetyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(thiophen-2-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-{[3-(trifluoromethyl)phenyl]acetyl}pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[4-(trifluoromethyl)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({(3R)-1-[4-(trifluoromethoxy)benzoyl]pyrrolidin-3-yl}oxy)phenyl]azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(3,3,3-trifluoropropanoyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[difluoro(phenyl)acetyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-(4-{1-[(2,4-difluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[(5-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methyl-2-phenylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[4-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-(4-{1-[difluoro(phenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(4,4-difluorocyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[4-(trifluoromethoxy)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-4-yl)-N-[4-(1-{[4-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(3-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-tert-butylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]sulfonyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2,5-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(4-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-dimethylbenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(3-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]azetidine-3-carboxamide;

N-[4-({1-[(3,5-difluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-({1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}sulfonyl)phenyl]azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,3-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,4-dichlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,5-difluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methoxybenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(phenylacetyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methylalanyl)piperidin-4-yl]phenyl}-1-(pyridin-3-yl)azetidine-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

tert-butyl 4-(2-methyl-1-oxo-1-{4-[4-({[1-(pyridin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidin-1-yl}propan-2-yl)piperazine-1-carboxylate;

N-(4-{1-[2-methyl-2-(piperazin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-chlorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-fluorophenyl)acetyl]piperidin-4-yl}sulfonyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)sulfonyl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]sulfonyl}phenyl)-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[(3R)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3R)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3S)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-2-carboxamide;

N-[(3R)-1-(5,6-dichloropyridazin-4-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3R)-1-(pyridazin-4-yl)pyrrolidin-3-yl]thiophene-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)piperidine-4-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)piperidine-4-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}piperidine-4-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]thiophene-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2S)-2-phenylbutanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2S)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2R)-2-methoxy-2-phenylacetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(ethoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-methylphenoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-1-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2,6-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-1-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[4-(thiophen-2-yl)butanoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(naphthalen-2-ylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[3-(phenylsulfonyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-[4-(1-{[3-(trifluoromethyl)phenyl]acetyl}piperidin-4-yl)phenyl]pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(furan-2-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(N-benzoylglycyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2,4-dichlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-methylcyclohexyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopentylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-5-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-fluoropyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-fluoro-6-methylpyridin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-heptanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-hexanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylpentanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3,5-dimethylphenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(4-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(furan-3-ylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,4-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[2-chloro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-ethoxypropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-dichlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,5-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(5-fluoro-2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(diphenylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[4-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(pent-4-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethoxy)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-phenylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[2-fluoro-5-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclohexylacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-tert-butylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-chlorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{1-[3-(trifluoromethyl)benzoyl]piperidin-4-yl}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(pent-4-ynoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(3-fluorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(1-acetylpiperidin-4-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(but-3-enoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluoro-4-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-chlorophenyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(N-acetyl-L-leucyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methoxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,3-dimethylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{1-[4-(propan-2-yl)benzoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclohexylcarbonyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-hydroxybenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-cyanobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoro-4-methylpyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-cyanopyridin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(5-methylpyridin-3-yl)azetidine-3-carboxamide;

2-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-1,3-thiazole-5-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(2-methylpyridin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(2-methylpyridin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}pyrrolidine-3-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]furan-2-carboxamide;

5-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]furan-2-carboxamide;

N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[(3S)-1-(6-chloropyridazin-3-yl)pyrrolidin-3-yl]-4-[1-(2-methylpropanoyl)piperidin-4-yl]benzamide;

N-(4-{1-[2-(piperazin-1-yl)ethyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

4-[1-(2-methylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]benzamide;

N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(3-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(4-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

(3S)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-hydroxy-2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

5-[1-(2-methylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-{1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-(1-benzoylpiperidin-4-yl)-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(tetrahydrofuran-3-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-{1-[(2R)-tetrahydrofuran-2-ylcarbonyl]piperidin-4-yl}thiophene-2-carboxamide;

5-{1-[(1-methylpiperidin-4-yl)acetyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]thiophene-2-carboxamide;

(3S)-N-{4-[1-(2-methylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(propan-2-yl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(cyclopropylmethyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-{4-[1-(tetrahydro-2H-pyran-2-ylmethyl)-1H-pyrazol-4-yl]phenyl}pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-tert-butyl-1H-pyrazol-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(3-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(4-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2-methylbenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({(3R)-1-[(4,4-difluorocyclohexyl)carbonyl]pyrrolidin-3-yl}oxy)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-1-(pyridazin-3-yl)-N-(4-{[(3R)-1-(4,4,4-trifluorobutanoyl)pyrrolidin-3-yl]oxy}phenyl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(5-propyl-1,2,4-oxadiazol-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(4-fluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylazetidin-3-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,5-difluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,4-difluorobenzoyl)azetidin-3-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(3-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[(1-benzoylpiperidin-4-yl)oxy]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(4-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}oxy)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,3,4-oxadiazol-2-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-imidazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[5-(2,2-dimethylpropyl)-1,2,4-oxadiazol-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-cyclopropyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-(5-{[1-(pyridazin-3-yl)azetidin-3-yl]carbamoyl}thiophen-2-yl)piperidine-1-carboxylate;

tert-butyl 4-fluoro-4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]piperidine-1-carboxylate;

5-(1-benzoylpiperidin-4-yl)-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2-methylbenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(3-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(4-fluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[3-cyclopropyl-1-(2-hydroxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

1-(6-fluoropyridazin-3-yl)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-fluoropyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-benzoylpyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(2-fluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(3,5-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[(3S)-1-(2,2-dimethylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-methylbenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(4-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,4-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,5-difluorobenzoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[(1-benzoylpiperidin-4-yl)oxy]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[8-(2-methylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[8-(4,4,4-trifluorobutanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}azetidine-3-carboxamide;

N-[4-(8-benzoyl-8-azabicyclo[3.2.1]oct-3-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2-fluorobenzoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[8-(2,2-dimethylpropanoyl)-8-azabicyclo[3.2.1]oct-3-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{8-[(1-methylcyclopropyl)carbonyl]-8-azabicyclo[3.2.1]oct-3-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-methoxyethyl)-3-(2-methylpropyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

5-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-[1-(pyridazin-3-yl)azetidin-3-yl]-5-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-fluoropiperidine-1-carboxylate;

benzyl 4-[4-({[1-(6-chloropyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-4-hydroxypiperidine-1-carboxylate;

N-[1-(pyridazin-3-yl)azetidin-3-yl]-5-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(cyclopropylcarbonyl)piperidin-4-yl]-N-[1-(pyridazin-3-yl)azetidin-3-yl]thiophene-2-carboxamide;

N-{4-[4-fluoro-1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylcarbonyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(2-fluoro-4-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoyl-4-fluoropiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)-4-fluoropiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(2-methoxyethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butyl-3-tert-butyl-1H-pyrazol-5-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[3-tert-butyl-1-(tetrahydro-2H-pyran-4-ylmethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-2-fluorophenyl]-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-2-fluorophenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-{2-fluoro-4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(6-chloropyridazin-3-yl)-N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(3-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)-3-fluorophenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{3-fluoro-4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(cyclopropylacetyl)piperidin-4-yl]-3-fluorophenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)-4-hydroxypiperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(6-methylpyridazin-3-yl)-N-(4-{1-[(4-methyltetrahydro-2H-pyran-4-yl)methyl]-1H-pyrazol-4-yl}phenyl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(6-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[(1-benzoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-fluorobenzoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylpropanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3,3-dimethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-ethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpropanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-acetylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2S)-2-methylbutanoyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-{[4-methyl-1-(oxetan-3-yl)piperidin-4-yl]methyl}-1H-pyrazol-4-yl)phenyl]-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(2-fluorobenzoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]furan-2-carboxamide;

N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide;

N-{4-[1-(2-fluorobenzoyl)piperidin-4-yl]phenyl}-1-(3-methylpyridazin-4-yl)azetidine-3-carboxamide;

N-(4-{1-[(2-aminopyridin-3-yl)carbonyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylic acid;

ethyl 1-methyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate;

ethyl 1-phenyl-5-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)phenyl]-1H-pyrazole-3-carboxylate;

N-{6-[1-(2-fluorobenzoyl)piperidin-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(3-methylbutanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2-methylpropanoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3R)-1-(2,4-difluorobenzoyl)pyrrolidin-3-yl]oxy}phenyl)-1-(6-methylpyridazin-3-yl)azetidine-3-carboxamide;

1-(6-methylpyridazin-3-yl)-N-(4-{[(3R)-1-(1,3-thiazol-4-ylcarbonyl)pyrrolidin-3-yl]oxy}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{6-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]pyridin-3-yl}azetidine-3-carboxamide;

N-{6-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-[4-(1-benzoylpiperidin-4-yl)phenyl]-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridazin-3-yl)pyrrolidine-3-carboxamide;

N-{4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{6-[1-(2,2-dimethylpropyl)-1H-pyrazol-4-yl]pyridin-3-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

tert-butyl 4-[4-({[1-(pyridazin-3-yl)azetidin-3-yl]carbonyl}amino)-1H-pyrazol-1-yl]piperidine-1-carboxylate;

N-(6-{1-[(4-methylpiperidin-4-yl)methyl]-1H-pyrazol-4-yl}pyridin-3-yl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(1H-pyrazol-4-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2,2-dimethylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(2-methylcyclopropyl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(methylsulfanyl)acetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1S,4R)-bicyclo[2.2.1]hept-2-ylacetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(4-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[3-(methylsulfanyl)propanoyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-4-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(1H-pyrazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(6-methylpyridin-3-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(3-methylthiophen-2-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(pent-4-ynoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-3-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(methoxyacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(tetrahydrofuran-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-[4-({1-[(2-methoxyethoxy)acetyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(ethoxyacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(thiophen-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-{4-[(1-hexanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperidin-4-yl}methyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(but-3-enoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(1,3-thiazol-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(1,2-oxazol-5-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-(4-{[1-(furan-3-ylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-propanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-butanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclobutylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-pentanoylpiperidin-4-yl)methyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopentylacetyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(2-methylbenzoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylpentanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclohexylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(3-methylbutanoyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[1-(cyclopropylcarbonyl)piperidin-4-yl]methyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]methyl}phenyl)azetidine-3-carboxamide;

N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(4-methylpyridazin-3-yl)azetidine-3-carboxamide;

N-{1-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-1H-pyrazol-4-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{1-[1-(2-fluorobenzoyl)piperidin-4-yl]-1H-pyrazol-4-yl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(phenylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2,2-dimethylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(3-methoxy-2,2-dimethylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-cyclopropylethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[2-(2-ethylpiperidin-1-yl)ethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(cyclobutylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2S)-butan-2-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(butylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2,2-dimethyltetrahydro-2H-pyran-4-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(1S)-1-cyclopropylethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-({2-[methyl(phenyl)amino]ethyl}carbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1,1'-bi(cyclopropyl)-1-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(thiophen-3-ylcarbamoyl)phenyl]azetidine-3-carboxamide;

N-(4-{[(1R)-1-cyclopropylethyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylpiperidin-4-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2R)-butan-2-ylcarbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-azabicyclo[2.2.2]oct-3-ylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(tetrahydrofuran-3-ylmethyl)carbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(oxetan-3-ylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-methylcyclopropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclobutylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylcyclopropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-methoxy-2-methylpropyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(cyclopropylmethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(2R)-tetrahydrofuran-2-ylmethyl]carbamoyl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3,3,3-trifluoropropyl)carbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(1-methylpiperidin-3-yl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{[(3-methyloxetan-3-yl)methyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-(4-{[(2S)-tetrahydrofuran-2-ylmethyl]carbamoyl}phenyl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(tetrahydro-2H-pyran-4-ylmethyl)carbamoyl]phenyl}azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-[4-(tetrahydro-2H-pyran-4-ylcarbamoyl)phenyl]azetidine-3-carboxamide;

N-(4-{[(1-methylpiperidin-3-yl)methyl]carbamoyl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclopropylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(cyclopentylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(benzylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(3-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(propylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(4-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(2-fluorophenyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[(1-methylcyclobutyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(prop-2-en-1-ylcarbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

5-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(2,2-dimethylbutanoyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-{1-[(1-methylcyclopropyl)carbonyl]piperidin-4-yl}-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]-5-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]thiophene-2-carboxamide;

5-[1-(cyclopropylacetyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

5-[1-(bicyclo[2.2.1]hept-2-ylacetyl)piperidin-4-yl]-N-[(3S)-1-(pyridazin-3-yl)pyrrolidin-3-yl]thiophene-2-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3S)-tetrahydrofuran-3-ylcarbamoyl]phenyl}azetidine-3-carboxamide;

N-[4-({4-[2-(dimethylamino)ethyl]phenyl}carbamoyl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[(3R)-tetrahydrofuran-3-ylcarbamoyl]phenyl}azetidine-3-carboxamide;

N-{4-[(2-methoxyethyl)carbamoyl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-amino-2,2-dimethylpropyl)-1H-pyrazol-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2,2-dimethyl-3-(piperazin-1-yl)propyl]-1H-pyrazol-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[2-methyl-2-(piperazin-1-yl)propanoyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide; and pharmaceutically acceptable salts thereof.

15. The compound of claim 1, selected from the group consisting of

N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(3,3,3-trifluoropropanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-{4-[1-(methoxyacetyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-(4-{1-[(methylsulfanyl)acetyl]piperidin-4-yl}phenyl)-1-(pyridazin-3-yl)azetidine-3-carboxamide;

N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)azetidine-3-carboxamide;

1-(pyridazin-3-yl)-N-{4-[1-(4,4,4-trifluorobutanoyl)piperidin-4-yl]phenyl}azetidine-3-carboxamide;

N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)azetidine-3-carboxamide;

(3S)-N-[4-(1-propanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-butanoylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-[4-(1-acetylpiperidin-4-yl)phenyl]-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(2-ethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3,3-dimethylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3S)-N-{4-[1-(3-methylbutanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide;

(3R)-N-{4-[1-(2,2-dimethylpropanoyl)piperidin-4-yl]phenyl}-1-(pyridazin-3-yl)pyrrolidine-3-carboxamide; and pharmaceutically acceptable salts thereof.

16. A composition for treating inflammatory and tissue repair disorders; particularly rheumatoid arthritis, inflammatory bowel disease, asthma and COPD (chronic obstructive pulmonary disease), osteoarthritis, osteoporosis and fibrotic diseases; dermatosis, including psoriasis, atopic dermatitis and ultra-violet induced skin damage; autoimmune diseases including systemic lupus erythematosis, multiple sclerosis, psoriatic arthritis, ankylosing spondylitis, tissue and organ rejection, Alzheimer's disease, stroke, athersclerosis, restenosis, diabetes, glomerulonephritis, cancer, particularly wherein the cancer is selected from breast, prostate, lung, colon, cervix, ovary, skin, CNS, bladder, pancreas, leukemia, lymphoma or Hodgkin's disease, cachexia, inflammation associated with infection and certain viral infections, including Acquired Immune Deficiency Syndrome (AIDS), adult respiratory distress syndrome, and ataxia telengiectasia, said composition comprising an excipient and a therapeutically effective amount of a compound of claim 1, or pharmaceutically acceptable salts thereof.

17. A method of treating inflammatory and tissue repair disorders; particularly rheumatoid arthritis, inflammatory bowel disease, asthma and COPD (chronic obstructive pulmonary disease), osteoarthritis, osteoporosis and fibrotic diseases; dermatosis, including psoriasis, atopic dermatitis and ultra-violet induced skin damage; autoimmune diseases including systemic lupus erythematosis, multiple sclerosis, psoriatic arthritis, ankylosing spondylitis, tissue and organ rejection, Alzheimer's disease, stroke, athersclerosis, restenosis, diabetes, glomerulonephritis, cancer, particularly wherein the cancer is selected from breast, prostate, lung, colon, cervix, ovary, skin, CNS, bladder, pancreas, leukemia, lymphoma or Hodgkin's disease, cachexia, inflammation associated with infection and certain viral infections, including Acquired Immune Deficiency Syndrome (AIDS), adult respiratory distress syndrome, and ataxia telengiectasia in a patient, said method comprising administering to the patient a therapeutically effective amount of a compound of claim 1, or pharmaceutically acceptable salts thereof.

18. A method of treating inflammatory and tissue repair disorders; particularly rheumatoid arthritis, inflammatory bowel disease, asthma and COPD (chronic obstructive pulmonary disease), osteoarthritis, osteoporosis and fibrotic diseases; dermatosis, including psoriasis, atopic dermatitis and ultra-violet induced skin damage; autoimmune diseases including systemic lupus erythematosis, multiple sclerosis, psoriatic arthritis, ankylosing spondylitis, tissue and organ rejection, Alzheimer's disease, stroke, atherscleros is, restenosis, diabetes, glomerulonephritis, cancer, particularly wherein the cancer is selected from breast, prostate, lung, colon, cervix, ovary, skin, CNS, bladder, pancreas, leukemia, lymphoma or Hodgkin's disease, cachexia, inflammation associated with infection and certain viral infections, including Acquired Immune Deficiency Syndrome (AIDS), adult respiratory distress syndrome, and ataxia telengiectasia or spleen cancer in a patient, said method comprising administering to the patient therapeutically effective amount of the compound of claim 1, or pharmaceutically acceptable salts thereof; and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent.

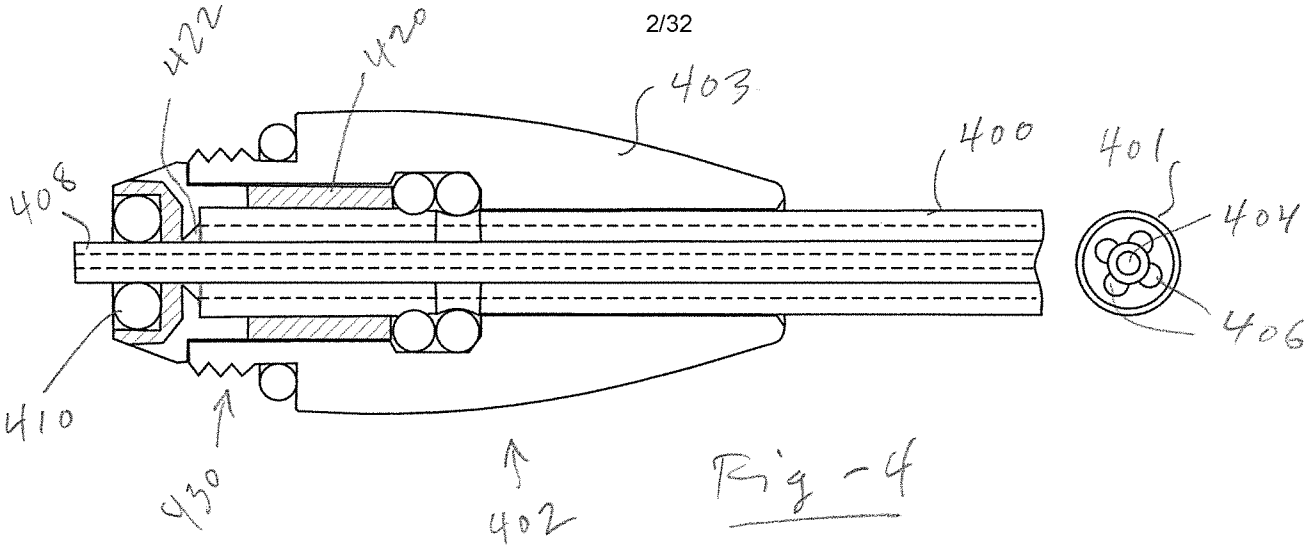


Fig - 4

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2013/040481

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D401/14 C07D405/14 C07D401/04 C07D403/04 C07D403/14
C07D409/14 C07D417/14 A61K31/501 A61K31/4427 A61P3/00
A61P11/00 A61P25/00 A61P31/00 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011/025799 A1 (GLAXO GROUP LTD [GB]; BULLION ANN MARIE [US]; BUSCH-PETERSEN JAKOB [US) 3 March 2011 (2011-03-03) the whole document	1-18
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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 June 2013	04/07/2013

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Bosma, Peter

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2013/040481

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	WO 2012/031199 A1 (FORMA THERAPEUTICS INC [US]; BAIR KENNETH W [US]; BUCKMELTER ALEXANDRE) 8 March 2012 (2012-03-08) the whole document -----	1-18

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2013/040481

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(71)申请人 艾伯维公司
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代理人 杜艳玲 梁谋
(51)Int.Cl.
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C07D 405/14(2006.01)
C07D 401/04(2006.01)
C07D 403/04(2006.01)
C07D 403/14(2006.01)
C07D 409/14(2006.01)
C07D 417/14(2006.01)
A61K 31/501(2006.01)
A61K 31/4427(2006.01)
A61P 3/00(2006.01)
A61P 11/00(2006.01)
A61P 25/00(2006.01)
A61P 31/00(2006.01)
A61P 35/00(2006.01)

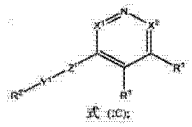
权利要求书57页 说明书492页 附图1页

(54)发明名称

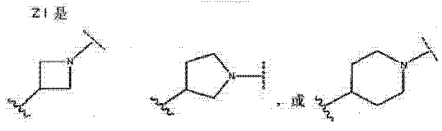
作为NAMPT抑制剂的哒嗪和吡啶衍生物

(57)摘要

公开了抑制NAMPT活性的式(IC)的化合物或其治疗上可接受的盐、包含所述化合物的组合物、和治疗在其过程中表达NAMPT的疾病的方法。

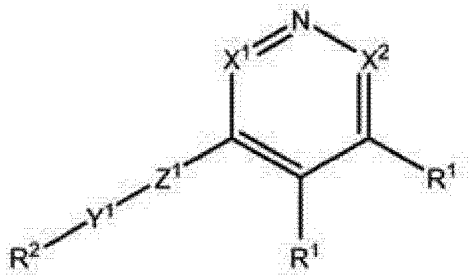


式(IC)



CN 104583194 A

1. 式 (IC) 的化合物，或其治疗上可接受的盐，



式 (IC);

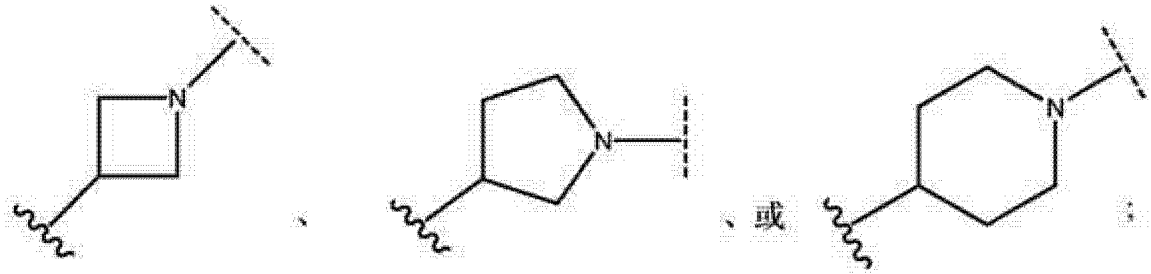
X^1为 N 且 X^2为 CR^1；或

X^1为 CR^1且 X^2为 N；或

X^1为 CR^1且 X^2为 CR^1；

Y^1为 C(O)NH、或 NHC(O)；

Z^1为



其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点；

R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I；

R^2独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2 中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：R^3、OR^3、SR^3、S(O)R^3、SO_2R^3、C(O)R^3、CO(O)R^3、OC(O)R^3、OC(O)OR^3、NH_2、NHR^3、N(R^3)$_2$、NHC(O)R^3、NR^3C(O)R^3、NHS(O)$_2R^3$、NR^3S(O)$_2R^3$、NHC(O)OR^3、NR^3C(O)OR^3、NHC(O)NH_2、NHC(O)NHR^3、NHC(O)N(R^3)$_2$、NR^3C(O)NHR^3、NR^3C(O)N(R^3)$_2$、C(O)NH_2、C(O)NHR^3、C(O)N(R^3)$_2$、C(O)NHOH、C(O)$NHOR^3$、C(O)$NHSO_2R^3$、C(O)$NR^3SO_2R^3$、SO_2NH_2、SO_2NHR^3、$SO_2N(R^3)_2$、C(O)H、C(O)OH、C(N)NH_2、C(N)NHR^3、C(N)N(R^3)$_2$、CNOH、$CNOCH_3$、OH、(O)、CN、N_3、NO_2、F、Cl、Br 和 I；其中 R^2 中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SR^4、S(O)R^4、SO_2R^4、C(O)R^4、OC(O)OR^4、NH_2、NHR^4、N(R^4)$_2$、NHC(O)R^4、NR^4C(O)R^4、NHS(O)$_2R^4$、NR^4S(O)$_2R^4$、NHC(O)OR^4、NR^4C(O)OR^4、NHC(O)NH_2、NHC(O)NHR^4、NHC(O)N(R^4)$_2$、NR^4C(O)NHR^4、NR^4C(O)N(R^4)$_2$、C(O)NH_2、C(O)NHR^4、C(O)N(R^4)$_2$、C(O)NHOH、C(O)$NHOR^4$、C(O)$NHSO_2R^4$、C(O)$NR^4SO_2R^4$、SO_2NH_2、SO_2NHR^4、$SO_2N(R^4)_2$、C(O)H、C(O)OH、C(N)NH_2、C(N)NHR^4、C(N)N(R^4)$_2$、CNOH、$CNOCH_3$、OH、CN、N_3、NO_2、F、Cl、和 I；

R^3在每次出现时独立地选自烷基、烯基、炔基、芳基、环烷基、环烯基、和杂环基；其中 R^3 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^5、OR^5、

SR^5、$S(O)R^5$、SO_2R^5、$C(O)R^5$、$CO(O)R^5$、$OC(O)R^5$、$OC(O)OR^5$、NH_2、NHR^5、$N(R^5)_2$、$NHC(O)R^5$、$NR^5C(O)R^5$、$NHS(O)_2R^5$、$NR^5S(O)_2R^5$、$NHC(O)OR^5$、$NR^5C(O)OR^5$、$NHC(O)NH_2$、$NHC(O)NHR^5$、$NHC(O)N(R^5)_2$、$NR^5C(O)NHR^5$、$NR^5C(O)N(R^5)_2$、$C(O)NH_2$、$C(O)NHR^5$、$C(O)N(R^5)_2$、$C(O)NHOH$、$C(O)NHOR^5$、$C(O)NHSO_2R^5$、$C(O)NR^5SO_2R^5$、SO_2NH_2、SO_2NHR^5、$SO_2N(R^5)_2$、$C(O)H$、$C(O)OH$、$C(N)NH_2$、$C(N)NHR^5$、$C(N)N(R^5)_2$、CNOH、$CNOCH_3$、OH、(O)、CN、N_3、NO_2、F、Cl、Br 和 I；其中 R^3中的芳基、环烷基、环烯基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^6、OR^6、SR^6、$S(O)R^6$、SO_2R^6、$C(O)R^6$、$CO(O)R^6$、$OC(O)R^6$、$OC(O)OR^6$、NH_2、NHR^6、$N(R^6)_2$、$NHC(O)R^6$、$NR^6C(O)R^6$、$NHS(O)_2R^6$、$NR^6S(O)_2R^6$、$NHC(O)OR^6$、$NR^6C(O)OR^6$、$NHC(O)NH_2$、$NHC(O)NHR^6$、$NHC(O)N(R^6)_2$、$NR^6C(O)NHR^6$、$NR^6C(O)N(R^6)_2$、$C(O)NH_2$、$C(O)NHR^6$、$C(O)N(R^6)_2$、$C(O)NHOH$、$C(O)NHOR^6$、$C(O)NHSO_2R^6$、$C(O)NR^6SO_2R^6$、SO_2NH_2、SO_2NHR^6、$SO_2N(R^6)_2$、$C(O)H$、$C(O)OH$、$C(N)NH_2$、$C(N)NHR^6$、$C(N)N(R^6)_2$、CNOH、$CNOCH_3$、OH、CN、N_3、NO_2、F、Cl、Br 和 I；

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^7、OR^7、SR^7、$S(O)R^7$、SO_2R^7、$C(O)R^7$、$CO(O)R^7$、$OC(O)R^7$、$OC(O)OR^7$、NH_2、NHR^7、$N(R^7)_2$、$NHC(O)R^7$、$NR^7C(O)R^7$、$NHS(O)_2R^7$、$NR^7S(O)_2R^7$、$NHC(O)OR^7$、$NR^7C(O)OR^7$、$NHC(O)NH_2$、$NHC(O)NHR^7$、$NHC(O)N(R^7)_2$、$NR^7C(O)NHR^7$、$NR^7C(O)N(R^7)_2$、$C(O)NH_2$、$C(O)NHR^7$、$C(O)N(R^7)_2$、$C(O)NHOH$、$C(O)NHOR^7$、$C(O)NHSO_2R^7$、$C(O)NR^7SO_2R^7$、SO_2NH_2、SO_2NHR^7、$SO_2N(R^7)_2$、$C(O)H$、$C(O)OH$、$C(N)NH_2$、$C(N)NHR^7$、$C(N)N(R^7)_2$、CNOH、$CNOCH_3$、OH、(O)、CN、N_3、NO_2、F、Cl、Br 和 I；

R^5在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^5 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^8、OR^8、SR^8、$S(O)R^8$、SO_2R^8、NHR^8、$N(R^8)_2$、$C(O)R^8$、$C(O)NH_2$、$C(O)NHR^8$、$C(O)N(R^8)_2$、$NHC(O)R^8$、$NR^8C(O)R^8$、$NHSO_2R^8$、$NHC(O)OR^8$、SO_2NH_2、SO_2NHR^8、$SO_2N(R^8)_2$、$NHC(O)NH_2$、$NHC(O)NHR^8$、OH、(O)、$C(O)OH$、N_3、CN、NH_2、F、Cl、Br 和 I；

R^6在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^6 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^9、OR^9、SR^9、$S(O)R^9$、SO_2R^9、NHR^9、$N(R^9)_2$、$C(O)R^9$、$C(O)NH_2$、$C(O)NHR^9$、$C(O)N(R^9)_2$、$NHC(O)R^9$、$NR^9C(O)R^9$、$NHSO_2R^9$、$NHC(O)OR^9$、SO_2NH_2、SO_2NHR^9、$SO_2N(R^9)_2$、$NHC(O)NH_2$、$NHC(O)NHR^9$、OH、(O)、$C(O)OH$、N_3、CN、NH_2、CF_3、CF_2CF_3、F、Cl、Br 和 I；

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^8在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^9在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中由 R^4、R^5、R^6、R^7、R^8、和 R^9表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、OR^{10}、SR^{10}、$S(O)R^{10}$、SO_2R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$OC(O)R^{10}$、$OC(O)OR^{10}$、$C(O)C(O)R^{10}$、NH_2、NHR^{10}、$N(R^{10})_2$、$NHC(O)R^{10}$、$NR^{10}C(O)R^{10}$、$NHS(O)_2R^{10}$、$NR^{10}S(O)_2R^{10}$、$NHC(O)OR^{10}$、$NR^{10}C(O)OR^{10}$、$NHC(O)NH_2$、$NHC(O)NHR^{10}$、$NHC(O)N(R^{10})_2$、$NR^{10}C(O)NHR^{10}$、$NR^{10}C(O)N(R^{10})_2$、$C(O)NH_2$、$C(O)NHR^{10}$、$C(O)N(R^{10})_2$、$C(O)NHOH$、$C(O)NHOR^{10}$、$C(O)NHSO_2R^{10}$、$C(O)NR^{10}SO_2R^{10}$、SO_2NH_2、SO_2NHR^{10}、$SO_2N(R^{10})_2$、$C(O)H$、$C(O)OH$、$C(N)NH_2$、$C(N)NHR^{10}$、$C(N)N(R^{10})_2$、CNOH、$CNOCH_3$、OH、CN、N_3、NO_2、F、Cl、Br 和 I；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其

中 R^{10} 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、$S(O)R^{11}$、SO_2R^{11}、$C(O)R^{11}$、$CO(O)R^{11}$、$OC(O)R^{11}$、$OC(O)OR^{11}$、NH_2、NHR^{11}、$N(R^{11})_2$、$NHC(O)R^{11}$、$NR^{11}C(O)R^{11}$、$NHS(O)_2R^{11}$、$NR^{11}S(O)_2R^{11}$、$NHC(O)OR^{11}$、$NR^{11}C(O)OR^{11}$、$NHC(O)NH_2$、$NHC(O)NHR^{11}$、$NHC(O)N(R^{11})_2$、$NR^{11}C(O)NHR^{11}$、$NR^{11}C(O)N(R^{11})_2$、$C(O)NH_2$、$C(O)NHR^{11}$、$C(O)N(R^{11})_2$、$C(O)NHOH$、$C(O)NHOR^{11}$、$C(O)NHSO_2R^{11}$、$C(O)NR^{11}SO_2R^{11}$、SO_2NH_2、SO_2NHR^{11}、$SO_2N(R^{11})_2$、$C(O)H$、$C(O)OH$、$C(N)NH_2$、$C(N)NHR^{11}$、$C(N)N(R^{11})_2$、$CNOH$、$CNOCH_3$、OH、(O)、CN、N_3、NO_2、F、Cl、Br 和 I；其中 R^{10} 中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、SR^{12}、$S(O)R^{12}$、SO_2R^{12}、$C(O)R^{12}$、$CO(O)R^{12}$、$OC(O)R^{12}$、$OC(O)OR^{12}$、NH_2、NHR^{12}、$N(R^{12})_2$、$NHC(O)R^{12}$、$NR^{12}C(O)R^{12}$、$NHS(O)_2R^{12}$、$NR^{12}S(O)_2R^{12}$、$NHC(O)OR^{12}$、$NR^{12}C(O)OR^{12}$、$NHC(O)NH_2$、$NHC(O)NHR^{12}$、$NHC(O)N(R^{12})_2$、$NR^{12}C(O)NHR^{12}$、$NR^{12}C(O)N(R^{12})_2$、$C(O)NH_2$、$C(O)NHR^{12}$、$C(O)N(R^{12})_2$、$C(O)NHOH$、$C(O)NHOR^{12}$、$C(O)NHSO_2R^{12}$、$C(O)NR^{12}SO_2R^{12}$、SO_2NH_2、SO_2NHR^{12}、$SO_2N(R^{12})_2$、$C(O)H$、$C(O)OH$、$C(N)NH_2$、$C(N)NHR^{12}$、$C(N)N(R^{12})_2$、$CNOH$、$CNOCH_3$、OH、CN、N_3、NO_2、CF_3、OCF_3、F、Cl、Br 和 I；

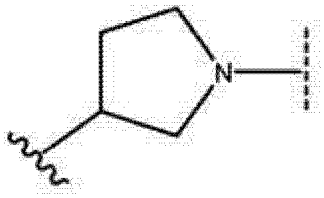
R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11} 中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11} 中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

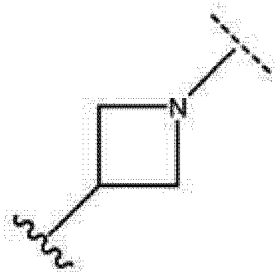
条件是

当 X^1为 CR^1且 X^2为 CR^1时；R^1为氢；Y^1为 NHC(O)；Z^1为



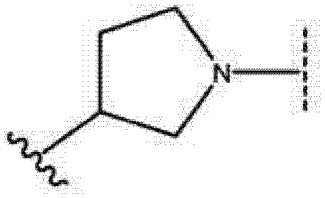
；且 R^2为吡咯基；所述 R^2 中的吡咯基未被两个烷基取代。

2. 权利要求 1 的化合物，或其治疗上可接受的盐，其中 Z^1为



；其中  表示连接至 Y^1的点且  表示连接至含氮杂芳基的点。

3. 权利要求 1 的化合物，或其治疗上可接受的盐，其中 Z^1为



；其中 表示连接至 Y^1 的点且 表示连接至含氮杂芳基的点。

4. 权利要求 2 的化合物，或其治疗上可接受的盐，其中 Y^1 为 C(O)NH。

5. 权利要求 3 的化合物，或其治疗上可接受的盐，其中 Y^1 为 C(O)NH。

6. 权利要求 4 的化合物，或其治疗上可接受的盐，其中 X^1 为 N 且 X^2 为 CR^1。

7. 权利要求 5 的化合物，或其治疗上可接受的盐，其中 X^1 为 N 且 X^2 为 CR^1。

8. 权利要求 6 的化合物，或其治疗上可接受的盐，其中 R^2 为苯基；其中 R^2 中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和 SO_2R^4。

9. 权利要求 7 的化合物，或其治疗上可接受的盐，其中 R^2 为苯基；其中 R^2 中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和 SO_2R^4。

10. 权利要求 8 的化合物，或其治疗上可接受的盐，其中 R^1 在每次出现时为氢。

11. 权利要求 9 的化合物，或其治疗上可接受的盐，其中 R^1 在每次出现时为氢。

12. 权利要求 10 的化合物，或其治疗上可接受的盐，其中 R^4 在每次出现时为杂环基。

13. 权利要求 11 的化合物，或其治疗上可接受的盐，其中 R^4 在每次出现时为杂环基。

14. 权利要求 1 的化合物，其选自

1-(吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(2-氰基吡啶-3-基)-N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-[2-(三氟甲基)吡啶-3-基]氮杂环丁烷-3-甲酰胺；

1-(2-甲基吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(4-甲基吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(4-氟吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-[4-(三氟甲基)吡啶-3-基]氮杂环丁烷-3-甲酰胺；

叔丁基 4-[4-({[(3S)-1-(吡啶-3-基)吡咯烷-3-基]羰基}氨基)苯氧基]哌啶-1-甲酸酯；

叔丁基 4-[4-({[(3R)-1-(吡啶-3-基)吡咯烷-3-基]羰基}氨基)苯氧基]哌啶-1-甲酸酯；

1-(吡啶-3-基)-N-(4-{1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

(3S)-1-(吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)吡咯烷-3-甲酰胺;

(3S)-1-(吡啶-3-基)-N-[4-({1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}氧基)苯基]吡咯烷-3-甲酰胺;

(3S)-1-(吡啶-3-基)-N-[4-({1-[(2R)-四氢呋喃-2-基羰基]哌啶-4-基}氧基)苯基]吡咯烷-3-甲酰胺;

(3S)-1-(吡啶-3-基)-N-(4-{[1-(四氢呋喃-3-基羰基)哌啶-4-基]氧基}苯基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[1-(环丙基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)吡咯烷-3-甲酰胺;

(3S)-1-(吡啶-3-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)吡咯烷-3-甲酰胺;

(3S)-N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)吡咯烷-3-甲酰胺;

N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-[1-(吡啶-3-基)氮杂环丁烷-3-基]-4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯甲酰胺;

N-(4-{1-[(2S)-2-甲基丁酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)-N-[1-(吡啶-3-基)氮杂环丁烷-3-基]苯甲酰胺;

4-{[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]氧基}-N-[1-(吡啶-3-基)氮杂环丁烷-3-基]苯甲酰胺;

1-(吡啶-3-基)-N-{4-[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

叔丁基 4-(4-{[(3S)-1-(吡啶-3-基)吡咯烷-3-基]氨基甲酰基}苯氧基)哌啶-1-甲酸酯;

叔丁基 4-(4-{[(3R)-1-(吡啶-3-基)吡咯烷-3-基]氨基甲酰基}苯氧基)哌啶-1-甲酸酯;

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-[4-({1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺；

N-{4-[(1-戊酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2-甲基环丙基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(1S,4R)-双环[2.2.1]庚-2-基乙酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-甲基戊酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基戊酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-乙氧基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,2-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3,3-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-丁酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(乙氧基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(N-乙酰基-L-亮氨酰)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环己基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环己基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁

烷 -3- 甲酰胺；

1-(吡啶 -3- 基)-N-(4-{[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(环戊基羰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基环己基) 羰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(呋喃 -3- 基羰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(吡啶 -3- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 乙酰基哌啶 -4- 基) 氧基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(甲氧基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(吡啶 -3- 基)-N-(4-{[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(吗啉 -4- 基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(吡啶 -3- 基)-N-(4-{[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(5- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(呋喃 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基 -1H- 吡咯 -2- 基) 羰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 丙酰基哌啶 -4- 基) 氧基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(N,N- 二甲基 -β- 丙氨酰) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(吡啶 -3- 基)-N-(4-{[1-(1,3- 噻唑 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(环戊基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,3-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(4-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(2-甲氧基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环丙基甲基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基戊基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基丙基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基丁基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-乙基丁基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,2-二甲基丙基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基丁基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-丙基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-环丙基乙基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-(4-{[1-(四氢呋喃-3-基甲基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,2-二甲基丁基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环己基甲基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,3-二甲基丁基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环戊基甲基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丁基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2- 甲基戊基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丁基哌啶 -4- 基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 乙基丁基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基丁基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基丙基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丙基哌啶 -4- 基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(4- 甲氧基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(4- 氰基吡啶 -3- 基)-N-{4-[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 戊酰基哌啶 -4- 基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1S,4R)- 双环 [2.2.1] 庚 -2- 基乙酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(吗啉 -4- 基乙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(呋喃 -3- 基羰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(吡啶 -3- 基)-N-{4-[1-(吡咯烷 -1- 基乙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(5- 氧代 -D- 脯氨酰) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(N,N- 二甲基 -β- 丙氨酰) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(吡啶 -3- 基)-N-{4-[1-(1,3- 噻唑 -2- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

1-(吡啶 -3- 基)-N-{4-[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(3- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(吡啶 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(4- 甲基哌嗪 -1- 基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(5- 氧代 -L- 脯氨酰) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 乙氧基丙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 甲基环己基) 羰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 乙酰基哌啶 -4- 基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环己基乙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(N- 乙酰基 -L- 亮氨酰) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丙酰基哌啶 -4- 基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(吡啶 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 甲氧基乙氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[3-(吗啉 -4- 基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(5- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(吡啶 -3- 基)-N-{4-[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 甲基 -1H- 吡咯 -2- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(呋喃 -2- 基羰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[3-(哌啶 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(乙氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲

酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁酰基哌啶 -4- 基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（甲氧基乙酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环己基羰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基丁酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环戊基羰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（环戊基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）吡咯烷 -3- 甲酰胺；

N-(4-{1-[(2S)-2- 甲基丁酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环戊基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-{4-[1-（四氢 -2H- 吡喃 -4- 基乙酰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-{4-[1-（四氢 -2H- 吡喃 -4- 基羰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基丙基）-1H- 吡唑 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁

烷 -3- 甲酰胺；

N-{4-[1-(3- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基）-N-(4-{1-[4-（三氟甲基）苯甲酰基］哌啶 -4- 基} 苯基）氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基）-N-{4-[1-（哒嗪 -3- 基羰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基）-N-[4-(1- 戊酰基哌啶 -4- 基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基戊酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1S,4R)- 双环 [2.2.1] 庚 -2- 基乙酰基］哌啶 -4- 基} 苯基）-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环戊基乙酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 甲基环丙基）羰基］哌啶 -4- 基} 苯基）-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基）-N-{4-[1-（吗啉 -4- 基乙酰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（呋喃 -3- 基羰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基）-N-{4-[1-（吡咯烷 -1- 基乙酰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基）-N-{4-[1-(5- 氧代 -D- 脯氨酰）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N,N- 二甲基 -β- 丙氨酰）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基）-N-{4-[1-（噻吩 -3- 基羰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环丙基）羰基］哌啶 -4- 基} 苯基）-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(3- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(4- 甲基哌嗪 -1- 基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(5- 氧代 -L- 脯氨酰) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 乙氧基丙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 甲基环己基) 羰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 乙酰基哌啶 -4- 基) 苯基]-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环己基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(N- 乙酰基 -L- 亮氨酰) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-[4-(1- 丙酰基哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 甲氧基乙氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[3-(吗啉 -4- 基) 丙酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(5- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(1- 甲基 -1H- 吡咯 -2- 基) 羰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(呋喃 -2- 基羰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[3-(哌啶 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基) 氮

杂环丁烷 -3- 甲酰胺；

N-{4-[1-(乙氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁酰基哌啶 -4- 基) 苯基]-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(甲氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环己基羰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氟苯甲酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[二氟 (苯基) 乙酰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4,4- 二氟环己基) 羰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4- 氟苯基) 乙酰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-[4-({1-[4-(三氟甲基) 苯甲酰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 苯甲酰基氮杂环丁烷 -3- 基) 氧基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 羟基 -2- 甲基丙酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[1-(四氢呋喃 -3- 基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(呋喃 -3- 基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1-戊酰基氮杂环丁烷-3-基)氧基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(1,3-噻唑-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[二氟(苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(4,4-二氟环己基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲基-2-苯基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(1,3-噻唑-4-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[(1-{[4-(三氟甲基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(四氢呋喃-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-({1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(噻吩-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-({1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(四氢呋喃-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(3-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2,4-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环

丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4- 氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基乙酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,4- 二氟苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-[4-({1-[4-（三氟甲氧基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2,4- 二氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-[4-({1-[4-（三氟甲基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-{4-[(1-{[4-（三氟甲氧基）苯基］乙酰基｝哌啶 -4- 基）氧基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-{4-[(1-{[3-（三氟甲基）苯基］乙酰基｝哌啶 -4- 基）氧基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-（吡啶 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 乙酰基哌啶 -4- 基）氧基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氯苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（甲氧基乙酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丁酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-3-基)-N-(4-{[1-(噻吩-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环丙基羰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3,3-二甲基丁酰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环己基羰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)氮杂环丁烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(2-甲基环丙基)羰基]氮杂环丁烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(3,3,3-三氟丙酰基)氮杂环丁烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环戊基羰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3,3-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环丁基羰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(四氢呋喃-2-基羰基)氮杂环丁烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-甲基戊酰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲基丙酰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(2S)-2-甲基丁酰基]氮杂环丁烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(甲氧基乙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)氮杂环

丁烷 -3- 甲酰胺；

N-[4-({1-[二氟（苯基）乙酰基] 哌啶 -4- 基 } 氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4,4- 二氟环己基）羰基] 哌啶 -4- 基 } 氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基）哌啶 -4- 基] 氧基 } 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基)-N-(4-{[1-(1,3- 噻唑 -4- 基羰基）哌啶 -4- 基] 氧基 } 苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基)-N-{4-[(1-{[4-（三氟甲基）苯基] 乙酰基 } 哌啶 -4- 基）氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,4- 二氟苯甲酰基）哌啶 -4- 基] 氧基 } 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基)-N-{4-[(1-{[4-（三氟甲氧基）苯基] 乙酰基 } 哌啶 -4- 基）氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4- 氟苯基）乙酰基] 哌啶 -4- 基 } 氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2,4- 二氟苯基）乙酰基] 哌啶 -4- 基 } 氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基)-N-(4-{[1-（噻吩 -3- 基羰基）哌啶 -4- 基] 氧基 } 苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氯苯甲酰基）哌啶 -4- 基] 氧基 } 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基] 氧基 } 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基 -2- 苯基丙酰基）哌啶 -4- 基] 氧基 } 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 乙酰基哌啶 -4- 基）氧基] 苯基 }-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基)-N-(4-{[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基] 氧基 } 苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基] 氧基 } 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基)-N-[4-({1-[3-（三氟甲基）苯甲酰基] 哌啶 -4- 基 } 氧基）苯基] 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氟苯甲酰基）哌啶 -4- 基] 氧基 } 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基)-N-[4-({1-[4-（三氟甲基）苯甲酰基] 哌啶 -4- 基 } 氧基）苯基] 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-[4-({1-[4-(三氟甲氧基) 苯甲酰基] 哌啶 -4- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(3,5- 二氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-[4-({1-[3-(三氟甲氧基) 苯甲酰基] 哌啶 -4- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环丙基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 氯苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[1-(吡啶 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(4- 氯苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[1-(四氢呋喃 -3- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环丙基羰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[1-(四氢呋喃 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(5- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-{4-[(1-{[3-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2S)-2- 甲基丁酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂

环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

5-[1-(2- 甲基丙基）-1H- 吡唑 -4- 基］-N-[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］呋喃 -2- 甲酰胺；

(3S)-N-{4-[1-(2- 甲基丙酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-（哒嗪 -3- 基）-N-{4-[1-（四氢 -2H- 吡喃 -4- 基乙酰基）哌啶 -4- 基］苯基｝吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

叔丁基 4-(4-{[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］氨基甲酰基｝苯基）哌啶 -1- 甲酸酯；

5-[1-(2- 甲基丙基）-1H- 吡唑 -4- 基］-N-[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］噻吩 -2- 甲酰胺；

N-[4-(1- 乙酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 戊酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基丁酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基丁酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 己酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基戊酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基戊酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 甲基戊酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丁酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,3- 二甲基丁酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 乙基丁酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 庚酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(丁-3-烯酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(戊-4-烯酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(甲基巯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-硝基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[3-(甲基巯基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(戊-4-炔酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环己基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环己基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(4-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(4-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲

酰胺；

N-{4-[1-(2-氯苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氯苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氰基苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氰基苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲基）苯甲酰基]哌啶-4-基}苯基）氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{1-[4-(三氟甲基）苯甲酰基]哌啶-4-基}苯基）氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲氧基）苯甲酰基]哌啶-4-基}苯基）氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,3-二甲基苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,4-二甲基苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,5-二甲基苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,4-二甲基苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,5-二甲基苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,4-二氯苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,5-二氯苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,4-二氯苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,5-二氯苯甲酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2-氟苯基）乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(3-氟苯基）乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(4-氟苯基）乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基）氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2- 氯苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 氯苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-(1-{[4-（三氟甲基）苯基］乙酰基｝哌啶 -4- 基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,5- 二甲基苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,5- 二氟苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,4- 二氯苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（呋喃 -3- 基羰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[1-（噻吩 -2- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(5- 甲基吡嗪 -2- 基）羰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环丙基）羰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 乙氧基丙酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 苯基环丙基）羰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{1-[（嘧啶 -2- 基巯基）乙酰基］哌啶 -4- 基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 乙酰基哌啶 -4- 基）羰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N- 乙酰基 -L- 亮氨酰）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（二苯基乙酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(5- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁

烷 -3- 甲酰胺；

N-{4-[1-(3- 氟 -4- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,3- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[4-（丙烷 -2- 基）苯甲酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 叔丁基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[2- 氟 -5-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[2- 氯 -5-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(4- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环戊基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基苯氧基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2S)-2- 苯基丁酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-(1-{[3-（三氟甲基）苯基］乙酰基｝哌啶 -4- 基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3- 氯苯基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,4- 二氯苯基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（萘 -1- 基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2R)-2- 甲氧基 -2- 苯基乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[N-(呋喃-2-基羰基)甘氨酰]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(苄基氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(萘-1-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[1-(N-苯甲酰基甘氨酰)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{1-[4-(噻吩-2-基)丁酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环丁基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-{N-[(4-甲基苯基)磺酰基]甘氨酰}哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2,3-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2S)-2-甲氧基-2-苯基乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(萘-2-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-苯基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2,6-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[3-(苯基磺酰基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2,5-二甲基呋喃-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环丙基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲

酰胺；

N-{4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[1-(1,3- 噻唑 -4- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[1-(1,3- 噻唑 -5- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（乙氧基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[1-(4,4,4- 三氟丁酰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(6- 甲基吡啶 -3- 基）羰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（呋喃 -2- 基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环己基）羰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氧代丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环戊基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丙酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氯苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-(1,3- 噻唑 -2- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-（环丙基乙酰基）吡咯烷 -3- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2S)-2- 甲基丁酰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-（四氢 -2H- 吡喃 -4- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-{[4-（三氟甲氧基）苯基］乙酰基｝吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(噻吩-3-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(4-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(3,5-二氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(3,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(3-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-({(3R)-1-[3-(三氟甲基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(2,4-二氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-{[4-(三氟甲基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(1,3-噻唑-4-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(四氢呋喃-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(5-甲基噻吩-2-基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(2-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(环丙基羰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(四氢呋喃-3-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-({(3R)-1-[3-(三氟甲氧基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(吡啶-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(3-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(4-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(2-甲基-2-苯基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(2,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)

氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(甲氧基乙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-(噻吩 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-{[3-(三氟甲基) 苯基] 乙酰基 } 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丁酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3,5- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-[4-({(3R)-1-[4-(三氟甲基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-[4-({(3R)-1-[4-(三氟甲氧基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 甲基丁酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-(3,3,3- 三氟丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[二氟 (苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(4,4- 二氟环己基) 羰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氯苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(1,3- 噻唑 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(环丙基乙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2S)-2- 甲基丁酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-3-基)-N-(4-{[(3R)-1-(四氢-2H-吡喃-4-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-{[4-(三氟甲氧基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(4-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-(噻吩-3-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(4-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(3,5-二氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(3,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(3-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-({(3R)-1-[3-(三氟甲基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(2,4-二氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-{[4-(三氟甲基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-(1,3-噻唑-4-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-(四氢呋喃-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(5-甲基噻吩-2-基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(2-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(环丙基羰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-(四氢呋喃-3-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-({(3R)-1-[3-(三氟甲氧基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-(吡啶-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(3-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮

杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(4- 氯苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基 -2- 苯基丙酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(甲氧基乙酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(噻吩 -2- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-{[3-(三氟甲基）苯基］乙酰基｝吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基丙酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丁酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3,5- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-[4-({(3R)-1-[4-(三氟甲基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-[4-({(3R)-1-[4-(三氟甲氧基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 甲基丁酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(3,3,3- 三氟丙酰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[二氟（苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丙酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(4,4- 二氟环己基）羰基］吡咯烷 -3- 基｝氧基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(1,3-噻唑-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环丙基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(4-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(3,5-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3,4-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(3-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2,4-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(1,3-噻唑-4-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(四氢呋喃-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(吡啶-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲

酰胺；

N-{4-[1-(2- 甲基 -2- 苯基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（甲氧基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-{4-[1-（噻吩 -2- 基羰基）哌啶 -4- 基］苯基}氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-(1-{[3-（三氟甲基）苯基］乙酰基}哌啶 -4- 基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{1-[4-（三氟甲基）苯甲酰基］哌啶 -4- 基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{1-[4-（三氟甲氧基）苯甲酰基］哌啶 -4- 基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基丁酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-{4-[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[二氟（苯基）乙酰基］哌啶 -4- 基} 苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4,4- 二氟环己基）羰基］哌啶 -4- 基} 苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-(1-{[4-（三氟甲氧基）苯基］乙酰基} 哌啶 -4- 基）苯基］氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{1-[3-（三氟甲氧基）苯甲酰基］哌啶 -4- 基} 苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-(1-{[4-（三氟甲基）苯基］乙酰基} 哌啶 -4- 基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氯苯甲酰基）哌啶 -4- 基］磺酰基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4-叔丁基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-甲氧基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环己基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环丙基乙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲氧基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2S)-2-苯基丁酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[4-(丙烷-2-基)苯甲酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-苯甲酰基哌啶-4-基)磺酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{[1-(4,4,4-三氟丁酰基)哌啶-4-基]磺酰基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,5-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(4-氟苯基)乙酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,3-二甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(3-氟苯基)乙酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-[4-({1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}磺酰基)苯基]

氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-[4-({1-[4-（三氟甲基）苯甲酰基］哌啶 -4- 基｝磺酰基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,3- 二氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氯苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（萘 -1- 基羰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基羰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲氧基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环戊基羰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（苯基乙酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 苯基环丙基）羰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基丙氨酰）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-（吡啶 -3- 基）吡咯烷 -3- 基］噻吩 -2- 甲酰胺；

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -4- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(哒嗪 -4- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

叔丁基 4-(2- 甲基 -1- 氧代 -1-{4-[4-({[1-(吡啶 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基] 哌啶 -1- 基 } 丙烷 -2- 基) 哌嗪 -1- 甲酸酯 ;

N-(4-{1-[2- 甲基 -2-(哌嗪 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 氯苯甲酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(4- 甲基戊酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2- 氟苯基) 乙酰基] 哌啶 -4- 基 } 磺酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 苯甲酰基哌啶 -4- 基) 磺酰基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环戊基羰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[(3R)-1-(5,6- 二氯哒嗪 -4- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -2- 甲酰胺 ;

N-[(3R)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -2- 甲酰胺 ;

N-[(3S)-1-(5,6- 二氯哒嗪 -4- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -2- 甲酰胺 ;

N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -2- 甲酰胺 ;

N-[(3R)-1-(5,6- 二氯哒嗪 -4- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -3- 甲酰胺 ;

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻

吩 -3- 甲酰胺；

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -4- 基) 吡咯烷 -3- 基] 噻吩 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 哌啶 -4- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 哌啶 -4- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 哌啶 -4- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 哌啶 -4- 甲酰胺；

N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(1,3- 噻唑 -5- 基羰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2S)-2- 苯基丁酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2S)-2- 甲氧基 -2- 苯基乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2R)-2- 甲氧基 -2- 苯基乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(乙氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(4- 甲基苯氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(四氢呋喃 -3- 基羰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(萘 -1- 基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2,6- 二氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(萘 -1- 基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-(4-{1-[4-(噻吩 -2- 基) 丁酰基] 哌啶 -4- 基 } 苯基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环丙基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(2,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(萘-2-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{1-[3-(苯基磺酰基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-1-(哒嗪-3-基)-N-[4-(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(呋喃-2-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(N-苯甲酰基甘氨酰)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{1-[(2,4-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-1-(哒嗪-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺;

(3S)-N-(4-{1-[(1-甲基环己基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-1-(哒嗪-3-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺;

(3S)-N-(4-{1-[(6-甲基吡啶-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{1-[(3-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(3,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(环戊基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 氟 -5- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(5- 氟吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(2- 氟 -6- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(4- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,4- 二甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 庚酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,4- 二氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(4- 氟苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,3- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 己酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(3- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 丁酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(3,5- 二甲基苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3,5- 二氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3- 氟 -2- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(4- 氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(呋喃 -3- 基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3,4- 二甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[2- 氯 -5-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 乙酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3,5- 二甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3- 乙氧基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,5- 二氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,5- 二甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(5- 氟 -2- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(二苯基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-1-(哒嗪 -3- 基)-N-(4-{1-[4-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(戊 -4- 烯酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-1-(哒嗪 -3- 基)-N-(4-{1-[3-(三氟甲氧基) 苯甲酰基] 哌啶 -4- 基 } 苯基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(1- 苯基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[2- 氟 -5-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(环己基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(4- 甲氧基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 乙基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(4- 叔丁基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(2- 氟苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-1-(哒嗪 -3- 基)-N-(4-{1-[3-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(戊 -4- 炔酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(3- 氟苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[3-(甲基巯基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(1- 乙酰基哌啶 -4- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(丁 -3- 烯酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3- 氟 -4- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3- 甲氧基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(2- 氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(2- 甲氧基乙氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(N- 乙酰基 -L- 亮氨酰) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯

烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 氰基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 甲氧基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,3- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[4-（丙烷 -2- 基）苯甲酰基］哌啶 -4- 基} 苯基）-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（环己基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-（哒嗪 -3- 基）-N-{4-[1-（噻吩 -2- 基羰基）哌啶 -4- 基］苯基} 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 羟基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氰基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-（哒嗪 -3- 基）-N-{4-[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基］苯基} 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（甲氧基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 甲基丁酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-(2- 氰基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-(4- 氰基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-(6- 氟 -4- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-(5- 氰基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-(5- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

2-[1-(2- 甲基丙基）-1H- 吡唑 -4- 基］-N-[(3S)-1-（哒嗪 -3- 基）吡咯烷 -3- 基］-1,3- 噻唑 -5- 甲酰胺；

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-(2- 甲基吡啶 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺 ;

N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 呋喃 -2- 甲酰胺 ;

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 呋喃 -2- 甲酰胺 ;

N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯甲酰胺 ;

N-(4-{1-[2-(哌嗪 -1- 基) 乙基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

4-[1-(2- 甲基丙酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 苯甲酰胺 ;

N-{4-[1-(2- 羟基 -2- 甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

5-[1-(3- 氟苯甲酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(4- 氟苯甲酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

(3S)-N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 羟基 -2- 甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(四氢 -2H- 吡喃 -4- 基羰基) 哌啶 -4- 基] 噻吩 -2- 甲酰胺 ;

(3S)-N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

5-[1-(2- 甲基丙酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-{1-[(2- 甲基环丙基) 羰基] 哌啶 -4- 基 }-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(2- 氟苯甲酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻

吩 -2- 甲酰胺；

5-(1- 苯甲酰基哌啶 -4- 基)-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(四氢呋喃 -3- 基羰基) 哌啶 -4- 基] 噻吩 -2- 甲酰胺；

N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基]-5-{1-[(2R)- 四氢呋喃 -2- 基羰基] 哌啶 -4- 基 } 噻吩 -2- 甲酰胺；

5-{1-[(1- 甲基哌啶 -4- 基) 乙酰基] 哌啶 -4- 基 }-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(1,3- 噻唑 -4- 基羰基) 哌啶 -4- 基] 噻吩 -2- 甲酰胺；

(3S)-N-{4-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(丙烷 -2- 基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环丙基甲基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(四氢 -2H- 吡喃 -2- 基甲基)-1H- 吡唑 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 叔丁基 -1H- 吡唑 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1- 苯甲酰基吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(2- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(3- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(4- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(3,5- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(2- 甲基苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(2,2- 二甲基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-[4-({(3R)-1-[(4,4- 二氟环己基) 羰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(4,4,4- 三氟丁酰基) 吡咯烷 -3- 基] 氧基 } 苯基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

N-[4-(5- 丙基 -1,2,4- 氧杂二唑 -3- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 氟苯甲酰基) 氮杂环丁烷 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3- 氟苯甲酰基) 氮杂环丁烷 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(4- 氟苯甲酰基) 氮杂环丁烷 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 苯甲酰基氮杂环丁烷 -3- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,2- 二甲基丙酰基) 氮杂环丁烷 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3,5- 二氟苯甲酰基) 氮杂环丁烷 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 甲基苯甲酰基) 氮杂环丁烷 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,4- 二氟苯甲酰基) 氮杂环丁烷 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3R)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3R)-N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3R)-N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[1-(环己基羰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[(1- 苯甲酰基哌啶 -4- 基) 氧基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-({1-[(2- 甲基环丙基) 羰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

N-{4-[5-(2,2-二甲基丙基)-1,3,4-氧杂二唑-2-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙基)-1H-咪唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(3-环丙基-1-甲基-1H-吡唑-5-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[5-(2,2-二甲基丙基)-1,2,4-氧杂二唑-3-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[3-环丙基-1-(2-甲氧基乙基)-1H-吡唑-5-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

叔丁基4-(5-{[1-(哒嗪-3-基)氮杂环丁烷-3-基]氨基甲酰基}噻吩-2-基)哌啶-1-甲酸酯；

叔丁基4-氟-4-[4-({[1-(哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]哌啶-1-甲酸酯；

5-(1-苯甲酰基哌啶-4-基)-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

5-[1-(2-氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

5-[1-(2-甲基苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

5-[1-(2,4-二氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

5-[1-(3-氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

5-[1-(4-氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

5-[1-(3,5-二氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

N-{4-[3-环丙基-1-(2-羟基乙基)-1H-吡唑-5-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(6-氟哒嗪-3-基)-N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-乙基丁酰基)哌啶-4-基]苯基}-1-(6-氟哒嗪-3-基)氮杂环丁

烷 -3- 甲酰胺；

N-{4-[1-(4- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(6- 氟哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

(3S)-N-(4-{[(3S)-1- 苯甲酰基吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3S)-1-(2- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3S)-1-(3,5- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3S)-1-(2,2- 二甲基丙酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基)-2- 氟苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(3- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(2- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(4- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基]-2- 氟苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基]-2- 氟苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基]-2- 氟苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-(6- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[(1- 苯甲酰基哌啶 -4- 基）氧基］苯基}-1-(6- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］氧基｝苯基)-1-(6- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(环己基羰基）哌啶 -4- 基］氧基｝苯基)-1-(6- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

N-{4-[8-(2- 甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[8-(4,4,4- 三氟丁酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-[4-(8- 苯甲酰基 -8- 氮杂双环 [3.2.1] 辛 -3- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[8-(2- 氟苯甲酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[8-(2,2- 二甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{8-[(1- 甲基环丙基) 羰基]-8- 氮杂双环 [3.2.1] 辛 -3- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲氧基乙基)-3-(2- 甲基丙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

5-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 }-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺 ;

N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基]-5-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺 ;

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基]-4- 氟哌啶 -1- 甲酸酯 ;

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基]-4- 羟基哌啶 -1- 甲酸酯 ;

N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基]-5-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(环丙基羰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺 ;

N-{4-[4- 氟 -1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环丙基羰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(2- 氟 -4-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂

环丁烷 -3- 甲酰胺；

N-{4-[1-(环丙基乙酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基 -4- 氟哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基)-4- 氟哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[3- 叔丁基 -1-(2- 甲氧基乙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁基 -3- 叔丁基 -1H- 吡唑 -5- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[3- 叔丁基 -1-(四氢 -2H- 吡喃 -4- 基甲基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基)-2- 氟苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1- 甲基 -3-(三氟甲基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(6- 氯哒嗪 -3- 基)-N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{3- 氟 -4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{3- 氟 -4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{3- 氟 -4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-3- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基)-3- 氟苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基]-3- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环丙基乙酰基) 哌啶 -4- 基]-3- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 氟苯甲酰基)-4- 羟基哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基)-4- 羟基哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(6- 甲基哒嗪 -3- 基)-N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

N-{4-[(1- 苯甲酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 乙基丁酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环

丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基）哌啶 -4- 基］甲基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 乙酰基哌啶 -4- 基）甲基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 甲基丁酰基］哌啶 -4- 基｝甲基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基环丙基）羰基］哌啶 -4- 基｝甲基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1-{[4- 甲基 -1-（氧杂环丁烷 -3- 基）哌啶 -4- 基］甲基}-1H- 吡唑 -4- 基）苯基]-1-(6- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(4- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

5-[1-(2- 氟苯甲酰基）哌啶 -4- 基]-N-[(3S)-1-（哒嗪 -3- 基）吡咯烷 -3- 基］呋喃 -2- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(3- 甲基哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(3- 甲基哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 氨基吡啶 -3- 基）羰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1- 甲基 -5-[4-({[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］羰基｝氨基）苯基]-1H- 吡唑 -3- 甲酸；

乙基 1- 甲基 -5-[4-({[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］羰基｝氨基）苯基]-1H- 吡唑 -3- 甲酸酯；

乙基 1- 苯基 -5-[4-({[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］羰基｝氨基）苯基]-1H- 吡唑 -3- 甲酸酯；

N-{6-[1-(2- 氟苯甲酰基）哌啶 -4- 基］吡啶 -3- 基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 甲基丁酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(6- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基丙酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(6- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(6- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(6- 甲基哒嗪 -3- 基)-N-(4-{[(3R)-1-(1,3- 噻唑 -4- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-{6-[1-(4,4,4- 三氟丁酰基）哌啶 -4- 基］吡啶 -3- 基｝氮杂环丁烷 -3- 甲酰胺；

N-{6-[1-(3,3-二甲基丁酰基)哌啶-4-基]吡啶-3-基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

(3S)-N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(4-甲基哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(4-甲基哒嗪-3-基)吡咯烷-3-甲酰胺；

N-{4-[1-苯基-3-(三氟甲基)-1H-吡唑-5-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{6-[1-(2,2-二甲基丙基)-1H-吡唑-4-基]吡啶-3-基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

叔丁基4-[4-({[1-(哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)-1H-吡唑-1-基]哌啶-1-甲酸酯；

N-(6-{1-[(4-甲基哌啶-4-基)甲基]-1H-吡唑-4-基}吡啶-3-基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{[1-(1,3-噻唑-5-基羰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环戊基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(1H-吡唑-4-基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,2-二甲基丁酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2-甲基环丙基)羰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(甲基巯基)乙酰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(1S,4R)-双环[2.2.1]庚-2-基乙酰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基戊酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-甲基戊酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[3-(甲基巯基)丙酰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{[1-(1,3-噻唑-4-基羰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(1H-吡唑-5-基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(6-甲基吡啶-3-基)羰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)

氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（戊 -4- 炔酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（噻吩 -3- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（甲氧基乙酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（四氢呋喃 -2- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 甲氧基乙氧基）乙酰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（乙氧基乙酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（噻吩 -2- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 己酰基哌啶 -4- 基）甲基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基 -1H- 吡咯 -2- 基）羰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（丁 -3- 烯酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（呋喃 -2- 基羰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(1,2- 唑 -5- 基羰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（吡啶 -2- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（呋喃 -3- 基羰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基乙酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丁酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 丙酰基哌啶 -4- 基）甲基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 丁酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环丁基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 戊酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环戊基乙酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基苯甲酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 甲基戊酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环己基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 甲基丁酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环丙基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(4- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{1-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-1H- 吡唑 -4- 基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{1-[1-(2- 氟苯甲酰基) 哌啶 -4- 基]-1H- 吡唑 -4- 基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(苯基氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(2,2- 二甲基丙基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(3- 甲氧基 -2,2- 二甲基丙基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(2- 环丙基乙基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[2-(2- 乙基哌啶 -1- 基) 乙基] 氨基甲酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(环丁基甲基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(2S)- 丁烷 -2- 基氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(丁基氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(2,2-二甲基四氢-2H-吡喃-4-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(1S)-1-环丙基乙基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({2-[甲基(苯基)氨基]乙基}氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1,1'-双(环丙基)-1-基氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-[4-(噻吩-3-基氨基甲酰基)苯基]氮杂环丁烷-3-甲酰胺；

N-(4-{[(1R)-1-环丙基乙基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-甲基哌啶-4-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(2R)-丁烷-2-基氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-氮杂双环[2.2.2]辛-3-基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[(四氢呋喃-3-基甲基)氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[(氧杂环丁烷-3-基甲基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(2-甲基环丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(环丁基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-甲基环丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(2-甲氧基-2-甲基丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(环丙基甲基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{[(2R)-四氢呋喃-2-基甲基]氨基甲酰基}苯基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[(3,3,3-三氟丙基)氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[(1-甲基哌啶-3-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3-甲基氧杂环丁烷-3-基)甲基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{[(2S)-四氢呋喃-2-基甲基]氨基甲酰基}苯基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[(四氢-2H-吡喃-4-基甲基)氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-(四氢-2H-吡喃-4-基氨基甲酰基)苯基]氮杂环丁烷-3-甲酰胺;

N-(4-{[(1-甲基哌啶-3-基)甲基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(环丙基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(环戊基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(苄基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(3-氟苯基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(丙基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(4-氟苯基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(2-氟苯基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-甲基环丁基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(丙-2-烯-1-基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

5-[1-(2,2-二甲基丙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(3,3-二甲基丁酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(2,2-二甲基丁酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-{1-[(1-甲基环丙基)羰基]哌啶-4-基}-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(3,3,3-三氟丙酰基)哌啶-4-基]噻吩-2-甲酰胺;

5-[1-(环丙基乙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(双环[2.2.1]庚-2-基乙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

1-(哒嗪-3-基)-N-{4-[(3S)-四氢呋喃-3-基氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺;

N-[4-({4-[2-(二甲基氨基)乙基]苯基}氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[(3R)-四氢呋喃-3-基氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[(2-甲氧基乙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3- 氨基 -2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[2,2- 二甲基 -3-(哌嗪 -1- 基) 丙基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[2- 甲基 -2-(哌嗪 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;及其药学上可接受的盐。

15. 权利要求 1 的化合物,其选自

N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

N-[4-(1- 乙酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丁酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(甲氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(甲基巯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丙酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 丙酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 丁酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 乙酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 乙基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3R)-N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;及其药学上可接受的盐。

16.组合物,其用于治疗炎性和组织修复病症;尤其是类风湿关节炎、炎性肠病、哮喘和COPD(慢性阻塞性肺病)、骨关节炎、骨质疏松和纤维化病;皮肤病,包括银屑病、特应性皮炎和紫外线引起的皮肤损伤;自身免疫性疾病,包括全身性红斑狼疮、多发性硬化、银屑病关节炎、强直性脊柱炎、组织和器官排斥、阿尔茨海默氏病、中风、动脉粥样硬化、再狭窄、糖尿病、肾小球肾炎、癌症,特别是其中所述癌症选自乳腺癌、前列腺癌、肺癌、结肠癌、宫颈癌、卵巢癌、皮肤癌、中枢神经系统癌、膀胱癌、胰腺癌、白血病、淋巴瘤或霍奇金氏病、恶病质、与感染和某些病毒感染相关的炎症,包括获得性免疫缺陷综合征(AIDS)、成人呼吸窘迫综合征和共济失调毛细血管扩张,所述组合物包含赋形剂和治疗有效量的权利要求1的化合物、或其药学上可接受的盐。

17.治疗患者中的炎性和组织修复病症的方法;尤其是类风湿关节炎、炎性肠病、哮喘和COPD(慢性阻塞性肺病)、骨关节炎、骨质疏松和纤维化病;皮肤病,包括银屑病、特应性皮炎和紫外线引起的皮肤损伤;自身免疫性疾病,包括全身性红斑狼疮、多发性硬化、银屑病关节炎、强直性脊柱炎、组织和器官排斥、阿尔茨海默氏病、中风、动脉粥样硬化、再狭窄、糖尿病、肾小球肾炎、癌症,特别是其中所述癌症选自乳腺癌、前列腺癌、肺癌、结肠癌、宫颈癌、卵巢癌、皮肤癌、中枢神经系统癌、膀胱癌、胰腺癌、白血病、淋巴瘤或霍奇金氏病、恶病质、与感染和某些病毒感染相关的炎症,包括获得性免疫缺陷综合征(AIDS)、成人呼吸窘迫综合征、和共济失调毛细血管扩张,所述方法包括向所述患者施用治疗有效量的权利要求1的化合物、或其药学上可接受的盐。

18.治疗患者中的炎性和组织修复病症的方法;尤其是类风湿关节炎、炎性肠病、哮喘和COPD(慢性阻塞性肺病)、骨关节炎、骨质疏松和纤维化病;皮肤病,包括银屑病、特应性皮炎和紫外线引起的皮肤损伤;自身免疫性疾病,包括全身性红斑狼疮、多发性硬化、银屑病关节炎、强直性脊柱炎、组织和器官排斥、阿尔茨海默氏病、中风、动脉粥样硬化、再狭窄、糖尿病、肾小球肾炎、癌症,特别是其中所述癌症选自乳腺癌、前列腺癌、肺癌、结肠癌、宫颈癌、卵巢癌、皮肤癌、中枢神经系统癌、膀胱癌、胰腺癌、白血病、淋巴瘤或霍奇金氏病、恶病质、与感染和某些病毒感染相关的炎症,包括获得性免疫缺陷综合征(AIDS)、成人呼吸窘迫综合征、和共济失调毛细血管扩张或脾癌,所述方法包括向所述患者施用治疗有效量的权利要求1的化合物、或其药学上可接受的盐;和治疗有效量的一种额外的治疗剂或多于一种额外的治疗剂。

作为 NAMPT 抑制剂的哒嗪和吡啶衍生物

[0001] 本申请要求享有于 2012 年 5 月 11 日提交的美国临时申请序列号 61/645692、于 2012 年 10 月 26 日提交的美国临时申请序列号 61/719013、和于 2013 年 3 月 13 日提交的美国临时申请序列号 61/779756 的优先权，其以其整体通过引用并入本文。

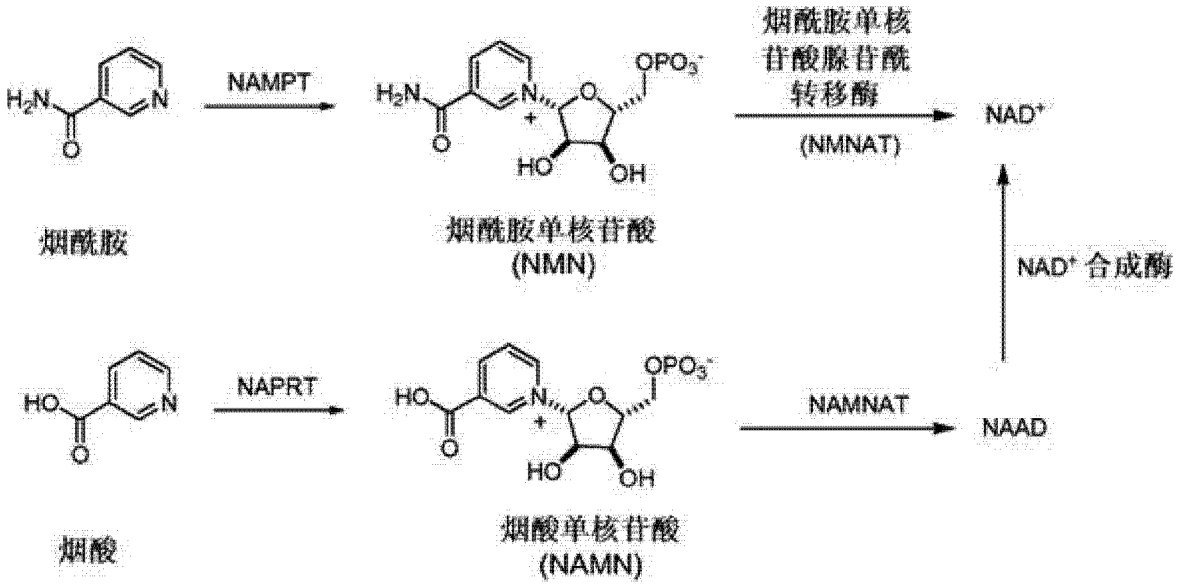
发明领域

[0002] 本发明涉及抑制 NAMPT 活性的化合物、包含所述化合物的组合物、和治疗在其过程中表达 NAMPT 的疾病的方法。

[0003] 发明背景

NAD+（烟酰胺腺嘌呤二核苷酸）是在许多生理学上重要的过程中起关键作用的辅酶 (Ziegkel, M. Eur. J. Biochem. 267, 1550-1564, 2000)。NAD 对于几种信号传递途径包括其中 DNA 修复中的多 ADP 核糖基化、在免疫系统和 G 蛋白偶联的信号传递中的单 ADP 核糖基化是必需的，并且 NAD 由于其脱乙酰基酶活性而对于沉默调节蛋白 (sirtuins) 是必需的 (Garten, A. 等人 Trends in Endocrinology and Metabolism, 20, 130-138, 2008)。

[0004] NAMPT（也称为前 B 细胞集落增强因子 (PBEF) 和内脂素 (visfatin)）是催化烟酰胺的磷酸核糖基化的酶，且是补救 NAD 的两条途径之一中的限速酶。



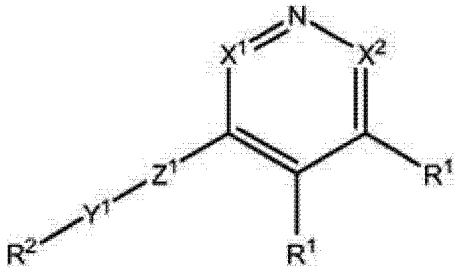
[0005] 渐增的证据表明 NAMPT 抑制剂具有作为抗癌剂的潜力。癌细胞相比于正常细胞具有更高的 NAD 周转且还展示更高的能量需要。此外，已在结肠直肠癌中报道了增加的 NAMPT 表达 (Van Beijnum, J. R. 等人 Int. J. Cancer 101, 118-127, 2002) 和 NAMPT 参与血管发生 (Kim, S. R. 等人 . Biochem. Biophys. Res. Commun. 357, 150-156, 2007)。NAMPT 的小分子抑制剂已在异种移植模型中显示引起胞内 NAD+ 水平的耗尽并最终诱导肿瘤细胞死亡 (Hansen, CM 等人 . Anticancer Res. 20, 42111-4220, 2000) 以及抑制肿瘤生长 (Olese, U. H. 等人 . Mol Cancer Ther. 9, 1609-1617, 2010)。

[0006] NAMPT 抑制剂还具有作为炎性和代谢病症中的治疗剂的潜力 (Galli, M. 等人 Cancer Res. 70, 8-11, 2010)。例如，NAMPT 为 T 淋巴细胞和 B 淋巴细胞中的优势酶。选择

性抑制 NAMPT 导致阻断膨胀（其伴随自身免疫疾病进展）的淋巴细胞中 NAD+ 耗尽，而表达其他 NAD+ 产生途径的细胞类型可能得以免除。小分子 NAMPT 抑制剂 (FK866) 已显示选择性阻断增殖并诱导活化的 T 细胞的凋亡，且在关节炎（胶原诱导的关节炎）的动物模型中是有效的 (Busso, N. 等人 .Plos One 3, e2267, 2008)。FK866 改善实验性自身免疫性脑脊髓炎 (EAE)（其为 T 细胞介导的自身免疫病症的模型）的表现 (Bruzzone, S 等人 Plos One 4, e7897, 2009)。NaMPT 活性增加人血管内皮细胞中 NF-kB 转录活性，导致 MMP-2 和 MMP-9 活化，表明 NAMPT 抑制剂在预防肥胖症和 2 型糖尿病的炎性介导的并发症中的作用 (Adya, R. 等人 Diabetes Care, 31, 758-760, 2008)。

[0007] 发明概述

因此，本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式 (IC)



式 (IC)；

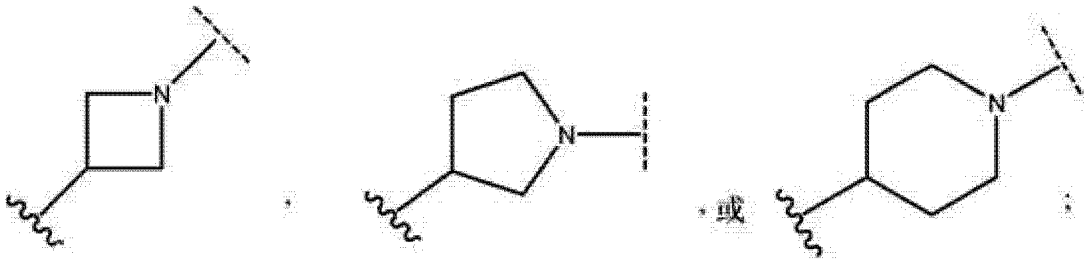
X^1 为 N 且 X^2 为 CR^1；或

X^1 为 CR^1 且 X^2 为 N；或

X^1 为 CR^1 且 X^2 为 CR^1；

Y^1 为 C(O)NH、或 NHC(O)；

Z^1 为



其中 表示连接至 Y^1 的点且 表示连接至含氮杂芳基的点；

R^1 在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I；

R^2 独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2 中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：

R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$,

$OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$,

$NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$,

$NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$,

$C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH,

$C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br

和 I;其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代:R^4, OR^4, SR^4, $S(O)R^4$,

SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$,

$NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$,

$NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH,

$C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H,

C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl,

和 I;

R^3在每次出现时独立地选自烷基、烯基、炔基、芳基、环烷基、环烯基、和杂环基;其中 R^3中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代:

R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$,

$OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$,

$NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$,

$NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, C(O)NHOH,

$C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, C(O)H,

C(O)OH, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F,

Cl, Br 和 I;其中 R^3中的芳基、环烷基、环烯基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代:

R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$,

$NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^5S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$,

$NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^5)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$,

$C(O)NHR^6$, $C(O)N(R^6)_2$, C(O)NHOH, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$,

SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$,

CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I;

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基;其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代:

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$,

$OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$,

$NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$,

$NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH,

$C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H,

C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F,

Cl, Br 和 I;

R^5在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基;其中 R^5中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代:

R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$,

$C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$,

SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), $C(O)OH$, N_3, CN, NH_2, F, Cl, Br 和 I；

R^6在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^6中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), $C(O)OH$, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br 和 I；

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^8在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^9在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中由 R^4、R^5、R^6、R^7、R^8、和 R^9表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br 和 I；

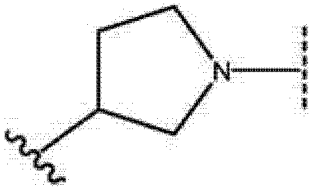
R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

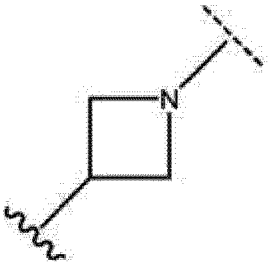
R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

条件是

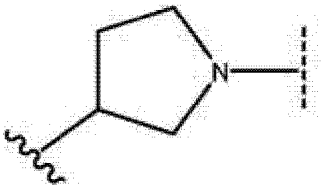
当 X^1为 CR^1且 X^2为 CR^1时；R^1为氢；Y^1为 NHC(O)；Z^1为



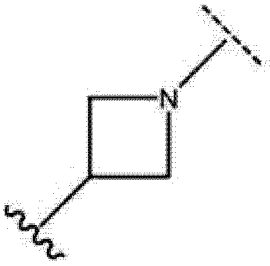
；且 R^2为吡咯基；所述 R^2中的吡咯基未被两个烷基取代。在式 (IC) 的另一个实施方案中，Z^1为



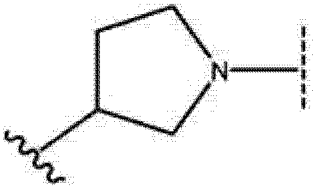
；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。在式 (IC) 的另一个实施方案中，Z^1为



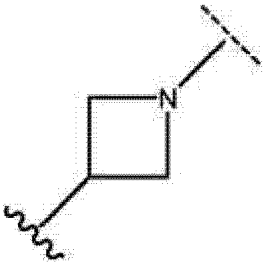
；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。在式 (IC) 的另一个实施方案中，Z^1为



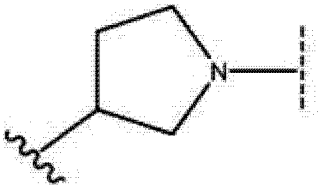
；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点；且 Y^1为 C(O)NH。在式 (IC) 的另一个实施方案中，Z^1为



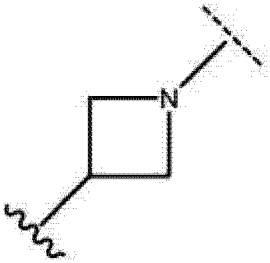
；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点；且 Y^1为 C(O)NH。在式 (IC) 的另一个实施方案中，Z^1为



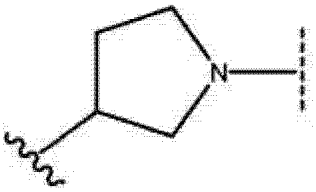
;其中 表示连接至 Y^1 的点且 表示连接至含氮杂芳基的点；Y^1 为 C(O)NH；且 X^1 为 N 且 X^2 为 CR^1。在式 (IC) 的另一个实施方案中，Z^1 为



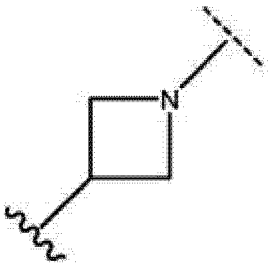
;其中 表示连接至 Y^1 的点且 表示连接至含氮杂芳基的点；Y^1 为 C(O)NH；X^1 为 N 且 X^2 为 CR^1。在式 (IC) 的另一个实施方案中，Z^1 为



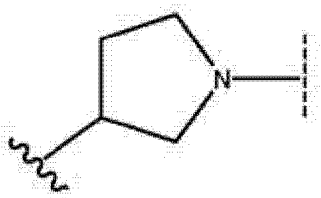
;其中 表示连接至 Y^1 的点且 表示连接至含氮杂芳基的点；Y^1 为 C(O)NH；X^1 为 N 且 X^2 为 CR^1；其中 R^2 为苯基；其中 R^2 中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和 SO_2R^4。在式 (IC) 的另一个实施方案中，Z^1 为



;其中 表示连接至 Y^1 的点且 表示连接至含氮杂芳基的点；Y^1 为 C(O)NH；X^1 为 N 且 X^2 为 CR^1；其中 R^2 为苯基；其中 R^2 中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和 SO_2R^4。在式 (IC) 的另一个实施方案中，Z^1 为

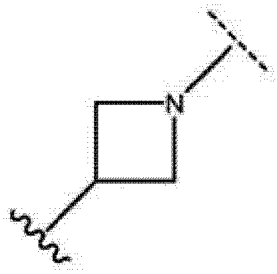


;其中 表示连接至 Y^1 的点且 表示连接至含氮杂芳基的点；Y^1 为 C(O)NH；X^1 为 N 且 X^2 为 CR^1；其中 R^2 为苯基；其中 R^2 中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和 SO_2R^4；且 R^1 在每次出现时为氢。在式 (IC) 的另一个实施方案中，Z^1 为

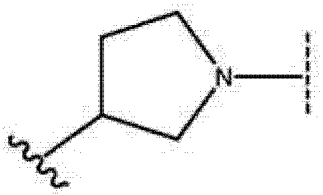


；其中 表示连接至 Y^1 的点且 表示连接至含氮杂芳

基的点；Y^1为C(O)NH；X^1为N且X^2为CR^1；其中R^2为苯基；其中R^2中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和SO_2R^4；且R^1在每次出现时为氢。在式(IC)的另一个实施方案中，Z^1为



；其中 表示连接至Y^1的点且 表示连接至含氮杂芳基的点；Y^1为C(O)NH；X^1为N且X^2为CR^1；其中R^2为苯基；其中R^2中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和SO_2R^4；R^1在每次出现时为氢；且R^4在每次出现时为杂环基。在式(IC)的另一个实施方案中，Z^1为



；其中 表示连接至Y^1的点且 表示连接至含氮杂芳基的点；Y^1为C(O)NH；X^1为N且X^2为CR^1；其中R^2为苯基；其中R^2中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和SO_2R^4；且R^1在每次出现时为氢；且R^4在每次出现时为杂环基。

[0008] 仍另一个实施方案涉及化合物，其为

1-(吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(2-氰基吡啶-3-基)-N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-[2-(三氟甲基)吡啶-3-基]氮杂环丁烷-3-甲酰胺；

1-(2-甲基吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(4-甲基吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(4-氟吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-[4-(三氟甲基)吡啶-3-基]氮杂环丁烷-3-甲酰胺；

叔丁基4-[4-({[(3S)-1-(吡啶-3-基)吡咯烷-3-基]羰基}氨基)苯氧基]哌啶-1-甲酸酯；

叔丁基4-[4-({[(3R)-1-(吡啶-3-基)吡咯烷-3-基]羰基}氨基)苯氧基]哌啶-1-甲酸酯；

1-(吡啶-3-基)-N-(4-{1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}苯基)氮杂环

丁烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 氧基 } 苯基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-[4-({1-[(2S)- 四氢呋喃 -2- 基羰基] 哌啶 -4- 基 } 氧基) 苯基] 吡咯烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-[4-({1-[(2R)- 四氢呋喃 -2- 基羰基] 哌啶 -4- 基 } 氧基) 苯基] 吡咯烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-(4-{[1-(四氢呋喃 -3- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(环丙基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 氧基 } 苯基) 吡咯烷 -3- 甲酰胺；

(3S)-N-[4-({1-[(2S)-2- 甲基丁酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[1-(吡啶 -3- 基) 氮杂环丁烷 -3- 基]-4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 氧基 } 苯甲酰胺；

N-(4-{1-[(2S)-2- 甲基丁酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

4-({1-[(2S)-2- 甲基丁酰基] 哌啶 -4- 基 } 氧基)-N-[1-(吡啶 -3- 基) 氮杂环丁烷 -3- 基] 苯甲酰胺；

4-{[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 氧基 }-N-[1-(吡啶 -3- 基) 氮杂环丁烷 -3- 基] 苯甲酰胺；

1-(吡啶 -3- 基)-N-{4-[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

叔丁基 4-(4-{[(3S)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 氨基甲酰基 } 苯氧基) 哌啶 -1- 甲酸酯；

叔丁基 4-(4-{[(3R)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 氨基甲酰基 } 苯氧基) 哌啶 -1- 甲酸酯；

N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲

酰胺；

N-(4-{[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-[4-({1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺；

N-{4-[(1-戊酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2-甲基环丙基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(1S,4R)-双环[2.2.1]庚-2-基乙酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-甲基戊酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基戊酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-乙氧基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,2-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3,3-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-丁酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(乙氧基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(N-乙酰基-L-亮氨酰)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环己基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环己基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-(4-{[1-(4,4,4-三氟丁酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环戊基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(1-甲基环己基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(呋喃-3-基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-乙酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(甲氧基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-(4-{[1-(噻吩-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(3-甲基噻吩-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(吗啉-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-(4-{[1-(噻吩-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(呋喃-2-基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(1-甲基-1H-吡咯-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-丙酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(1-甲基环丙基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(N,N-二甲基-β-丙氨酰)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-(4-{[1-(1,3-噻唑-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环戊基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁

烷 -3- 甲酰胺；

N-(4-{[1-(2,3- 二甲基丁酰基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(4- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(2- 甲氧基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(环丙基甲基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基戊基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 乙基丁基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丁基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 丙基哌啶 -4- 基）氧基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 环丙基乙基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(吡啶 -3- 基)-N-(4-{[1-(四氢呋喃 -3- 基甲基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丁基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环己基甲基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环戊基甲基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丁基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲

酰胺；

N-{4-[1-(2- 甲基戊基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁基哌啶 -4- 基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 乙基丁基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基丁基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基丙基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丙基哌啶 -4- 基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(4- 甲氧基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(4- 氰基吡啶 -3- 基）-N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 戊酰基哌啶 -4- 基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基戊酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1S,4R)- 双环 [2.2.1] 庚 -2- 基乙酰基］哌啶 -4- 基} 苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环戊基乙酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 甲基环丙基）羰基］哌啶 -4- 基} 苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（吗啉 -4- 基乙酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（呋喃 -3- 基羰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-{4-[1-（吡咯烷 -1- 基乙酰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(5- 氧代 -D- 脯氨酰）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N, N- 二甲基 -β- 丙氨酰）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-{4-[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-{4-[1-（噻吩 -3- 基羰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环丙基）羰基］哌啶 -4- 基} 苯基）-1-（吡啶 -3- 基）氮杂环丁

烷 -3- 甲酰胺；

N-(4-{1-[(3- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基哌嗪 -1- 基）乙酰基］哌啶 -4- 基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(5- 氧代 -L- 脯氨酰）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 乙氧基丙酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 甲基戊酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环己基）羰基］哌啶 -4- 基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 乙酰基哌啶 -4- 基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环己基乙酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N- 乙酰基 -L- 亮氨酰）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丙酰基哌啶 -4- 基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 甲氧基乙氧基）乙酰基］哌啶 -4- 基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[3-（吗啉 -4- 基）丙酰基］哌啶 -4- 基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基)-N-{4-[1-（噻吩 -2- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基 -1H- 吡咯 -2- 基）羰基］哌啶 -4- 基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（呋喃 -2- 基羰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[3-（哌啶 -1- 基）丙酰基］哌啶 -4- 基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(乙氧基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,2-二甲基丁酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-丁酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环己基羰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环戊基羰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

(3S)-N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)吡咯烷-3-甲酰胺;

N-(4-{1-[(2S)-2-甲基丁酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(四氢-2H-吡喃-4-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,5- 二氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[4-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(哒嗪 -3- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-[4-(1- 戊酰基哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1S,4R)- 双环 [2.2.1] 庚 -2- 基乙酰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(吗啉 -4- 基乙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(呋喃 -3- 基羰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(吡咯烷 -1- 基乙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(5- 氧代 -D- 脯氨酰) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(N,N- 二甲基 -β- 丙氨酰) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂

环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(3- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基哌嗪 -1- 基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(5- 氧代 -L- 脯氨酰) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 乙氧基丙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环己基) 羰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 乙酰基哌啶 -4- 基) 苯基]-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环己基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N- 乙酰基 -L- 亮氨酰) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-[4-(1- 丙酰基哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 甲氧基乙氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[3-(吗啉 -4- 基) 丙酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(5- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(1- 甲基 -1H- 吡咯 -2- 基) 羰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(呋喃 -2- 基羰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[3-(哌啶 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(乙氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丁酰基哌啶 -4- 基) 苯基]-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(甲氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环己基羰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(4- 氟苯甲酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,4- 二氟苯甲酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[二氟 (苯基) 乙酰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(4,4- 二氟环己基) 羰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(4- 氟苯基) 乙酰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-[4-({1-[4-(三氟甲基) 苯甲酰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 苯甲酰基氮杂环丁烷 -3- 基) 氧基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 羟基 -2- 甲基丙酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[1-(四氢呋喃 -3- 基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(呋喃 -3- 基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮

杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 戊酰基氮杂环丁烷 -3- 基）氧基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氯苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 甲基丁酰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-（四氢 -2H- 吡喃 -4- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[二氟（苯基）乙酰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4,4- 二氟环己基）羰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基 -2- 苯基丙酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-(1,3- 噻唑 -4- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-{4-[(1-{[4-（三氟甲基）苯基］乙酰基｝哌啶 -4- 基）氧基］苯基｝氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-（四氢呋喃 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-[4-({1-[3-（三氟甲基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-（噻吩 -3- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-[4-({1-[3-（三氟甲氧基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-（四氢呋喃 -3- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(4- 氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环丙基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3,4- 二氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-[4-({1-[4-(三氟甲氧基) 苯甲酰基] 哌啶 -4- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2,4- 二氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-[4-({1-[4-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[(1-{[4-(三氟甲氧基) 苯基] 乙酰基 } 哌啶 -4- 基) 氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(3,5- 二氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[(1-{[3-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(吡啶 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 乙酰基哌啶 -4- 基) 氧基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(4- 氯苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(甲氧基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2- 氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环

丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氯苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(环丙基羰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,3- 二甲基丁酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(环己基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 甲基环丙基) 羰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(环戊基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(环丁基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[1-(四氢呋喃 -2- 基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 甲基戊酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 甲基丁酰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(甲氧基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-4-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[二氟(苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(4,4-二氟环己基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(1,3-噻唑-4-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[(1-{[4-(三氟甲基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3,4-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[(1-{[4-(三氟甲氧基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(4-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(2,4-二氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(噻吩-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲基-2-苯基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-乙酰基哌啶-4-基)氧基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(1,3-噻唑-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2,4-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-({1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-({1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}氧基)苯基]

氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({1-[4-（三氟甲氧基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({1-[3-（三氟甲氧基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基乙酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氯苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（吡啶 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氯苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（四氢呋喃 -3- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丁酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基羰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（四氢呋喃 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（噻吩 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-{4-[(1-{[3-（三氟甲基）苯基］乙酰基｝哌啶 -4- 基）氧基］苯基｝氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（四氢 -2H- 吡喃 -4- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 甲基丁酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2- 氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 呋喃 -2- 甲酰胺 ;

(3S)-N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

叔丁基 4-(4-{[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 氨基甲酰基 } 苯基) 哌啶 -1- 甲酸酯 ;

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺 ;

N-[4-(1- 乙酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丁酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 戊酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 己酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 乙基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1-庚酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(丁-3-烯酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(戊-4-烯酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(甲基巯基(methylsulfanyl))乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-硝基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[3-(甲基巯基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(戊-4-炔酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环己基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环己基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(4-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,3-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,4-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,5-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3,4-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3,5-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,4-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,5-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3,4-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3,5-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(3-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(4-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁

烷 -3- 甲酰胺；

N-(4-{1-[(2- 氯苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 氯苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-[4-(1-{[4-(三氟甲基）苯基］乙酰基｝哌啶 -4- 基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,5- 二甲基苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,5- 二氟苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,4- 二氯苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(呋喃 -3- 基羰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(噻吩 -2- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(5- 甲基吡嗪 -2- 基）羰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环丙基）羰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 乙氧基丙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 苯基环丙基）羰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{1-[(嘧啶 -2- 基巯基 (ylsulfanyl)) 乙酰基］哌啶 -4- 基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 乙酰基哌啶 -4- 基）羰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N- 乙酰基 -L- 亮氨酰）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(二苯基乙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(5- 氟 -2- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 氟 -4- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,3- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[4-(丙烷 -2- 基) 苯甲酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 叔丁基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[2- 氟 -5-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[2- 氯 -5-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(4- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(4- 甲基苯氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2S)-2- 苯基丁酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-[4-(1-{[3-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(3- 氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2,4- 二氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(萘 -1- 基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2R)-2- 甲氧基 -2- 苯基乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮

杂环丁烷 -3- 甲酰胺；

N-(4-{1-[N-(呋喃 -2- 基羰基）甘氨酰］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(苄基氧基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(萘 -1- 基乙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环丙基羰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(四氢呋喃 -2- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N- 苯甲酰基甘氨酰）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(四氢呋喃 -3- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{1-[4-(噻吩 -2- 基）丁酰基］哌啶 -4- 基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,5- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环丁基羰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1-{N-[(4- 甲基苯基）磺酰基］甘氨酰｝哌啶 -4- 基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,3- 二氟苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2S)-2- 甲氧基 -2- 苯基乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(萘 -2- 基乙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 苯基丙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,6- 二氯苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[3-(苯基磺酰基）丙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(噻吩 -3- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,5- 二甲基呋喃 -3- 基）羰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环丙基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[1-(1,3-噻唑-4-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[1-(1,3-噻唑-5-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[1-(乙氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(6-甲基吡啶-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(呋喃-2-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(1-甲基环己基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-氧代丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环戊基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(4-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(2-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(1,3-噻唑-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(环丙基乙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(2S)-2-甲基丁酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(四氢-2H-吡喃-4-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-{[4-(三氟甲氧基)苯基]乙酰基}吡咯烷-3-基]

氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-（噻吩 -3- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(4- 氟苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(3,5- 二氟苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3,4- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(3- 氟苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({(3R)-1-[3-（三氟甲基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2,4- 二氟苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-{[4-（三氟甲基）苯基］乙酰基｝吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-(1,3- 噻唑 -4- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-（四氢呋喃 -2- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(5- 甲基噻吩 -2- 基）羰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2- 氟苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-（环丙基羰基）吡咯烷 -3- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-（四氢呋喃 -3- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({(3R)-1-[3-（三氟甲氧基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-（吡啶 -2- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氯苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(4- 氯苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基 -2- 苯基丙酰基）吡咯烷 -3- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(甲氧基乙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(噻吩-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-(4-{[(3R)-1-{[3-(三氟甲基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(2-甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(2-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(2,2-二甲基丁酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(3,5-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-[4-({(3R)-1-[4-(三氟甲基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(3-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-[4-({(3R)-1-[4-(三氟甲氧基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(3-甲基丁酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(3,3,3-三氟丙酰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

N-[4-({(3R)-1-[二氟(苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(2,2-二甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-[4-({(3R)-1-[(4,4-二氟环己基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(2-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{[(3R)-1-(1,3-噻唑-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(环丙基乙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({(3R)-1-[(2S)-2-甲基丁酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)

氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(四氢 -2H- 吡喃 -4- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-{[4-(三氟甲氧基) 苯基] 乙酰基 } 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(4- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(噻吩 -3- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(4- 氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(3,5- 二氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3,4- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(3- 氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-[4-({(3R)-1-[3-(三氟甲基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2,4- 二氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-{[4-(三氟甲基) 苯基] 乙酰基 } 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(1,3- 噻唑 -4- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(四氢呋喃 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(5- 甲基噻吩 -2- 基) 羰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2- 氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(环丙基羰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(四氢呋喃 -3- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-[4-({(3R)-1-[3-(三氟甲氧基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(吡啶 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氯苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(4- 氯苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(2- 甲基 -2- 苯基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(甲氧基乙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(噻吩 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-{[3-(三氟甲基) 苯基] 乙酰基 } 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(2- 甲基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(2- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(2,2- 二甲基丁酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(3,5- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-[4-({(3R)-1-[4-(三氟甲基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(3- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-[4-({(3R)-1-[4-(三氟甲氧基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(3- 甲基丁酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(3,3,3- 三氟丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[二氟 (苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(2,2- 二甲基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(4,4- 二氟环己基) 羰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲

酰胺；

1-(哒嗪-4-基)-N-{4-[1-(1,3-噻唑-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环丙基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(4-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(3,5-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,4-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(3-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-(4-{1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2,4-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(1,3-噻唑-4-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(四氢呋喃-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(吡啶-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基 -2- 苯基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(甲氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-{4-[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-[4-(1-{[3-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{1-[4-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{1-[4-(三氟甲氧基) 苯甲酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-{4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[二氟 (苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(4,4- 二氟环己基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-[4-(1-{[4-(三氟甲氧基) 苯基] 乙酰基 } 哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{1-[3-(三氟甲氧基) 苯甲酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-[4-(1-{[4-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 氯苯甲酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁

烷 -3- 甲酰胺；

N-(4-{[1-(4- 叔丁基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 甲氧基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 甲基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环己基羰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基乙酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲氧基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 苯基丁酰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[4-（丙烷 -2- 基）苯甲酰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氯苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 苯甲酰基哌啶 -4- 基）磺酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-(4,4,4- 三氟丁酰基）哌啶 -4- 基］磺酰基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,5- 二氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4- 氟苯基）乙酰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,3- 二甲基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 氟苯基）乙酰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-3-基)-N-[4-({1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}磺酰基)苯基]氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(3,5-二氟苯基)乙酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2,4-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-({1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}磺酰基)苯基]氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2,3-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2,4-二氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(萘-1-基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环丙基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3,5-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3,3-二甲基丁酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-甲氧基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环戊基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(苯基乙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(1-苯基环丙基)羰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-甲基丙氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3R)-1-(吡啶-3-基)吡咯烷-3-基]噻

吩 -2- 甲酰胺；

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -4- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(哒嗪 -4- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

叔丁基 4-(2- 甲基 -1- 氧代 -1-{4-[4-({[1-(吡啶 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基] 哌啶 -1- 基 } 丙烷 -2- 基) 哌嗪 -1- 甲酸酯；

N-(4-{1-[2- 甲基 -2-(哌嗪 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氯苯甲酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 甲基戊酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 氟苯基) 乙酰基] 哌啶 -4- 基 } 磺酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 苯甲酰基哌啶 -4- 基) 磺酰基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(环戊基羰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[(3R)-1-(5,6- 二氯哒嗪 -4- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -2- 甲酰胺；

N-[(3R)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -2- 甲酰胺；

N-[(3S)-1-(5,6- 二氯哒嗪 -4- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -2- 甲酰胺；

N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -2- 甲酰胺；

N-[(3R)-1-(5,6- 二氯哒嗪 -4- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -3- 甲酰胺；

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3R)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-3-甲酰胺；

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3R)-1-(哒嗪-4-基)吡咯烷-3-基]噻吩-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)哌啶-4-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)哌啶-4-甲酰胺；

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)哌啶-4-甲酰胺；

1-(哒嗪-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}哌啶-4-甲酰胺；

N-[(3S)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(1,3-噻唑-5-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2S)-2-苯基丁酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2S)-2-甲氧基-2-苯基乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2R)-2-甲氧基-2-苯基乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(乙氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(4-甲基苯氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-3-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(萘-1-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2,6-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(萘-1-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-(4-{1-[4-(噻吩-2-基)丁酰基]哌啶-4-基}苯基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环丙基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲

酰胺；

(3S)-N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(萘-2-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[3-(苯基磺酰基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-[4-(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(呋喃-2-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(N-苯甲酰基甘氨酰)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2,4-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(1-甲基环己基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(6-甲基吡啶-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(3-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环戊基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲

酰胺；

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-氟-5-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-氟吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-氟-6-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

(3S)-N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,4-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-庚酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,4-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(4-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,3-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-己酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(3-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-丁酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(3,5-二甲基苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3,5-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯

烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(4- 氯苯基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(呋喃 -3- 基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,4- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[2- 氯 -5-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 乙酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,5- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 乙氧基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,5- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,5- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(5- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（二苯基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-（哒嗪 -3- 基）-N-(4-{1-[4-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（戊 -4- 烯酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-（哒嗪 -3- 基）-N-(4-{1-[3-（三氟甲氧基）苯甲酰基］哌啶 -4- 基｝苯基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(1- 苯基环丙基）羰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[2- 氟 -5-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（环己基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲

酰胺；

(3S)-N-{4-[1-(4- 甲氧基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 甲基丁酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 乙基丁酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 叔丁基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2- 氟苯基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-（哒嗪 -3- 基)-N-(4-{1-[3-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(1- 甲基环丙基）羰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（戊 -4- 炔酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(3- 氟苯基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[3-（甲基巯基）丙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(1- 乙酰基哌啶 -4- 基）羰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（丁 -3- 烯酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,2- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氟 -4- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 甲氧基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2- 氯苯基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2- 甲氧基乙氧基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(N-乙酰基-L-亮氨酰)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,3-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[4-(丙烷-2-基)苯甲酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环己基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(噻吩-2-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(4-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-氟-4-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

2-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-1,3-噻唑-5-甲酰胺；

(3S)-N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-甲基吡啶-3-基)吡咯烷-3-甲

酰胺；

(3S)-N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(2-甲基吡啶-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

N-[(3S)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]呋喃-2-甲酰胺；

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]呋喃-2-甲酰胺；

N-(4-{1-[(4-甲基四氢-2H-吡喃-4-基)甲基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[(3S)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-4-[1-(2-甲基丙酰基)哌啶-4-基]苯甲酰胺；

N-(4-{1-[2-(哌嗪-1-基)乙基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丁基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

4-[1-(2-甲基丙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]苯甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

5-[1-(3-氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺；

5-[1-(4-氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺；

(3S)-N-(4-{1-[(4-甲基四氢-2H-吡喃-4-基)甲基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-羟基-2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(四氢-2H-吡喃-4-基羰基)哌啶-4-基]噻吩-2-甲酰胺；

(3S)-N-{4-[1-(2,2-二甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

5-[1-(2-甲基丙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺；

5-[1-(2,4-二氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺；

5-{1-[(2-甲基环丙基)羰基]哌啶-4-基}-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺；

5-[1-(2-氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺；

5-(1-苯甲酰基哌啶-4-基)-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺；

N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(四氢呋喃-3-基羰基)哌啶-4-基]噻吩-2-甲酰胺；

N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-{1-[(2R)-四氢呋喃-2-基羰基]哌啶-4-基}噻吩-2-甲酰胺；

5-{1-[(1-甲基哌啶-4-基)乙酰基]哌啶-4-基}-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺；

N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(1,3-噻唑-4-基羰基)哌啶-4-基]噻吩-2-甲酰胺；

(3S)-N-{4-[1-(2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(丙烷-2-基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环丙基甲基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢-2H-吡喃-2-基甲基)-1H-吡唑-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-叔丁基-1H-吡唑-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-苯甲酰基吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-(2-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-(3-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-(4-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-(3,5-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-(2-甲基苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-(2,2-二甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-({(3R)-1-[(4,4-二氟环己基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-(4-{[(3R)-1-(4,4,4-三氟丁酰基)吡咯烷-3-基]氧基}

苯基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

N-[4-(5- 丙基 -1,2,4- 氧杂二唑 -3- 基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 氟苯甲酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氟苯甲酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 氟苯甲酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 苯甲酰基氮杂环丁烷 -3- 基）苯基]-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,2- 二甲基丙酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,5- 二氟苯甲酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 甲基苯甲酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,4- 二氟苯甲酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3R)-N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3R)-N-{4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3R)-N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(环己基羰基）哌啶 -4- 基］氧基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(3- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[(1- 苯甲酰基哌啶 -4- 基）氧基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(4- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］氧基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-({1-[(2- 甲基环丙基）羰基］哌啶 -4- 基｝氧基）苯基]-1-(哒嗪 -3- 基）

吡咯烷 -3- 甲酰胺；

N-{4-[5-(2,2- 二甲基丙基)-1,3,4- 氧杂二唑 -2- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙基)-1H- 咪唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(3- 环丙基 -1- 甲基 -1H- 吡唑 -5- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[5-(2,2- 二甲基丙基)-1,2,4- 氧杂二唑 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[3- 环丙基 -1-(2- 甲氧基乙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

叔丁基 4-(5-{[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 氨基甲酰基 } 噻吩 -2- 基) 哌啶 -1- 甲酸酯；

叔丁基 4- 氟 -4-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基] 哌啶 -1- 甲酸酯；

5-(1- 苯甲酰基哌啶 -4- 基)-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(2- 氟苯甲酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(2- 甲基苯甲酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(3- 氟苯甲酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(4- 氟苯甲酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺；

N-{4-[3- 环丙基 -1-(2- 羟基乙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(6- 氟哒嗪 -3- 基)-N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 乙基丁酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

(3S)-N-(4-{[(3S)-1- 苯甲酰基吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[(3S)-1-(2- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[(3S)-1-(3,5- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[(3S)-1-(2,2- 二甲基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基)-2- 氟苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(2- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

(3S)-N-(4-{[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[(1- 苯甲酰基哌啶 -4- 基) 氧基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[1-(环己基羰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

N-{4-[8-(2- 甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[8-(4,4,4- 三氟丁酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯

基}氮杂环丁烷-3-甲酰胺；

N-[4-(8-苯甲酰基-8-氮杂双环[3.2.1]辛-3-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[8-(2-氟苯甲酰基)-8-氮杂双环[3.2.1]辛-3-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[8-(2,2-二甲基丙酰基)-8-氮杂双环[3.2.1]辛-3-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{8-[(1-甲基环丙基)羰基]-8-氮杂双环[3.2.1]辛-3-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲氧基乙基)-3-(2-甲基丙基)-1H-吡唑-5-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

5-[1-(2,2-二甲基丙酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

5-{1-[(1-甲基环丙基)羰基]哌啶-4-基}-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]-5-[1-(3,3,3-三氟丙酰基)哌啶-4-基]噻吩-2-甲酰胺；

5-[1-(2,2-二甲基丁酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

苄基4-[4-({[1-(6-氯哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]-4-氟哌啶-1-甲酸酯；

苄基4-[4-({[1-(6-氯哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]-4-羟基哌啶-1-甲酸酯；

N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]-5-[1-(4,4,4-三氟丁酰基)哌啶-4-基]噻吩-2-甲酰胺；

5-[1-(环丙基羰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

N-{4-[4-氟-1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{2-氟-4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]-2-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环丙基羰基)哌啶-4-基]-2-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(2- 氟 -4-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环丙基乙酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基 -4- 氟哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基)-4- 氟哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[3- 叔丁基 -1-(2- 甲氧基乙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丁基 -3- 叔丁基 -1H- 吡唑 -5- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[3- 叔丁基 -1-(四氢 -2H- 吡喃 -4- 基甲基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基)-2- 氟苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1- 甲基 -3-(三氟甲基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(6- 氯哒嗪 -3- 基)-N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁

烷 -3- 甲酰胺；

N-{3- 氟 -4-[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基］苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基]-3- 氟苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{3- 氟 -4-[1-(4,4,4- 三氟丁酰基）哌啶 -4- 基］苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基)-3- 氟苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{3- 氟 -4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基]-3- 氟苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{3- 氟 -4-[1-(3- 甲基丁酰基）哌啶 -4- 基］苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环丙基乙酰基）哌啶 -4- 基]-3- 氟苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基)-4- 羟基哌啶 -4- 基］苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基)-4- 羟基哌啶 -4- 基］苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(6- 甲基哒嗪 -3- 基)-N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基）甲基]-1H- 吡唑 -4- 基 } 苯基）氮杂环丁烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基 }-1-(6- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(6- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基 }-1-(6- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

N-{4-[(1- 苯甲酰基哌啶 -4- 基）甲基］苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氟苯甲酰基）哌啶 -4- 基］甲基 } 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］甲基 } 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］甲基 } 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 乙基丁酰基）哌啶 -4- 基］甲基 } 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-3-基)-N-(4-{[1-(4,4,4-三氟丁酰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-乙酰基哌啶-4-基)甲基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(1-甲基环丙基)羰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-{[4-甲基-1-(氧杂环丁烷-3-基)哌啶-4-基]甲基}-1H-吡唑-4-基)苯基]-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(4-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

5-[1-(2-氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]呋喃-2-甲酰胺;

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(3-甲基哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(3-甲基哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2-氨基吡啶-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-甲基-5-[4-({[1-(哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]-1H-吡唑-3-甲酸;

乙基1-甲基-5-[4-({[1-(哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]-1H-吡唑-3-甲酸酯;

乙基1-苯基-5-[4-({[1-(哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]-1H-吡唑-3-甲酸酯;

N-{6-[1-(2-氟苯甲酰基)哌啶-4-基]吡啶-3-基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(3-甲基丁酰基)吡咯烷-3-基]氧基}苯基)-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(2-甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(2,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(6-甲基哒嗪-3-基)-N-(4-{[(3R)-1-(1,3-噻唑-4-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{6-[1-(4,4,4-三氟丁酰基)哌啶-4-基]吡啶-3-基}氮杂环

丁烷 -3- 甲酰胺；

N-{6-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］吡啶 -3- 基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-(4- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基}-1-(4- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

N-{4-[1- 苯基 -3-（三氟甲基）-1H- 吡唑 -5- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{6-[1-(2,2- 二甲基丙基）-1H- 吡唑 -4- 基］吡啶 -3- 基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

叔丁基 4-[4-({[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］羰基} 氨基）-1H- 吡唑 -1- 基］哌啶 -1- 甲酸酯；

N-(6-{1-[(4- 甲基哌啶 -4- 基）甲基］-1H- 吡唑 -4- 基} 吡啶 -3- 基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-(1,3- 噻唑 -5- 基羰基）哌啶 -4- 基］甲基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环戊基羰基）哌啶 -4- 基］甲基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(1H- 吡唑 -4- 基羰基）哌啶 -4- 基］甲基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丁酰基）哌啶 -4- 基］甲基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 甲基环丙基）羰基］哌啶 -4- 基} 甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[（甲基巯基）乙酰基］哌啶 -4- 基} 甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1S,4R)- 双环 [2.2.1] 庚 -2- 基乙酰基］哌啶 -4- 基} 甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基戊酰基）哌啶 -4- 基］甲基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 甲基戊酰基）哌啶 -4- 基］甲基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[3-（甲基巯基）丙酰基］哌啶 -4- 基} 甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-(1,3- 噻唑 -4- 基羰基）哌啶 -4- 基］甲基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(1H- 吡唑 -5- 基羰基）哌啶 -4- 基］甲基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(6- 甲基吡啶 -3- 基) 羰基] 哌啶 -4- 基 } 甲基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(3- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 甲基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(戊 -4- 炔酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(甲氧基乙酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(四氢呋喃 -2- 基羰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2- 甲氧基乙氧基) 乙酰基] 哌啶 -4- 基 } 甲基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(乙氧基乙酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 己酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(1- 甲基 -1H- 吡咯 -2- 基) 羰基] 哌啶 -4- 基 } 甲基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(丁 -3- 烯酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(1,3- 噻唑 -2- 基羰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(呋喃 -2- 基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(1,2- 唑 -5- 基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(吡啶 -2- 基羰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(呋喃 -3- 基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环丙基乙酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基丁酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 丙酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰

胺；

N-{4-[(1- 丁酰基哌啶 -4- 基）甲基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丁基羰基）哌啶 -4- 基］甲基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 戊酰基哌啶 -4- 基）甲基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环戊基乙酰基）哌啶 -4- 基］甲基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基苯甲酰基）哌啶 -4- 基］甲基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基戊酰基）哌啶 -4- 基］甲基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环己基羰基）哌啶 -4- 基］甲基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁酰基）哌啶 -4- 基］甲基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基羰基）哌啶 -4- 基］甲基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-(4- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{1-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基]-1H- 吡唑 -4- 基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{1-[1-(2- 氟苯甲酰基）哌啶 -4- 基]-1H- 吡唑 -4- 基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（苯基氨基甲酰基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2,2- 二甲基丙基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(3- 甲氧基 -2,2- 二甲基丙基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2- 环丙基乙基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[2-(2- 乙基哌啶 -1- 基）乙基］氨基甲酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[（环丁基甲基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2S)- 丁烷 -2- 基氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(丁基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(2,2-二甲基四氢-2H-吡喃-4-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(1S)-1-环丙基乙基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({2-[甲基(苯基)氨基]乙基}氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1,1′-双(环丙基)-1-基氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-[4-(噻吩-3-基氨基甲酰基)苯基]氮杂环丁烷-3-甲酰胺；

N-(4-{[(1R)-1-环丙基乙基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-甲基哌啶-4-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(2R)-丁烷-2-基氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-氮杂双环[2.2.2]辛-3-基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[(四氢呋喃-3-基甲基)氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[(氧杂环丁烷-3-基甲基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(2-甲基环丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(环丁基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-甲基环丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(2-甲氧基-2-甲基丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(环丙基甲基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{[(2R)-四氢呋喃-2-基甲基]氨基甲酰基}苯基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[(3,3,3-三氟丙基)氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[(1-甲基哌啶-3-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3-甲基氧杂环丁烷-3-基)甲基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{[(2S)-四氢呋喃-2-基甲基]氨基甲酰基}苯基)氮杂环丁

烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[（四氢 -2H- 吡喃 -4- 基甲基）氨基甲酰基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-（四氢 -2H- 吡喃 -4- 基氨基甲酰基）苯基] 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(1- 甲基哌啶 -3- 基）甲基] 氨基甲酰基 } 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（环丙基氨基甲酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（环戊基氨基甲酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（苄基氨基甲酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(3- 氟苯基）氨基甲酰基] 苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（丙基氨基甲酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(4- 氟苯基）氨基甲酰基] 苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2- 氟苯基）氨基甲酰基] 苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 甲基环丁基）氨基甲酰基] 苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（丙 -2- 烯 -1- 基氨基甲酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

5-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基]-N-[(3S)-1-（哒嗪 -3- 基）吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基]-N-[(3S)-1-（哒嗪 -3- 基）吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(2,2- 二甲基丁酰基）哌啶 -4- 基]-N-[(3S)-1-（哒嗪 -3- 基）吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

5-{1-[(1- 甲基环丙基）羰基] 哌啶 -4- 基 }-N-[(3S)-1-（哒嗪 -3- 基）吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

N-[(3S)-1-（哒嗪 -3- 基）吡咯烷 -3- 基]-5-[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基] 噻吩 -2- 甲酰胺；

5-[1-（环丙基乙酰基）哌啶 -4- 基]-N-[(3S)-1-（哒嗪 -3- 基）吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-（双环 [2.2.1] 庚 -2- 基乙酰基）哌啶 -4- 基]-N-[(3S)-1-（哒嗪 -3- 基）吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[(3S)- 四氢呋喃 -3- 基氨基甲酰基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-[4-({4-[2-（二甲基氨基）乙基] 苯基 } 氨基甲酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[(3R)- 四氢呋喃 -3- 基氨基甲酰基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2- 甲氧基乙基）氨基甲酰基] 苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰

胺；

N-{4-[1-(3-氨基-2,2-二甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[2,2-二甲基-3-(哌嗪-1-基)丙基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[2-甲基-2-(哌嗪-1-基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；及其药学上可接受的盐。

[0009] 仍另一个实施方案涉及式(1A)的化合物，其选自

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

(3S)-N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

N-[4-(1-乙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-丁酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(甲基巯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

(3S)-N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-丁酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-乙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-乙基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲

酰胺；

(3R)-N-{4-[1-(2,2-二甲基丙酰基）哌啶-4-基]苯基}-1-(哒嗪-3-基）吡咯烷-3-甲酰胺；及其药学上可接受的盐。

[0010] 另一实施方案涉及用于治疗炎性和组织修复病症的组合物；尤其是类风湿关节炎、炎性肠病、哮喘和COPD(慢性阻塞性肺病)、骨关节炎、骨质疏松和纤维化病；皮肤病，包括银屑病、特应性皮炎和紫外线引起的皮肤损伤；自身免疫性疾病包括全身性红斑狼疮、多发性硬化、银屑病关节炎、强直性脊柱炎、组织和器官排斥、阿尔茨海默氏病、中风、动脉粥样硬化、再狭窄、糖尿病、肾小球肾炎、癌症，特别是其中所述癌症选自乳腺癌、前列腺癌、肺癌、结肠癌、宫颈癌、卵巢癌、皮肤癌、中枢神经系统癌、膀胱癌、胰腺癌、白血病、淋巴瘤或霍奇金氏病、恶病质、与感染和某些病毒感染相关的炎症，包括获得性免疫缺陷综合征(AIDS)、成人呼吸窘迫综合征和共济失调毛细血管扩张，所述组合物包含赋形剂和治疗有效量的式(IC)的化合物、或其药学上可接受的盐。

[0011] 另一实施方案涉及治疗患者中的炎性和组织修复病症的方法；尤其是类风湿关节炎、炎性肠病、哮喘和COPD(慢性阻塞性肺病)、骨关节炎、骨质疏松和纤维化病；皮肤病，包括银屑病、特应性皮炎和紫外线引起的皮肤损伤；自身免疫性疾病包括全身性红斑狼疮、多发性硬化、银屑病关节炎、强直性脊柱炎、组织和器官排斥、阿尔茨海默氏病、中风、动脉粥样硬化、再狭窄、糖尿病、肾小球肾炎、癌症，特别是其中所述癌症选自乳腺癌、前列腺癌、肺癌、结肠癌、宫颈癌、卵巢癌、皮肤癌、中枢神经系统癌、膀胱癌、胰腺癌、白血病、淋巴瘤或霍奇金氏病、恶病质、与感染和某些病毒感染相关的炎症，包括获得性免疫缺陷综合征(AIDS)、成人呼吸窘迫综合征和共济失调毛细血管扩张，所述方法包括向患者施用治疗有效量的式(IC)的化合物、或其药学上可接受的盐。

[0012] 另一实施方案涉及治疗患者中的炎性和组织修复病症的方法；尤其是类风湿关节炎、炎性肠病、哮喘和COPD(慢性阻塞性肺病)、骨关节炎、骨质疏松和纤维化病；皮肤病，包括银屑病、特应性皮炎和紫外线引起的皮肤损伤；自身免疫性疾病包括全身性红斑狼疮、多发性硬化、银屑病关节炎、强直性脊柱炎、组织和器官排斥、阿尔茨海默氏病、中风、动脉粥样硬化、再狭窄、糖尿病、肾小球肾炎、癌症，特别是其中所述癌症选自乳腺癌、前列腺癌、肺癌、结肠癌、宫颈癌、卵巢癌、皮肤癌、中枢神经系统癌、膀胱癌、胰腺癌、白血病、淋巴瘤或霍奇金氏病、恶病质、与感染和某些病毒感染相关的炎症，包括获得性免疫缺陷综合征(AIDS)、成人呼吸窘迫综合征、和共济失调毛细血管扩张或脾癌，所述方法包括向患者施用治疗有效量的式(IC)的化合物、或其药学上可接受的盐；和治疗有效量的一种额外的治疗剂或多于一种额外的治疗剂。

[0013] 发明详述

该详细描述仅旨在使本领域技术人员熟悉申请人的发明、其原理以及其实际应用，从而使得本领域技术人员可以以它的许多形式来改变和应用本发明，只要它们可以最适合于具体用途的需要。本描述及其具体实施例仅旨在说明的目的。因此，本发明不限于本专利申请中描述的实施方案，并且可以不同地修改。

[0014] 缩写和定义

除非本文另有定义，否则在本发明上下文中使用的科技术语均具有本领域普通技术人员通常理解的含义。术语的含义和范围应当清楚，然而，在任何潜在模糊的情况下，本文所

提供的定义采用相对于任何字典或外在定义的惯例。在本申请中,“或 (or)”的使用意指“和 / 或 (and/or)”,除非另有说明。此外,术语“包括 (including)”以及其他形式诸如“包括 (includes)”和“包括 (included)”的使用并无限制。本专利申请 (包括权利要求) 中关于使用词语“包含 (comprise)”或“包含 (comprises)”或“包含 (comprising)”,申请人指出除非上下文另有要求,这些词语均以其被包括性而非排他性解释的基础和明确理解来使用,并且申请人旨在这些词语的每一个均如此解释以理解本专利申请 (包括下文的权利要求)。对于在任何取代基中或本发明的化合物中或本文的任何其他式中出现超过一次的变量,其在每次出现时的定义独立于其在另外每次出现时的定义。取代基的组合仅在此类组合物产生稳定的化合物时是允许的。稳定的化合物是其可以以可用的纯度程度从反应混合物中分离的化合物。

[0015] 意在理解本文所有组合均维持合适的化合价,具有多于一个原子的单价基团经其左端连接,且二价基团从左向右绘制。

[0016] 如本说明书和所附的权利要求中所用,除非相反地说明,以下术语具有所指出的含义 :

术语“烷基”(单独地或与其他术语组合) 意指直链或支链饱和烃基取代基,其通常含有从 1 至约 10 个碳原子 ;或在另一实施方案中,从 1 至约 8 个碳原子 ;在另一个实施方案中,从 1 至约 6 个碳原子 ;和在另一个实施方案中,从 1 至约 4 个碳原子。此类取代基的实例包括甲基、乙基、正丙基、异丙基、正丁基、异丁基、仲丁基、叔丁基、戊基、异戊基、和己基等。

[0017] 术语“烯基”(单独地或与其他术语组合) 意指直链或支链烃基取代基,其含有一个或多个双键和通常含有从 2 至约 10 个碳原子 ;或在另一实施方案中,从 2 至约 8 个碳原子 ;在另一个实施方案中,从 2 至约 6 个碳原子 ;和在另一个实施方案中,从 2 至约 4 个碳原子。此类取代基的实例包括乙烯基 (ethenyl)(乙烯基 (vinyl))、2- 丙烯基、3- 丙烯基、1,4- 戊二烯基、1,4- 丁二烯基、1- 丁烯基、2- 丁烯基、和 3- 丁烯基等。

[0018] 术语“炔基”(单独地或与其他术语组合) 意指直链或支链烃基取代基,其含有一个或多个三键和通常含有从 2 至约 10 个碳原子 ;或在另一实施方案中,从 2 至约 8 个碳原子 ;在另一个实施方案中,从 2 至约 6 个碳原子 ;和在另一个实施方案中,从 2 至约 4 个碳原子。此类取代基的实例包括乙炔基、2- 丙炔基、3- 丙炔基、2- 丁炔基和 3- 丁炔基等。

[0019] 术语“碳环基 (carbocyclyl)”(单独地或与其他术语组合) 意指饱和的环状 (即“环烷基”)、部分饱和的环状 (即“环烯基”)、或完全不饱和的 (即“芳基”) 烃基取代基,其含有 3-14 个碳环原子 (“环原子”是结合在一起以形成环状取代基的一个或多个环的原子)。碳环基可以是单环 (single-ring)(单环 (monocyclic)) 或多环的环结构。

[0020] 碳环基可以是单环结构,其通常含有 3-8 个环原子,更通常 3-6 个环原子,和甚至更通常 5-6 个环原子。此类单环碳环基的实例包括环丙基 (cyclopropyl(cyclopropanyl))、环丁基 (cyclobutyl(cyclobutanyl))、环戊基 (cyclopentyl(cyclopentanyl))、环戊烯基、环戊二烯基、环己基 (cyclohexyl(cyclohexanyl))、环己烯基、环己二烯基和苯基。碳环基可以可选地为多环的 (即,可以含有多于一个环)。多环碳环基的实例包括桥连的、稠合的和螺环的碳环基。在螺环的碳环基中,一个原子由两个不同环共有。螺环的碳环基的实例是螺戊基 (spiropentanyl)。在桥连的碳环基中,环共有至少两个共同的非相邻原子。桥连的碳环基

的实例包括二环 [2.2.1] 庚烷基、二环 [2.2.1] 庚 -2- 烯基和金刚烷基。在稠合环碳环基系统中，两个或多个环可以稠合在一起，从而使得两个环共有一个共同的键。两个或三个稠合环的碳环基的实例包括萘基、四氢萘基 (tetrahydronaphthalenyl(tetralinyl))、茚基、茚满基（二氢茚基）、蒽基、菲基、和十氢萘基。

[0021] 术语“环烷基”（单独地或与其他术语组合）意指饱和的环状烃基取代基，其含有 3-14 个碳环原子。环烷基可以是单一碳环，其通常含有 3-8 个碳环原子，并更通常 3-6 个环原子。单环环烷基的实例包括环丙基、环丁基、环戊基和环己基。环烷基可以可选地为多环的或含有多于一个环。多环环烷基的实例包括桥连的、稠合的和螺环的碳环基。

[0022] 术语“芳基”（单独地或与其他术语组合）意指芳族碳环基，其含有 6-14 个碳环原子。芳基可以为单环的或多环的（即，可以含有多于一个环）。在多环芳族环的情况下，多环系统中仅一个环需要是不饱和的，而其余的环可以是饱和的，部分饱和的或不饱和的。芳基的实例包括苯基、萘基、茚基、茚满基、和四氢萘基。

[0023] 在一些情况下，烃基取代基（例如烷基、烯基、炔基、或环烷基）中的碳原子数目由前缀“C_x-C_y-”所表示，其中 x 为取代基中碳原子数的最小值且 y 为最大值。因此，例如“C_1-C_6- 烷基”指含有 1-6 个碳原子的烷基取代基。进一步说明，C_3-C_8- 环烷基表示含有 3-8 个碳环原子的饱和的烃基环。

[0024] 术语“氢”（单独地或与其他术语组合）意指氢基 (hydrogen radical)，并可以表示为 -H。

[0025] 术语“羟基”（单独地或与其他术语组合）意指 -OH。

[0026] 术语“羧基”（单独地或与其他术语组合）意指 -C(O)-OH。

[0027] 术语“氨基”（单独地或与其他术语组合）意指 $-NH_2$。

[0028] 术语“卤素”或“卤代 (halo)”（单独地或与其他术语组合）意指氟基（其可以表示为 -F）、氯基（其可以表示为 -Cl）、溴基（其可以表示为 -Br）、或碘基（其可以表示为 -I）。

[0029] 如果取代基被描述为“取代的”，则非氢基位于取代基的碳或氮上的氢基位置处。因此，例如，取代的烷基取代基是其中至少一个非氢基位于烷基取代基上的氢基位置处的烷基取代基。为了说明，单氟烷基是由氟基取代的烷基，并且二氟烷基是由两个氟基取代的烷基。应该认识到如果在取代基上存在多于一个取代，则每一个非氢基可以是相同的或不同的（除非另有说明）。

[0030] 如果取代基被描述为“任选取代的”，则取代基可以是 (1) 未取代的或 (2) 取代的。如果取代基被描述为任选用高至特定数目的非氢基取代的，则该取代基可以是 (1) 未取代的；或 (2) 由高至特定数目的非氢基或由高至取代基上可取代位置的最大数目（以较少者为准）所取代。因此，例如，如果取代基被描述为任选用高至 3 个非氢基取代的杂芳基，则任何具有少于 3 个可取代位置的杂芳基将任选由高至仅和所述杂芳基具有的可取代位置一样多的非氢基所取代。为了说明，四唑基（其仅具有一个可取代位置）将任选由高至一个非氢基取代。为了进一步说明，如果氨基氮被描述为任选由高至 2 个非氢基取代，则伯氨基氮将任选由高至 2 个非氢基取代，尽管仲氨基氮将任选由高至仅 1 个非氢基取代。如果取代基被描述为任选用一个或多个非氢基取代的，则该取代基可以是 (1) 未取代的；或 (2) 由高至取代基上的可取代位置的最大数目所取代。因此，例如，如果取代基被描述为任选用一个或多个非氢基取代的杂芳基，则任何具有 3 个可取代位置的杂芳基将任选由一个、两

个或三个非氢基所取代。为了说明，四唑基（其仅具有一个可取代位置）将任选由高至一个非氢基取代。

[0031] 本专利申请可互换使用术语“取代基”和“基”。

[0032] 前缀“卤代”表示连有该前缀的取代基被一个或多个独立选择的卤素基所取代。例如，卤代烷基表示其中至少一个氢基被卤素基所取代的烷基取代基。卤代烷基的实例包括氯甲基、1-溴乙基、氟甲基、二氟甲基、三氟甲基、和1,1,1-三氟乙基。应该认识到如果取代基被多于一个卤素基所取代，则那些卤素基可以是相同的或不同的（除非另有说明）。

[0033] 前缀“全卤代”表示连有该前缀的取代基上的每一个氢基均由独立选择的卤素基所取代，即取代基上的每个氢基被卤素基所取代。如果所有的卤素基是相同的，则前缀通常将辨别该卤素基。因此，例如，术语“全氟代”表示与该前缀相连的取代基上的每一个氢基均由氟基所取代。为了说明，术语“全氟代烷基”表示其中氟基位于每一氢基的位置处的烷基取代基。

[0034] 术语“羰基”（单独地或与其他术语组合）意指 -C(O)-。

[0035] 术语“氨基羰基”（单独地或与其他术语组合）意指 -C(O)-NH_2。

[0036] 术语“氧代”（单独地或与其他术语组合）意指（＝O）。

[0037] 术语“氧基”（单独地或与其他术语组合）意指醚取代基，并可以表示为 -O-。

[0038] 术语“烷基羟基”（单独地或与其他术语组合）意指 - 烷基 -OH。

[0039] 术语“烷基氨基”（单独地或与其他术语组合）意指 - 烷基 -NH_2。

[0040] 术语“烷基氧基”（单独地或与其他术语组合）意指烷基醚取代基，即 -O- 烷基。此类取代基的实例包括甲氧基（-O-CH_3）、乙氧基、正丙氧基、异丙氧基、正丁氧基、异丁氧基、仲丁氧基和叔丁氧基。

[0041] 术语“烷基羰基”（单独地或与其他术语组合）意指 -C(O)- 烷基。

[0042] 术语“氨基烷基羰基”（单独地或与其他术语组合）意指 -C(O)- 烷基 -NH_2。

[0043] 术语“烷基氧基羰基”（单独地或与其他术语组合）意指 -C(O)-O- 烷基。

[0044] 术语“碳环基羰基”（单独地或与其他术语组合）意指 -C(O)- 碳环基。

[0045] 类似地，术语“杂环基羰基”（单独地或与其他术语组合）意指 -C(O)- 杂环基。

[0046] 术语“碳环基烷基羰基”（单独地或与其他术语组合）意指 -C(O)- 烷基 - 碳环基。

[0047] 类似地，术语“杂环基烷基羰基”（单独地或与其他术语组合）意指 -C(O)- 烷基 - 杂环基。

[0048] 术语“碳环基氧基羰基”（单独地或与其他术语组合）意指 -C(O)-O- 碳环基。

[0049] 术语“碳环基烷基氧基羰基”（单独地或与其他术语组合）意指 -C(O)-O- 烷基 - 碳环基。

[0050] 术语“硫代（thio）”或“硫代（thia）”（单独地或与其他术语组合）意指硫醚取代基，即其中二价硫原子代替醚氧原子的醚取代基。此类取代基可以表示为 -S-。例如，该“烷基 - 硫代 - 烷基”意指烷基 -S- 烷基（烷基 - 巯基 - 烷基）。

[0051] 术语“硫氢基（thiol）”或“硫氢基（sulfhydryl）”（单独地或与其他术语组合）意指硫氢基取代基，并可以表示为 -SH。

[0052] 术语“（硫代羰基）”（单独地或与其他术语组合）意指其中氧原子已由硫代替的羰基。此类取代基可以表示为 -C(S)-。

[0053] 术语“磺酰基”(单独地或与其他术语组合)意指 $-S(O)_2-$。

[0054] 术语“氨基磺酰基”(单独地或与其他术语组合)意指 $-S(O)_2-NH_2$。

[0055] 术语“亚磺酰基”或“亚砜(sulfoxido)”(单独地或与其他术语组合)意指-S(O)-。

[0056] 术语“杂环基”(单独地或与其他术语组合)意指饱和的(即“杂环烷基”)、部分饱和的(即“杂环烯基”)、或完全不饱和的(即“杂芳基”)环结构,其含有总计 3-14 个环原子。至少一个环原子是杂原子(即,氧、氮、或硫),其余环原子独立地选自碳、氧、氮和硫。杂环基可以是单环 (single-ring)(单环 (monocyclic)) 或多环的环结构。

[0057] 杂环基可以是单环,其通常含有 3-7 个环原子,更通常 3-6 个环原子,和甚至更通常 5-6 个环原子。单环杂环基的实例包括 1,2,3,6- 四氢吡啶、硫代吗啉基、四氢吡喃基、呋喃基、二氢呋喃基、四氢呋喃基、噻吩基(硫代呋喃基 (thiofuranyl))、二氢噻吩基、四氢噻吩基、吡咯基、吡咯啉基、吡咯烷基、咪唑基、咪唑啉基、咪唑烷基、吡唑基、吡唑啉基、吡唑烷基、三唑基、四唑基、噁唑基、噁唑烷基、异噁唑烷基、异噁唑基、噻唑基、异噻唑基、噻唑啉基、异噻唑啉基、噻唑烷基、异噻唑烷基、噻二唑基 (thiodiazolyl)、噁二唑基 (oxadiazolyl)(包括 1,2,3- 噁二唑基、1,2,4- 噁二唑基、1,2,5- 噁二唑基(呋咱基 (furazanyl))、或 1,3,4- 噁二唑基)、噁三唑基 (oxatriazolyl)(包括 1,2,3,4- 噁三唑基或 1,2,3,5- 噁三唑基)、二噁唑基 (dioxazolyl)(包括 1,2,3- 二噁唑基、1,2,4- 二噁唑基、1,3,2- 二噁唑基、或 1,3,4- 二噁唑基)、噁噻唑基 (oxathiazolyl)、噁硫酚基 (oxathiolyl)、氧硫杂戊环基 (oxathiolanyl)、吡喃基、二氢吡喃基、噻喃基 (thiopyranyl)、四氢噻喃基、吡啶基(吖嗪基 (azinyl))、哌啶基、二嗪基(包括哒嗪基 (1,2- 二嗪基)、嘧啶基 (1,3- 二嗪基)、或吡嗪基 (1,4- 二嗪基))、哌嗪基、吡咯烷 -2- 酮基 (pyrrolidin-2-only)、三嗪基(包括 1,3,5- 三嗪基、1,2,4- 三嗪基、和 1,2,3- 三嗪基))、噁嗪基(包括 1,2- 噁嗪基、1,3- 噁嗪基或 1,4- 噁嗪基))、噁噻嗪基 (oxathiazinyl)(包括 1,2,3- 噁噻嗪基、1,2,4- 噁噻嗪基、1,2,5- 噁噻嗪基、或 1,2,6- 噁噻嗪基))、噁二嗪基 (oxadiazinyl)(包括 1,2,3- 噁二嗪基、1,2,4- 噁二嗪基、1,4,2- 噁二嗪基、或 1,3,5- 噁二嗪基))、吗啉基、氮杂卓基 (azepinyl)、氧杂卓基 (oxepinyl)、硫杂卓基 (thiepinyl)、和二氮杂卓基 (diazepinyl)。

[0058] 杂环基可以可选地为多环的(即,可以含有多于一个环)。多环杂环基的实例包括桥连的、稠合的和螺环的碳环基。在螺环的杂环基中,一个原子由两个不同环共有。在桥连的杂环基中,环共有至少两个共同的非相邻原子。在稠合环杂环基中,两个或多个环可以稠合在一起,从而使得两个环共有一个共同的键。稠合环杂环基的实例包括六氢 - 呋喃并 [3,4-c] 吡咯、六氢 - 呋喃并 [3,4-B] 吡咯、八氢 - 吡咯并 [3,4-b] 吡啶、八氢 - 吡咯并 [3,4-c] 吡啶、(3aR,6aR)-5- 甲基 - 八氢 - 吡咯并 [3,4-b] 吡咯、(3aR,6aR)- 八氢 - 吡咯并 [3,4-b] 吡咯、6- 甲基 -2,6- 二氮杂 - 二环 [3.2.0] 庚烷、(3aS,6aR)-2- 甲基 - 八氢 - 吡咯并 [3,4-c] 吡咯、十氢 -[1,5] 萘啶、2,3- 二氢苯并呋喃基、2,3,4,9- 四氢 -1H- 吡啶并 [3,4-b] 吲哚基、噻吩并 [3,2-c] 吡啶基、呋喃并 [3,2-c] 吡啶基、酞嗪 -1(2H)- 酮基、异喹啉基、异喹啉 -1(2H)- 酮基、5,6,7,8- 四氢酞嗪 -1(2H)- 酮基、氟代酞嗪 -1(2H)- 酮基、(Z)-3H- 苯并 [d][1,2] 二氮杂卓 -4(5H)- 酮基、(三氟甲基)酞嗪 -1(2H)- 酮基、吡咯并 [1,2-d][1,2,4] 三嗪 -1(2H)- 酮基、1,2,3,4- 四氢异喹啉基、2,3- 二氢苯并 [b][1,4] 二氧杂环己烯基 (dioxinyl)、5,6,7,8- 四氢酞嗪 -1(2H)- 酮基、5,6,7,8- 四氢 -[1,2,4] 三唑并 [4,3-a]

吡嗪基、5,6,7,8- 四氢咪唑并 [1,5-a] 吡嗪基、噻吩并 [3,2-c] 吡啶基、呋喃并 [3,2-c] 吡啶基、吲嗪基、吡喃并吡咯基 (pyranopyrrolyl)、4H- 喹嗪基、嘌呤基、萘啶基、吡啶并吡啶基 (pyridopyridinyl)(包括吡啶并 [3,4-b]- 吡啶基、吡啶并 [3,2-b]- 吡啶基、或吡啶并 [4,3-b]- 吡啶基) 和蝶啶基。稠合环杂环基的其他实例包括苯并稠合的杂环基,诸如苯并咪唑基、苯并 [d][1,3] 二氧杂环戊烯基、吲哚基、异吲哚基 (异氮茚基 (isobenzazolyl)、假异吲哚基 (pseudoisoindolyl))、假吲哚基 (indoleninyl(pseudoindolyl))、异吲唑基 (isoindazolyl(benzpyrazolyl))、benzazinyl(包括喹啉基 (1-benzazinyl) 或异喹啉基 (2-benzazinyl))、酞嗪基、喹喔啉基、喹唑啉基、苯并二嗪基 (benzodiazinyl)(包括噌啉基 (1,2- 苯并二嗪基) 或喹唑啉基 (1,3- 苯并二嗪基))、苯并吡喃基 (包括苯并二氢吡喃基或异苯并二氢吡喃基)、苯并噁嗪基 (包括 1,3,2- 苯并噁嗪基、1,4,2- 苯并噁嗪基、2,3,1- 苯并噁嗪基、或 3,1,4- 苯并噁嗪基)、和苯并异噁唑基 (benzisoxazinyl)(包括 1,2- 苯并异噁唑基或 1,4- 苯并异噁唑基)。螺环杂环基的实例包括 1,4- 二氧杂 -8- 氮杂螺 [4.5] 癸基 (decanyl)。

[0059] 术语“5-6 元杂芳基”(单独地或与其他术语组合) 意指含有总计 5-6 个环原子的芳族杂环基。至少一个环原子是杂原子 (即,氧、氮、或硫),其余环原子独立地选自碳、氧、氮和硫。

[0060] 术语“杂环烷基”(单独地或与其他术语组合) 意指饱和的杂环基。

[0061] 术语“杂芳基”(单独地或与其他术语组合) 意指芳族杂环基,其含有 5-14 个环原子。杂芳基可以是单环或 2 个或 3 个稠合环。杂芳基取代基的实例包括 6 元环取代基诸如吡啶基、吡嗪基 (pyrazyl)、嘧啶基、哒嗪基、和 1,3,5-、1,2,4- 或 1,2,3- 三嗪基 ;5 元环取代基如咪唑基 (imidazyl)、呋喃基、噻吩基、吡唑基、噁唑基、异噁唑基、噻唑基、1,2,3-、1,2,4-、1,2,5- 或 1,3,4- 噁二唑基和异噻唑基 ;6/5 元稠合环取代基诸如苯并噻吩基、苯并异噁唑基、苯并噁唑基、和嘌呤基 ;和 6/6 元稠合环例如苯并吡喃基、喹啉基、异喹啉基、噌啉基、喹唑啉基、和苯并噁嗪基。

[0062] 与多组分取代基相连的前缀仅应用于第一组分。为了说明,术语“烷基环烷基”含有两种组分 :烷基和环烷基。因此,C_1-C_6- 烷基环烷基上的 C_1-C_6- 前缀表示烷基环烷基的烷基组分含有 1-6 个碳原子 ;C_1-C_6- 前缀不描述环烷基组分。为了进一步说明,卤代烷基氧基烷基上的前缀“卤代”表示仅烷基氧基烷基取代基的烷基氧基组分被一个或多个卤素基取代。如果卤素取代可以可选地或另外出现在烷基组分上,则取代基将改为描述成“卤素取代的烷基氧基烷基”而非“卤代烷基氧基烷基”。并且最后,如果卤素取代可能仅出现在烷基组分上,则取代基将改为描述成“烷基氧基卤代烷基”。

[0063] 术语“治疗 (treat)”、“治疗 (treating)”和“治疗 (treatment)”指减轻或消除疾病和 / 或其伴随的症状的方法。

[0064] 术语“预防 (prevent)”、“预防 (preventing)”和“预防 (prevention)”指预防疾病和 / 或其伴随的症状的发作或防止主体获得疾病的方法。如本文所用,“预防 (prevent)”、“预防 (preventing)”和“预防 (prevention)”还包括延迟疾病和 / 或其伴随的症状的发作和降低主体获得疾病的风险。

[0065] 术语“治疗有效量”指所施用的足以预防所治疗的病况或病症的一种或多种症状的发生或将其减轻至一定程度的化合物的量。

[0066] 术语“调节”指化合物增加或降低激酶的功能或活性的能力。如本文所用,“调节”以其多种形式旨在包括与激酶相关的活性的拮抗、激动、部分拮抗和/或部分激动。激酶抑制剂是例如结合以部分地或全部阻断刺激,降低、阻止、延迟活化,失活,脱敏,或下调信号转导的化合物。激酶活化剂是例如结合以刺激,增加,打开,活化,促进,增强活化,敏化或上调信号转导的化合物。

[0067] 如本文所用的术语“组合物”旨在包括包含以特定量的特定成分的产品、以及任何直接或间接产生自以特定量的特定成分的组合的产品。“药学上可接受的”意指载体、稀释剂或赋形剂必须与制剂的其他成分相容且对其受体无害。

[0068] “主体”在本文定义为包括动物诸如哺乳动物,包括但不限于灵长类动物(例如人)、牛、绵羊、山羊、马、犬、猫、兔、大鼠、小鼠等。在优选的实施方案中,主体是人。

[0069] 同位素富集或标记的化合物

本发明的化合物可以以同位素标记或同位素富集的形式存在,其含有一个或多个具有不同于自然界中最大量发现的原子量或质量数的原子量或质量数的原子。同位素可以是有放射性的或无放射性的同位素。原子诸如氢、碳、磷、硫、氟、氯和碘的同位素包括但不限于^{2}H、^{3}H、^{13}C、^{14}C、^{15}N、^{18}O、^{32}P、^{35}S、^{18}F、^{36}Cl、和^{125}I。含有这些和/或其他原子的其他同位素的化合物在本发明的范围内。

[0070] 在另一个实施方案中,同位素标记的化合物包含氘(^{2}H)、氚(^{3}H)或^{14}C同位素。本发明的同位素标记的化合物可以通过本领域普通技术人员熟知的一般方法来制备。此类同位素标记的化合物可以方便地通过进行本文实施例中公开的程序和方案通过用容易可得的同位素标记的试剂代替未标记的试剂来制备。在一些情况下,化合物可以用同位素标记的试剂处理来交换正常原子与其同位素,例如,氢交换为氘可以通过氘酸(deuteric acid)诸如D_2SO_4/D_2O的作用来交换。除了上述内容,相关程序和中间产物例如公开于Lizondo,J等人,Drugs Fut,21(11),1116(1996);Brickner,S J等人,J Med Chem,39(3),673(1996);Mallesham,B等人,Org Lett,5(7),963(2003);PCT公开WO1997010223,WO2005099353,WO1995007271,WO2006008754;美国专利号7538189;7534814;7531685;7528131;7521421;7514068;7511013;和美国专利申请公开号20090137457;20090131485;20090131363;20090118238;20090111840;20090105338;20090105307;20090105147;20090093422;20090088416;和20090082471,所述方法通过引用并入本文。

[0071] 本发明的同位素标记化合物可以用作标准品以确定结合测定法中的有效性。含同位素的化合物已用于药物研究中以通过评价未同位素标记的母体化合物的作用机制和代谢途径来研究化合物的体内代谢归宿(Blake等人J.Pharm.Sci.64,3,367-391(1975))。此类代谢研究在安全、有效的治疗药物的设计中是重要的,因为施用于患者的体内活性化合物或因为从母体化合物产生的代谢物证实是有毒性的或致癌的(Foster等人,Advances in Drug Research Vol.14,pp.2-36,Academic press,London,1985;Kato等人,J.Labelled Comp.Radiopharmaceut.,36(10):927-932(1995);Kushner等人,Can.J.Physiol.Pharmacol.,77,79-88(1999)。

[0072] 此外,含无放射性同位素的药物诸如称为“重药(heavy drug)”的氘化药物可用于治疗与NAMPT活性相关的疾病和病况。增加化合物中存在的同位素的量高于其天然丰度被称为富集。富集的量的实例包括从约0.5、1、2、3、4、5、6、7、8、9、10、12、16、21、25、

29、33、37、42、46、50、54、58、63、67、71、75、79、84、88、92、96 至约 100mol％。用重同位素替代高至约 15％的正常原子已在哺乳动物（包括啮齿类动物和犬）中起效且维持数天至数周的周期，具有最小的观察到的不利作用 (Czajka D M 和 FinkelA J，Ann.N.Y.Acad.Sci.1960 84：770；Thomson J F，Ann.New York Acad.Sci 1960 84：736；Czakja D M 等人，Am.J.Physiol.1961 201：357)。发现在人流体中用氘精确替代高至 15％ -23％没有导致毒性 (Blagojevic N 等人在 "Dosimetry&Treatment Planning for Neutron Capture Therapy" 中，Zamenhof R，Solares G 和 Harling O 编辑 1994.Advanced Medical Publishing，Madison Wis.pp.125-134；Diabetes Metab.23：251(1997))。

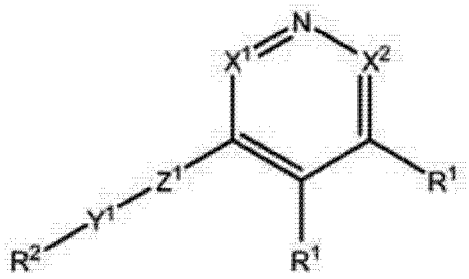
[0073] 稳定同位素标记药物可以改变其物理化学特性诸如 pKa 和脂质溶解性。如果同位素取代影响参与配体 - 受体相互作用的区域，则这些作用和改变可以影响药物分子的药代动力学应答。尽管稳定同位素标记的分子的一些物理特性不同于未标记分子的那些，但化学和生物特性是相同的，且一点重要的例外是：由于重同位素增加的质量，参与重同位素与另一原子的任何键将强于轻同位素与该原子之间的相同的键。因此，在代谢和酶促转化的位点处的同位素的掺入将减缓所述反应，潜在地改变与无同位素化合物相关的药代动力学概况或效力。

[0074] 化合物

所有式的化合物中的 X^1、X^2、Y^1、Z^1、R^1、和 R^2的合适组是独立选择的。本发明所描述的实施方案可以组合。此类组合被考虑并在本发明的范围内。例如，考虑任何的 X^1、X^2、Y^1、Z^1、R^1、和 R^2的实施方案与对任何其他的 X^1、X^2、Y^1、Z^1、R^1、和 R^2定义的实施方案组合。

[0075] 式 (I) 的实施方案

因此，本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式 (I)



式 (I)；

其中

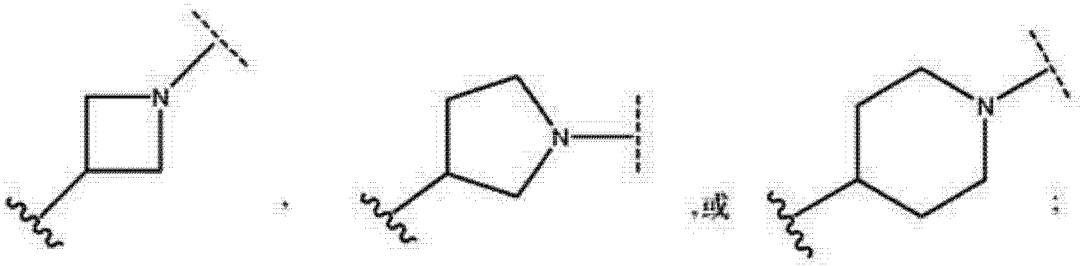
X^1为 N 且 X^2为 CR^1；或

X^1为 CR^1且 X^2为 N；或

X^1为 CR^1且 X^2为 CR^1；

Y^1为 C(O)NH、或 NHC(O)；

Z^1为



其中 表示连接至 Y^1 的点且 表示连接至含氮杂芳基的点；

R^1 在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I；

R^2 独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2 中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：

R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$,
$OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$,
$NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$,
$NR^3C(O)N(R^3)2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$,
$C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, $C(O)H$, $C(O)OH$,
$C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br
和 I；其中 R^2 中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4, OR^4, SR^4, $S(O)R^4$,
SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$,
$NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$,
$NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$,
$C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, $C(O)H$,
$C(O)OH$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl,
和 I；

R^3 在每次出现时独立地选自烷基、烯基、炔基、芳基、环烷基、环烯基、和杂环基；其中 R^3 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：
R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$,
$OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$,
$NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$,
$NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, $C(O)NHOH$,
$C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, $C(O)H$,
$C(O)OH$, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F,
Cl, Br 和 I；其中 R^3 中的芳基、环烷基、环烯基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：

R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$,
$NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$,

$NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^5)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, $C(O)NHOH$, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；

R^5在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^5中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), $C(O)OH$, N_3, CN, NH_2, F, Cl, Br 和 I；

R^6在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^6中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), $C(O)OH$, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br 和 I；

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^8在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^9在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中由 R^4、R^5、R^6、R^7、R^8、和 R^9表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$,

$OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$,

$OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})^2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $CO(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NHR^{12}, $SO_2N(R^{12})^2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3OH$, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br 和 I；

R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：

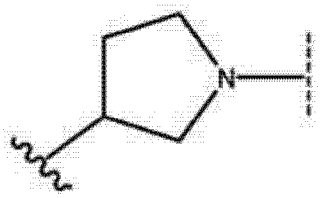
R^{13}, OR^{13}, $C(O)OR^{13}$, OCF_3, CF_3, F, Cl, Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

R^{13}在每次出现时独立地选自烷基、烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

条件是

当 X^1为 CR^1且 X^2为 CR^1时；R^1为氢；Y^1为 NHC(O)；Z^1为



；且 R^2为吡咯基；所述 R^2中的吡咯基未被两个烷基取代。

[0076] 在式 (I) 的一个实施方案中，X^1为 N 且 X^2为 CR^1；或 X^1为 CR^1且 X^2为 N；或 X^1为 CR^1且 X^2为 CR^1。在式 (I) 的另一个实施方案中，X^1为 N 且 X^2为 CR^1。在式 (I) 的另一个实施方案中，X^1为 CR^1且 X^2为 N。在式 (I) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1。

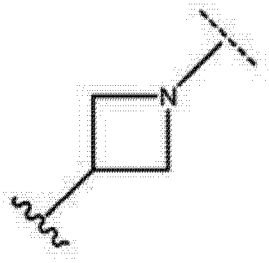
[0077] 在式 (I) 的一个实施方案中，R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (I) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (I) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、和 F。在式 (I) 的另一个实施方案中，R^1在每次出现时为氢。

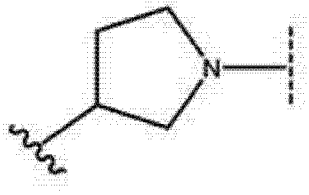
[0078] 在式 (I) 的一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (I) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (I) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、和 F。在式 (I) 的另一个实施方

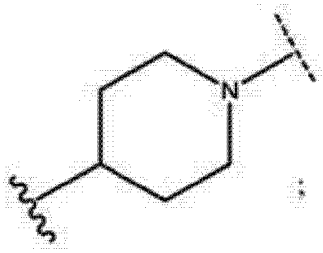
案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时为氢。

[0079] 在式 (I) 的一个实施方案中，Y^1为 C(O)NH、或 NHC(O)。在式 (I) 的另一个实施方案中，Y^1为 C(O)NH。在式 (I) 的另一个实施方案中，Y^1为 NHC(O)。

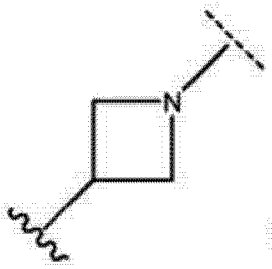
[0080] 在式 (I) 的一个实施方案中，Z^1为

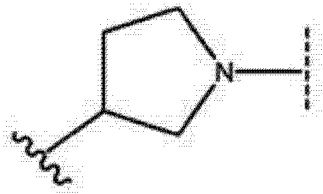

，

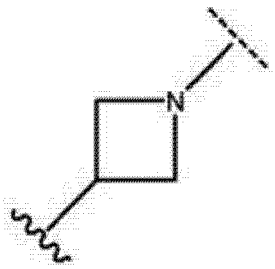

，或

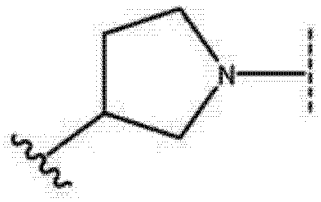

；

其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。在式 (I) 的另一个实施方案中，Z^1为


，或


；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。在式 (I) 的另一个实施方案中，Z^1为


；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。在式 (I) 的另一个实施方案中，Z^1为


；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。

[0081] 在式 (I) 的一个实施方案中，R^2独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：R^3，OR^3，SR^3，$S(O)R^3$，

SO_2R^3，$C(O)R^3$，$CO(O)R^3$，$OC(O)R^3$，$OC(O)OR^3$，NH_2，NHR^3，$N(R^3)_2$，$NHC(O)R^3$，

$NR^3C(O)R^3$，$NHS(O)_2R^3$，$NR^3S(O)_2R^3$，$NHC(O)OR^3$，$NR^3C(O)OR^3$，$NHC(O)NH_2$，

$NHC(O)NHR^3$，$NHC(O)N(R^3)_2$，$NR^3C(O)NHR^3$，$NR^3C(O)N(R^3)_2$，$C(O)NH_2$，$C(O)NHR^3$，

$C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2,

SO_2NHR^3, $SO_2N(R^3)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH,

$CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I ;其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代 :

R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4,

$N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$,

$NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$,

$C(O)NHR^4$, $C(O)N(R^4)_3$, $C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$,

SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, $C(O)H$, $C(O)H$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$,

CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, 和 I。在式 (I) 的另一个实施方案中, R^2为芳基 ;其中

R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、OR^4、SO_2R^4、F、Cl、和 I。在式 (I) 的另一个实施方案中, R^2为芳基 ;其中 R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、OR^4、和 SO_2R^4。在式 (I) 的另一个实施方案中, R^2为苯基 ;其中 R^2中的苯基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、OR^4、和 SO_2R^4。

[0082] 在式 (I) 的另一个实施方案中, R^2为 5-6 元杂芳基 ;其中 R^2中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、OR^4、SO_2R^4、F、Cl、和 I。在式 (I) 的另一个实施方案中, R^2为 5-6 元杂芳基 ;其中 R^2中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、OR^4、和 SO_2R^4。在式 (I) 的另一个实施方案中, R^2为呋喃基或噻吩基 ;其中 R^2中的呋喃基和噻吩基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、OR^4、和 SO_2R^4。

[0083] 在式 (I) 的一个实施方案中, R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 :R^7, OR^7, SR^7, $S(O)R^7$,

SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$,

$NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$,

$NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$,

$C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2,

SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH,

$CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (I) 的另一个实施方案中, R^4在每次出现时为杂环基。

[0084] 在式 (I) 的一个实施方案中, R^4中的杂环基各自任选被一个或多个独立地选自以下的取代基取代 :R^{10}, OR^{10}, SR^{10},

$S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$,

$NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$,

$NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$,

$C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$,

$C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$,

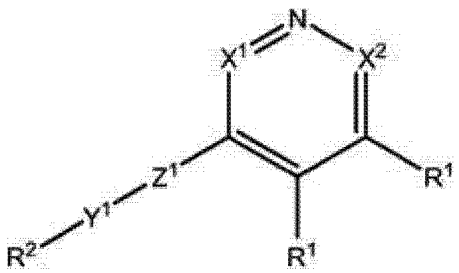
$C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I ;R^{10}在每次出现时

独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10} 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br

和 I；其中 R^{10} 中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；R^{11} 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11} 中的烷基、烯基、和炔基各自任选被烷氧基取代；其中 R^{11} 中的芳基、杂环基、环烷基、和环烯基各自任选被烷基或烷氧基取代；且 R^{12} 在每次出现时为独立选择的烷基。在式 (I) 的另一个实施方案中，R^4 中的杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、F、Cl、Br 和 I；R^{10} 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10} 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10} 中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl；R^{11} 在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11} 中的烷基各自任选被烷氧基或芳基取代；其中 R^{11} 中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl；R^{12} 在每次出现时独立地选自烷基和芳基；且 R^{13} 在每次出现时独立地选自烷基、和杂环基。

[0085] 本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式 (I)



式 (I)；

其中

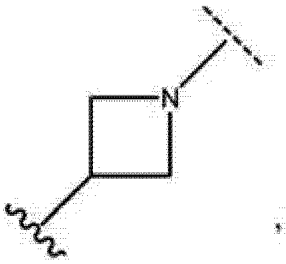
X^1 为 N 且 X^2 为 CR^1；或

X^1为 CR^1且 X^2为 N；或

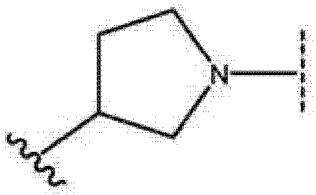
X^1为 CR^1且 X^2为 CR^1；

Y^1为 C(O)NH、或 NHC(O)；

Z^1为



，或



；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点；

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、和 F；

R^2为芳基或 5-6 元杂芳基，其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、SO_2R^4、和 OR^4；

R^4在每次出现时为杂环基；

其中由 R^4表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、C(O)R^{10}、C(O)C(O)R^{10}、和 CO(O)R^{10}；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、NHC(O)R^{11}、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代：R^{12}、OR^{12}、C(O)R^{12}、OH、CN、CF_3、OCF_3、F、和 Cl；

R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、C(O)OR^{13}、OCF_3、CF_3、F、和 Cl；

R^{12}在每次出现时独立地选自烷基、和芳基；和

R^{13}在每次出现时独立地选自烷基、和杂环基。

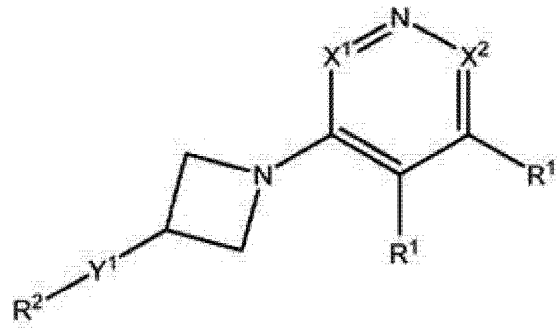
[0086] 仍另一个实施方案涉及具有式 (I) 的化合物，其包括实施例

1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,

254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613，及其药学上可接受的盐。

[0087] 式(II)的实施方案

在另一个方面，本发明提供式(II)的化合物



(II);

及其药学上可接受的盐；其中X^1、X^2、Y^1、R^1、和R^2如本文式(I)中所述。

[0088] 本发明的一个实施方案涉及式(II)的化合物及其药学上可接受的盐；

其中

X^1为N且X^2为CR^1；或

X^1为CR^1且X^2为N；或

X^1为CR^1且X^2为CR^1；

Y^1为C(O)NH、或NHC(O)；

R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br和I；

R^2独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：

R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$,

$OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$,

$NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$,

$NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$,

$C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, $C(O)H$, $C(O)OH$,

$C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br

和 I；其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4, OR^4, SR^4, $S(O)R^4$,

SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$,

$NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$,

$NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$,

$C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, $C(O)H$,

$C(O)OH$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl,

和 I；

R^3在每次出现时独立地选自烷基、烯基、炔基、芳基、环烷基、环烯基、和杂环基；其中 R^3中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$,

$OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$,

$NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$,

$NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, $C(O)NHOH$,

$C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, $C(O)H$,

$C(O)OH$, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F,

Cl, Br 和 I；其中 R^3中的芳基、环烷基、环烯基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：

R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$,

$NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^5S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$,

$NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^6)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$,

$C(O)NHR^6$, $C(O)N(R^6)_2$, $C(O)NHOH$, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$,

SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$,

$CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$,

$OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$,

$NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$,

$NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$,

$C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I ;

R^5在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^5中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 : R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), C(O)OH, N_3, CN, NH_2, F, Cl, Br 和 I ;

R^6在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^6中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 : R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), C(O)OH, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br 和 I ;

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;

R^8在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;

R^9在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;

其中由 R^4、R^5、R^6、R^7、R^8、和 R^9表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代 : R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I ;

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 : R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I ;其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代 : R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$,

$NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br 和 I；

R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中

R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

R^{13}在每次出现时独立地选自烷基、烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0089] 在式（II）的一个实施方案中，X^1为 N 且 X^2为 CR^1；或 X^1为 CR^1且 X^2为 N；或 X^1为 CR^1且 X^2为 CR^1。在式（II）的另一个实施方案中，X^1为 N 且 X^2为 CR^1。在式（II）的另一个实施方案中，X^1为 CR^1且 X^2为 N。在式（II）的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1。

[0090] 在式（II）的一个实施方案中，R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式（II）的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式（II）的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、和 F。在式（II）的另一个实施方案中，R^1在每次出现时为氢。

[0091] 在式（II）的一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式（II）的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、CL、Br 和 I。在式（II）的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、和 F。在式（II）的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时为氢。

[0092] 在式（II）的一个实施方案中，Y^1为 C(O)NH、或 NHC(O)。在式（II）的另一个实施方案中，Y^1为 C(O)NH。在式（II）的另一个实施方案中，Y^1为 NHC(O)。

[0093] 在式（II）的一个实施方案中，R^2独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$, $OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：

R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$,

$C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, 和 I。在式 (II) 的另一个实施方案中, R^2为芳基 ; 其中

R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代 : R^4、OR^4、SO_2R^4、F、Cl、和 I。在式 (II) 的另一个实施方案中, R^2为芳基 ; 其中 R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代 : R^4、OR^4、和 SO_2R^4。在式 (II) 的另一个实施方案中, R^2为苯基 ; 其中 R^2中的苯基各自任选被一个或多个独立地选自以下的取代基取代 : R^4、OR^4、和 SO_2R^4。

[0094] 在式 (II) 的另一个实施方案中, R^2为 5-6 元杂芳基 ; 其中 R^2中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代 : R^4、OR^4、SO_2R^4、F、Cl、和 I。在式 (II) 的另一个实施方案中, R^2为 5-6 元杂芳基 ; 其中 R^2中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代 : R^4、OR^4、和 SO_2R^4。在式 (II) 的另一个实施方案中, R^2为呋喃基或噻吩基 ; 其中 R^2中的呋喃基和噻吩基各自任选被一个或多个独立地选自以下的取代基取代 : R^4、OR^4、和 SO_2R^4。

[0095] 在式 (II) 的一个实施方案中, R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ; 其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 : R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (II) 的另一个实施方案中, R^4在每次出现时为杂环基。

[0096] 在式 (II) 的一个实施方案中, R^4中的杂环基各自任选被一个或多个独立地选自以下的取代基取代 : R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I ; R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ; 其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 :

R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, C(O)NHOH, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, C(O)H, C(O)OH,

$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，CNOH，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br

和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}，OR^{12}，

SR^{12}，$S(O)R^{12}$，SO_2R^{12}，$C(O)R^{12}$，$CO(O)R^{12}$，$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_2，NHR^{12}，$N(R^{12})_2$，

$NHC(O)R^{12}$，$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，

$NHC(O)NH_2$，$NHC(O)NHR^{12}$，$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，

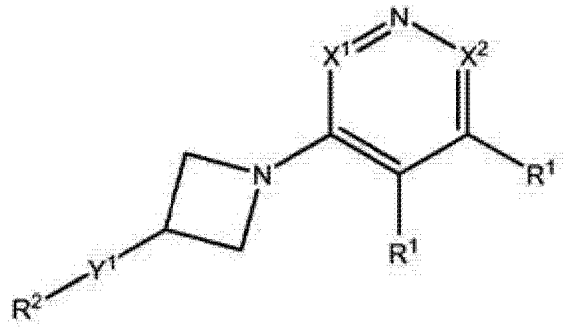
$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，

$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，$SO_2N(R^{12})_2$，C(O)H，C(O)OH，$C(N)NH_2$，

$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被烷基或烷氧基取代；且 R^{12}在每次出现时为独立选择的烷基。在式 (II) 的另一个实施方案中，R^4中的杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、F、Cl、Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl；

R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl；R^{12}在每次出现时独立地选自烷基和芳基；且 R^{13}在每次出现时独立地选自烷基、和杂环基。

[0097] 本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式 (II)



式 (II)；

其中

X^1为 N 且 X^2为 CR^1；或

X^1为 CR^1且 X^2为 N；或

X^1为 CR^1且 X^2为 CR^1；

Y^1为 C(O)NH、或 NHC(O)；

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、和 F；

R^2为芳基或 5-6 元杂芳基，其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独

立地选自以下的取代基取代：R^4、SO_2R^4、和 OR^4；

R^4在每次出现时为杂环基；

其中由 R^4表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$C(O)C(O)R^{10}$、和 $CO(O)R^{10}$；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代：R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl；

R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl；

R^{12}在每次出现时独立地选自烷基、和芳基；和

R^{13}在每次出现时独立地选自烷基、和杂环基。

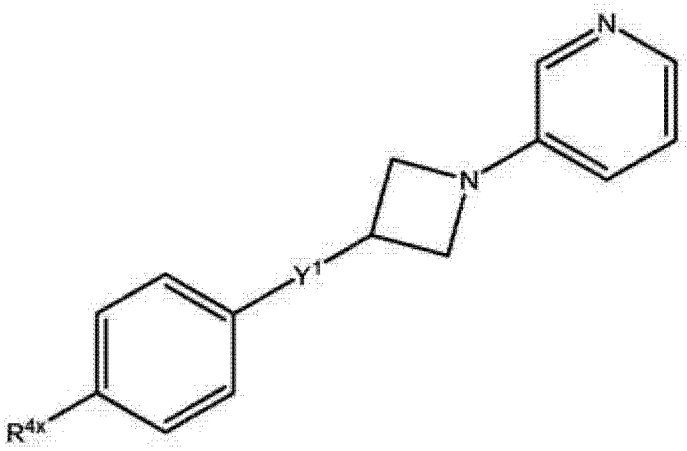
[0098] 仍另一个实施方案涉及具有式 (II) 的化合物，其包括实施例

1,2,3,4,5,6,7,10,20,21,22,23,24,25,26,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,

517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,609,610,611,612,613,及其药学上可接受的盐。

[0099] 式(III)的实施方案

在另一个方面,本发明提供式(III)的化合物



(III);

及其药学上可接受的盐;其中当式(I)中R^2为芳基时,Y^1如本文式(I)中所述且R^{4x}如本文对R^2上的取代基所描述的。

[0100] 本发明的一个实施方案涉及式(III)的化合物或其药学上可接受的盐;

其中

Y^1为C(O)NH、或NHC(O);

R^{4x}独立地选自R^4,OR^4,SR^4,$S(O)R^4$,

SO_2R^4,$C(O)R^4$,$OC(O)OR^4$,NH_2,NHR^4,$N(R^4)_2$,$NHC(O)R^4$,$NR^4C(O)R^4$,$NHS(O)_2R^4$,

$NR^4S(O)_2R^4$,$NHC(O)OR^4$,$NR^4C(O)OR^4$,$NHC(O)NH_2$,$NHC(O)NHR^4$,$NHC(O)N(R^4)_2$,

$NR^4C(O)NHR^4$,$NR^4C(O)N(R^4)_2$,$C(O)NH_2$,$C(O)NHR^4$,$C(O)N(R^4)_2$,C(O)NHOH,

$C(O)NHOR^4$,$C(O)NHSO_2R^4$,$C(O)NR^4SO_2R^4$,SO_2NH_2,SO_2NHR^4,$SO_2N(R^4)_2$,C(O)H,

C(O)OH,$C(N)NH_2$,$C(N)NHR^4$,$C(N)N(R^4)_2$,CNOH,$CNOCH_3$,OH,CN,N_3,NO_2,F,Cl,

和I;

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基;其中R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代:

R^7,OR^7,SR^7,$S(O)R^7$,SO_2R^7,$C(O)R^7$,$CO(O)R^7$,

$OC(O)R^7$,$OC(O)OR^7$,NH_2,NHR^7,$N(R^7)_2$,$NHC(O)R^7$,$NR^7C(O)R^7$,$NHS(O)_2R^7$,

$NR^7S(O)_2R^7$,$NHC(O)OR^7$,$NR^7C(O)OR^7$,$NHC(O)NH_2$,$NHC(O)NHR^7$,$NHC(O)N(R^7)_2$,

$NR^7C(O)NHR^7$,$NR^7C(O)N(R^7)_2$,$C(O)NH_2$,$C(O)NHR^7$,$C(O)N(R^7)_2$,C(O)NHOH,

$C(O)NHOR^7$,$C(O)NHSO_2R^7$,$C(O)NR^7SO_2R^7$,SO_2NH_2,SO_2NHR^7,$SO_2N(R^7)_2$,C(O)H,

C(O)OH,$C(N)NH_2$,$C(N)NHR^7$,$C(N)N(R^7)_2$,CNOH,$CNOCH_3$,OH,(O),CN,N_3,NO_2,F,

Cl，Br 和 I；

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中由 R^4和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：

R^{10}，OR^{10}，SR^{10}，$S(O)R^{10}$，SO_2R^{10}，$C(O)R^{10}$，$CO(O)R^{10}$，$OC(O)R^{10}$，$OC(O)OR^{10}$，$C(O)C(O)R^{10}$，NH_2，NHR^{10}，$N(R^{10})_2NHC(O)R^{10}$，$NR^{10}C(O)R^{10}$，$NHS(O)_2R^{10}$，$NR^{10}S(O)_2R^{10}$，$NHC(O)OR^{10}$，$NR^{10}C(O)OR^{10}$，$NHC(O)NH_2$，$NHC(O)NHR^{10}$，$NHC(O)N(R^{10})_2$，$NR^{10}C(O)NHR^{10}$，$NR^{10}C(O)N(R^10)_2$，$C(O)NH_2$，$C(O)NHR^{10}$，$C(O)N(R^{10})_2$，$C(O)NHOH$，$C(O)NHOR^{10}$，$C(O)NHSO_2R^{10}$，$C(O)NR^{10}SO_2R^{10}$，SO_2NH_2，SO_2NHR^{10}，$SO_2N(R^{10})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{10}$，$C(N)N(R^{10})_2$，$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}，OR^{11}，SR^{11}，$S(O)R^{11}$，SO_2R^{11}，$C(O)R^{11}$，$CO(O)R^{11}$，$OC(O)R^{11}$，$OC(O)OR^{11}$，NH_2，NHR^{11}，$N(R^{11})_2$，$NHC(O)R^{11}$，$NR^{11}C(O)R^{11}$，$NHS(O)_2R^{11}$，$NR^{11}S(O)_2R^{11}$，$NHC(O)OR^{11}$，$NR^{11}C(O)OR^{11}$，$NHC(O)NH_2$，$NHC(O)NHR^{11}$，$NHC(O)N(R^{11})_2$，$NR^{11}C(O)NHR^{11}$，$NR^{11}C(O)N(R^{11})_2$，$C(O)NH_2$，$C(O)NHR^{11}$，$C(O)N(R^{11})_2$，$C(O)NHOH$，$C(O)NHOR^{11}$，$C(O)NHSO_2R^{11}$，$C(O)NR^{11}SO_2R^{11}$，SO_2NH_2，SO_2NHR^{11}，$SO_2N(R^{11})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，$CNOH$，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}，OR^{12}，SR^{12}，$S(O)R^{12}$，SO_2R^{12}，$C(O)R^{12}$，$CO(O)R^{12}$，$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_2，NHR^{12}，$N(R^{12})_2$，$NHC(O)R^{12}$，$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{11}$，$NR^{12}C(O)OR^{12}$，$NHC(O)NH_2$，$NHC(O)NHR^{12}$，$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，CF_3，OCF_3，F，Cl，Br 和 I；

R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

R^{13}在每次出现时独立地选自烷基、烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0101] 在式（III）的一个实施方案中，Y^1为 C(O)NH、或 NHC(O)。在式（III）的另一个实施方案中，Y^1为 C(O)NH。在式（III）的另一个实施方案中，Y^1为 NHC(O)。

[0102] 在式（III）的一个实施方案中，R^{4x}选自 R^4，

OR^4，SR^4，$S(O)R^4$，SO_2R^4，$C(O)R^4$，$OC(O)OR^4$，NH_2，NHR^4，$N(R^4)_2$，$NHC(O)R^4$，$NR^4C(O)R^4$，$NHS(O)_2R^4$，$NR^4S(O)_2R^4$，$NHC(O)OR^4$，$NR^4C(O)OR^4$，$NHC(O)NH_2$，$NHC(O)NHR^4$，

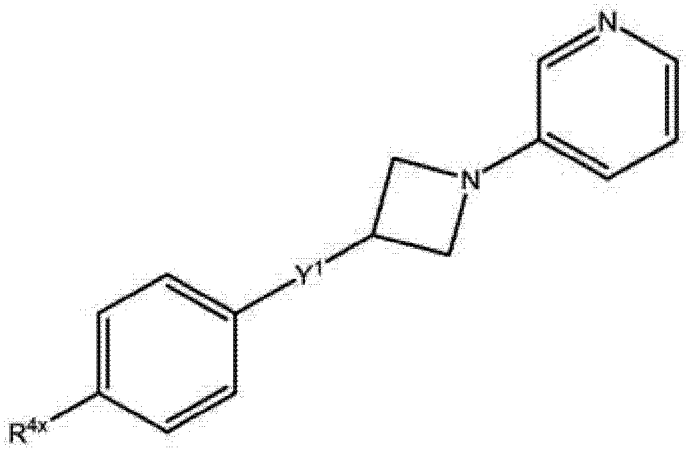
$NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$,
$C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$,
$C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2,
F, Cl, 和 I。在式 (III) 的另一个实施方案中, R^{4x}选自 R^4、OR^4、SO_2R^4、F、Cl、和 I。在式 (III) 的另一个实施方案中, R^{4x}选自 R^4、SO_2R^4、和 OR^4。

[0103] 在式 (III) 的一个实施方案中, R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 :R^7, OR^7, SR^7, $S(O)R^7$,
SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$,
$NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$,
$NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$,
$C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2,
SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$,
$CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (III) 的另一个实施方案中, R^4在每次出现时为杂环基。

[0104] 在式 (III) 的一个实施方案中, R^4中的杂环基各自任选被一个或多个独立地选自以下的取代基取代 :R^{10}, OR^{10},
SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$,
$NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$,
$NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$,
$C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$,
$C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$,
$C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I ;R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 :
R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$,
NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$,
$NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$,
$NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$,
$C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$,
$C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br
和 I ;其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代 :R^{12}, OR^{12},
SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$,
$NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$,
$NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$,
$C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$,
$C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$,
$C(N)NHR^{12}$, $C(N)N(R^{12})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I ;R^{11}在每次出现时独

立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11} 中的烷基、烯基、和炔基各自任选被烷氧基取代；其中 R^{11} 中的芳基、杂环基、环烷基、和环烯基各自任选被烷基或烷氧基取代；且 R^{12} 在每次出现时为独立选择的烷基。在式 (III) 的另一个实施方案中，R^4 中的杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、F、Cl、Br 和 I；R^{10} 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10} 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10} 中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl；R^{11} 在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11} 中的烷基各自任选被烷氧基或芳基取代；其中 R^{11} 中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl；R^{12} 在每次出现时独立地选自烷基和芳基；和 R^{13} 在每次出现时独立地选自烷基、和杂环基。

[0105] 本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式 (III)



式 (III)；

其中

Y^1 为 $C(O)NH$、或 $NHC(O)$；

R^{4x} 独立地选自 R^4、SO_2R^4、和 OR^4；

R^4 在每次出现时为杂环基；

其中由 R^4 表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$C(O)C(O)R^{10}$、和 $CO(O)R^{10}$；

R^{10} 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10} 中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10} 中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代：R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl；

R^{11} 在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11} 中的烷基各自任选被烷氧基或芳基取代；其中 R^{11} 中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl；

R^{12} 在每次出现时独立地选自烷基、和芳基；和

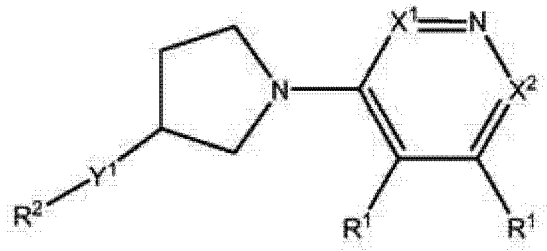
R^{13}在每次出现时独立地选自烷基、和杂环基。

[0106] 仍另一个实施方案涉及具有式 (III) 的化合物,其包括实施例

1,2,3,4,5,6,7,10,20,21,22,23,24,25,26,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,602,609,610,及其药学上可接受的盐。

[0107] 式 (IV) 的实施方案

在另一方面,本发明提供式 (IV) 的化合物



(IV);

及其药学上可接受的盐 ;其中 X^1、X^2、Y^1、R^1、和 R^2如本文对式 (I) 所述。

[0108] 本发明的一个实施方案涉及式 (IV) 的化合物及其药学上可接受的盐 ;

其中

X^1为 N 且 X^2为 CR^1;或

X^1为 CR^1且 X^2为 N ;或

X^1为 CR^1且 X^2为 CR^1;

Y^1为 C(O)NH、或 NHC(O) ;

R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I ;

R^2独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基 ;其中 R^2中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代 :

R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$,

$OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$,

$NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$,

$NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$,

$C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH,

$C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br

和 I ;其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代 :R^4, OR^4, SR^4, $S(O)R^4$,

SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$,

$NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$,

$NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$,
$C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, $C(O)H$,
$C(O)OH$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl,
和 I；

R^3在每次出现时独立地选自烷基、烯基、炔基、芳基、环烷基、环烯基、和杂环基；其中R^3中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$,
$OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$,
$NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$,
$NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, $C(O)NHOH$,
$C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SC_2NHR^5, $SO_2N(R^5)_2$, $C(O)H$,
$C(O)OH$, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F,
Cl, Br 和 I；其中R^3中的芳基、环烷基、环烯基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：

R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$,
$NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^5S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$,
$NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^5)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$,
$C(O)NHR^6$, $C(O)N(R^6)_2$, $C(O)NHOH$, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$,
SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$,
$CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$,
$OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$,
$NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$,
$NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$,
$C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$,
$C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F,
Cl, Br 和 I；

R^5在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中R^5中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$,
$C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$,
SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), $C(O)OH$, N_3, CN,
NH_2, F, Cl, Br 和 I；

R^6在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中R^6中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$,
$C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$,

SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), $C(O)OH$, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br 和 I ;

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;

R^8在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;

R^9在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;

其中由 R^4、R^5、R^6、R^7、R^8、和 R^9表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代 :R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_{2+}C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I ;

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 :R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I ;其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代 :R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br 和 I ;

R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代 ;其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代 :R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I ;

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;和

R^{13}在每次出现时独立地选自烷基、烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0109] 在式 (IV) 的一个实施方案中，X^1为 N 且 X^2为 CR^1;或 X^1为 CR^1且 X^2为 N ;或 X^1为 CR^1且 X^2为 CR^1。在式 (IV) 的另一个实施方案中，X^1为 N 且 X^2为 CR^1。在式 (IV) 的另一个实施方案中，X^1为 CR^1且 X^2为 N。在式 (IV) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1。

[0110] 在式(IV)的一个实施方案中，R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br和I。在式(IV)的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br和I。在式(VI)的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、和F。在式(VI)的另一个实施方案中，R^1在每次出现时为氢。

[0111] 在式(IV)的一个实施方案中，X^1为CR^1且X^2为CR^1；且R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br和I。在式(IV)的另一个实施方案中，X^1为CR^1且X^2为CR^1；且R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br和I。在式(IV)的另一个实施方案中，X^1为CR^1且X^2为CR^1；且R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、和F。在式(IV)的另一个实施方案中，X^1为CR^1且X^2为CR^1；且R^1在每次出现时为氢。

[0112] 在式(IV)的一个实施方案中，Y^1为C(O)NH、或NHC(O)。在式(IV)的另一个实施方案中，Y^1为C(O)NH。在式(IV)的另一个实施方案中，Y^1为NHC(O)。

[0113] 在式(IV)的一个实施方案中，R^2独立地选自C_4-C_6-烷基、C_4-C_6-烯基、C_4-C_6-炔基、芳基、和5-6元杂芳基；其中R^2中的C_4-C_6-烷基、C_4-C_6-烯基、和C_4-C_6-炔基各自被一个或多个独立地选自以下的取代基取代：R^3，OR^3，SR^3，$S(O)R^3$，

SO_2R^3，$C(O)R^3$，$CO(O)R^3$，$OC(O)R^3$，$OC(O)OR^3$，NH_2，NHR^3，$N(R^3)_2$，$NHC(O)R^3$，

$NR^3C(O)R^3$，$NHS(O)_2R^3$，$NR^3S(O)_2R^3$，$NHC(O)OR^3$，$NR^3C(O)OR^3$，$NHC(O)NH_2$，

$NHC(O)NHR^3$，$NHC(O)N(R^3)_2$，$NR^3C(O)NHR^3$，$NR^3C(O)N(R^3)_2$，$C(O)NH_2$，$C(O)NHR^3$，

$C(O)N(R^3)_2$，$C(O)NHOH$，$C(O)NHOR^3$，$C(O)NHSO_2R^3$，$C(O)NR^3SO_2R^3$，SO_2NH_2，

SO_2NHR^3，$SO_2N(R^3)_2$，C(O)H，C(O)OH，$C(N)NH_2$，$C(N)NHR^3$，$C(N)N(R^3)_2$，CNOH，

$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br和I；其中R^2中的芳基和5-6元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：

R^4，OR^4，SR^4，$S(O)R^4$，SO_2R^4，$C(O)R^4$，$OC(O)OR^4$，NH_2，NHR^4，

$N(R^4)_2$，$NHC(O)R^4$，$NR^4C(O)R^4$，$NHS(O)_2R^4$，$NR^4S(O)_2R^4$，$NHC(O)OR^4$，$NR^4C(O)OR^4$，

$NHC(O)NH_2$，$NHC(O)NHR^4$，$NHC(O)N(R^4)_2$，$NR^4C(O)NHR^4$，$NR^4C(O)N(R^4)_2$，$C(O)NH_2$，

$C(O)NHR^4$，$C(O)N(R^4)_2$，$C(O)NHOH$，$C(O)NHOR^4$，$C(O)NHSO_2R^4$，$C(O)NR^4SO_2R^4$，

SO_2NH_2，SO_2NHR^4，$SO_2N(R^4)_2$，C(O)H，C(O)OH，$C(N)NH_2$，$C(N)NHR^4$，$C(N)N(R^4)_2$，

CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，和I。在式(IV)的另一个实施方案中，R^2为芳基；其中R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、F、Cl、和I。在式(IV)的另一个实施方案中，R^2为芳基；其中R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、和SO_2R^4。在式(IV)的另一个实施方案中，R^2为苯基；其中R^2中的苯基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、和SO_2R^4。

[0114] 在式(IV)的另一个实施方案中，R^2为5-6元杂芳基；其中R^2中的5-6元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、F、Cl、和I。在式(IV)的另一个实施方案中，R^2为5-6元杂芳基；其中R^2中的5-6元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、和SO_2R^4。在式(IV)的另一个实施方案中，R^2为呋喃基或噻吩基；其中R^2中的呋喃基和噻吩基各自任选被一个或多个独立地选自以下的取

代基取代：R^4、OR^4、和 SO_2R^4。

[0115] 在式（IV）的一个实施方案中，R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^7，OR^7，SR^7，$S(O)R^7$，

SO_2R^7，$C(O)R^7$，$CO(O)R^7$，$OC(O)R^7$，$OC(O)OR^7$，NH_2，NHR^7，$N(R^7)_2$，$NHC(O)R^7$，

$NR^7C(O)R^7$，$NHS(O)_2R^7$，$NR^7S(O)_2R^7$，$NHC(O)OR^7$，$NR^7C(O)OR^7$，$NHC(O)NH_2$，

$NHC(O)NHR^7$，$NHC(O)N(R^7)_2$，$NR^7C(O)NHR^7$，$NR^7C(O)N(R^7)_2$，$C(O)NH_2$，$C(O)NHR^7$，

$C(O)N(R^7)_2$，$C(O)NHOH$，$C(O)NHOR^7$，$C(O)NHSO_2R^7$，$C(O)NR^7SO_2R^7$，SO_2NH_2，

SO_2NHR^7，$SO_2N(R^7)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^7$，$C(N)N(R^7)_2$，CNOH，

$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I。在式（IV）的另一个实施方案中，R^4在每次出现时为杂环基。

[0116] 在式（IV）的一个实施方案中，R^4中的杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{10}，OR^{10}，

SR^{10}，$S(O)R^{10}$，SO_2R^{10}，$C(O)R^{10}$，$CO(O)R^{10}$，$OC(O)R^{10}$，$OC(O)OR^{10}$，NH_2，NHR^{10}，$N(R^{10})_2$，

$NHC(O)R^{10}$，$NR^{10}C(O)R^{10}$，$NHS(O)_2R^{10}$，$NR^{10}S(O)_2R^{10}$，$NHC(O)OR^{10}$，$NR^{10}C(O)OR^{10}$，

$NHC(O)NH_2$，$NHC(O)NHR^{10}$，$NHC(O)N(R^{10})_2$，$NR^{10}C(O)NHR^{10}$，$NR^{10}C(O)N(R^{10})_2$，

$C(O)NH_2$，$C(O)NHR^{10}$，$C(O)N(R^{10})_2$，$C(O)NHOH$，$C(O)NHOR^{10}$，$C(O)NHSO_2R^{10}$，

$C(O)NR^{10}SO_2R^{10}$，SO_2NH_2，SO_2NHR^{10}，$SO_2N(R^{10})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，

$C(N)NHR^{10}$，$C(N)N(R^{10})_2$，CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}，OR^{11}，SR^{11}，$S(O)R^{11}$，SO_2R^{11}，$C(O)R^{11}$，$CO(O)R^{11}$，$OC(O)R^{11}$，$OC(O)OR^{11}$，

NH_2，NHR^{11}，$N(R^{11})_2$，$NHC(O)R^{11}$，$NR^{11}C(O)R^{11}$，$NHS(O)_2R^{11}$，$NR^{11}S(O)_2R^{11}$，$NHC(O)OR^{11}$，

$NR^{11}C(O)OR^{11}$，$NHC(O)NH_2$，$NHC(O)NHR^{11}$，$NHC(O)N(R^{11})_2$，$NR^{11}C(O)NHR^{11}$，

$NR^{11}C(O)N(R^{11})_2$，$C(O)NH_2$，$C(O)NHR^{11}$，$C(O)N(R^{11})_2$，$C(O)NHOH$，$C(O)NHOR^{11}$，

$C(O)NHSO_2R^{11}$，$C(O)NR^{11}SO_2R^{11}$，SO_2NH_2，SO_2NHR^{11}，$SO_2N(R^{11})_2$，$C(O)H$，$C(O)OH$，

$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，CNOH，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}，OR^{12}，

SR^{12}，$S(O)R^{12}$，SO_2R^{12}，$C(O)R^{12}$，$CO(O)R^{12}$，$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_2，NHR^{12}，$N(R^{12})_2$，

$NHC(O)R^{12}$，$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，

$NHC(O)NH_2$，$NHC(O)NHR^{12}$，$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，

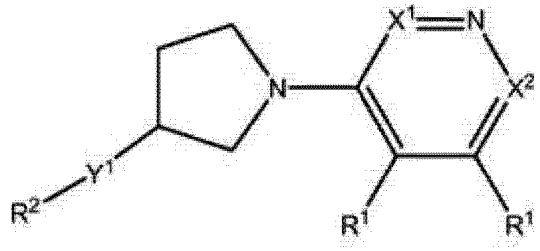
$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，

$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，

$C(N)NHR^{12}C(N)N(R^{12})_2$，CNOH，$CNOCH_3$，OH，CN，$N_3$，$NO_2$，F，Cl，Br 和 I；$R^{11}$在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被烷基或烷氧基取代；且 R^{12}在每次出现时为独立选择的烷基。在式（IV）的另一个实施方案中，R^4中的杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、C(O)

C(O)R^{10}、F、Cl、Br 和 I ;R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基 ;其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 :R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F ;其中 R^{10}中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代 :R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl ;R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基 ;其中 R^{11}中的烷基各自任选被烷氧基或芳基取代 ;其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代 :R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl ;R^{12}在每次出现时独立地选自烷基和芳基 ;和 R^{13}在每次出现时独立地选自烷基、和杂环基。

[0117] 本发明的一个实施方案涉及化合物或其药学上可接受的盐,其用作 NAMPT 的抑制剂,所述化合物具有式 (IV)



式 (IV);

其中

X^1为 N 且 X^2为 CR^1;或

X^1为 CR^1且 X^2为 N ;或

X^1为 CR^1且 X^2为 CR^1;

Y^1为 C(O)NH、或 NHC(O) ;

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、和 F ;

R^2为芳基或 5-6 元杂芳基,其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、SO_2R^4、和 OR^4;

R^4在每次出现时为杂环基 ;

其中由 R^4表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代 :R^{10}、$C(O)R^{10}$、$C(O)C(O)R^{10}$、和 $CO(O)R^{10}$;

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基 ;其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代 :R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F ;其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代 :R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl ;

R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基 ;其中 R^{11}中的烷基各自任选被烷氧基或芳基取代 ;其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代 :R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl ;

R^{12}在每次出现时独立地选自烷基、和芳基 ;和

R^{13}在每次出现时独立地选自烷基、和杂环基 ;

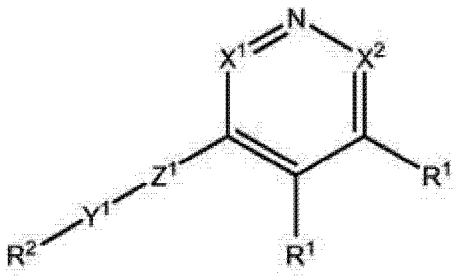
条件是

当 X^1为 CR^1且 X^2为 CR^1时 ;R^1为氢 ;Y^1为 NHC(O) ;且 R^2为吡咯基 ;所述 R^2中的吡咯基未被两个烷基取代。

[0118] 仍另一个实施方案涉及具有式 (IV) 的化合物，其包括实施例 8、9、11、12、13、14、15、16、17、18、19、27、28、141、142、204、310、311、312、313，及其药学上可接受的盐。

[0119] 式 (IA) 的实施方案

因此，本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式 (IA)



式 (IA)；

其中

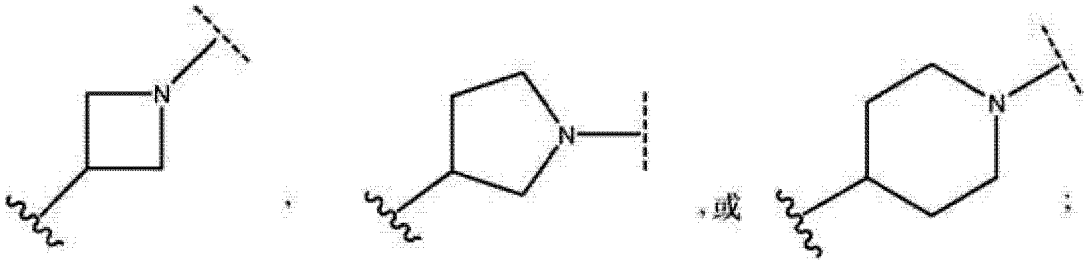
X^1 为 N 且 X^2 为 CR^1；或

X^1 为 CR^1 且 X^2 为 N；或

X^1 为 CR^1 且 X^2 为 CR^1；

Y^1 为 C(O)NH、或 NHC(O)；

Z^1 为



其中 表示连接至 Y^1 的点且 表示连接至含氮杂芳基的点；

R^1 在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I；

R^2 独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2 中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：

R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$,

$OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$,

$NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$,

$NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$,

$C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH,

$C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br

和 I；其中 R^2 中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4, OR^4, SR^4, $S(O)R^4$,

SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$,

$NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^2)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, 和 I；

R^3在每次出现时独立地选自烷基、烯基、炔基、芳基、环烷基、环烯基、和杂环基；其中 R^3中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, $C(O)NHOH$, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中 R^3中的芳基、环烷基、环烯基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：

R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^5S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^5)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, $C(O)NHOH$, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；

R^5在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^5中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), $C(O)OH$, N_3, CN, NH_2, F, Cl, Br 和 I；

R^6在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^6中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$,

$C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), $C(O)OH$, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br 和 I ;

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;

R^8在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;

R^9在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;

其中由 R^4、R^5、R^6、R^7、R^8、和 R^9表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代 :R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I ;

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 :$R^{11}OR^{11}$, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I ;其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代 :R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br 和 I ;

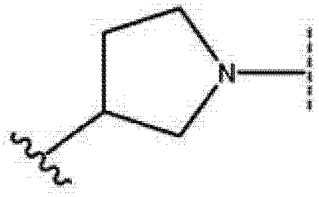
R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代 ;其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代 :R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I ;

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;和

R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;

条件是

当 X^1 为 CR^1 且 X^2 为 CR^1 时；R^1 为氢；Y^1 为 NHC(O)；Z^1 为



；且 R^2 为吡咯基；所述 R^2 中的吡咯基未被两个烷基取代。

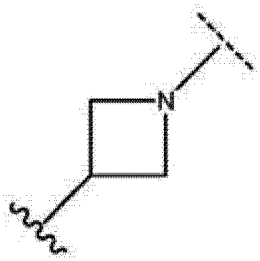
[0120] 在式 (IA) 的一个实施方案中，X^1 为 N 且 X^2 为 CR^1；或 X^1 为 CR^1 且 X^2 为 N；或 X^1 为 CR^1 且 X^2 为 CR^1。在式 (IA) 的另一个实施方案中，X^1 为 N 且 X^2 为 CR^1。在式 (IA) 的另一个实施方案中，X^1 为 CR^1 且 X^2 为 N。在式 (IA) 的另一个实施方案中，X^1 为 CR^1 且 X^2 为 CR^1。

[0121] 在式 (IA) 的一个实施方案中，R^1 在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (IA) 的另一个实施方案中，R^1 在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IA) 的另一个实施方案中，R^1 在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IA) 的另一个实施方案中，R^1 在每次出现时为氢。

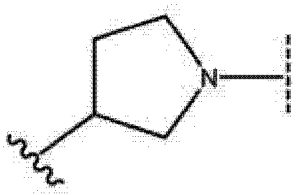
[0122] 在式 (IA) 的一个实施方案中，X^1 为 CR^1 且 X^2 为 CR^1；且 R^1 在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (IA) 的另一个实施方案中，X^1 为 CR^1 且 X^2 为 CR^1；且 R^1 在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IA) 的另一个实施方案中，X^1 为 CR^1 且 X^2 为 CR^1；且 R^1 在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IA) 的另一个实施方案中，X^1 为 CR^1 且 X^2 为 CR^1；且 R^1 在每次出现时为氢。

[0123] 在式 (IA) 的一个实施方案中，Y^1 为 C(O)NH、或 NHC(O)。在式 (IA) 的另一个实施方案中，Y^1 为 C(O)NH。在式 (IA) 的另一个实施方案中，Y^1 为 NHC(O)。

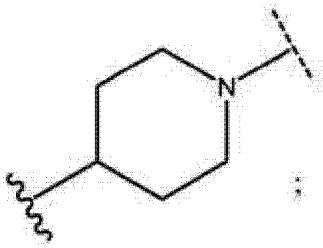
[0124] 在式 (IA) 的一个实施方案中，Z^1 为



，

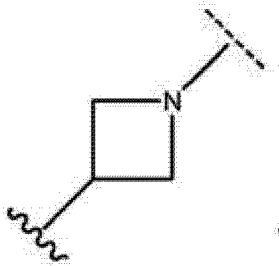


，或

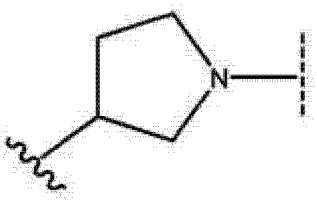


；

其中  表示连接至 Y^1 的点且  表示连接至含氮杂芳基的点。在式 (IA) 的另一个实施方案中，Z^1 为

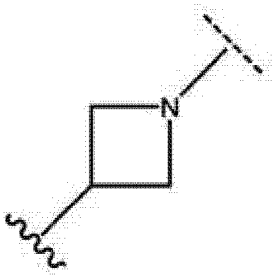


，或

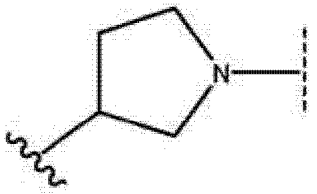


；其中 表示连接至 Y^1 的点

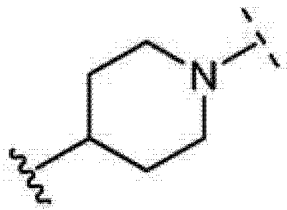
且 表示连接至含氮杂芳基的点。在式 (IA) 的另一个实施方案中，Z^1为



；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。在式 (IA) 的另一个实施方案中，Z^1为



；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。在式 (IA) 的另一个实施方案中，Z^1为



；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。

[0125] 在式 (IA) 的一个实施方案中，R^2独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：R^3，OR^3，SR^3，$S(O)R^3$，

SO_2R^3，$C(O)R^3$，$CO(O)R^3$，$OC(O)R^3$，$OC(O)OR^3$，NH_2，NHR^3，$N(R^3)_2$，$NHC(O)R^3$，

$NR^3C(O)R^3$，$NHS(O)_2R^3$，$NR^3S(O)_2R^3$，$NHC(O)OR^3$，$NR^3C(O)OR^3$，$NHC(O)NH_2$，

$NHC(O)NHR^3$，$NHC(O)N(R^3)_2$，$NR^3C(O)NHR^3NR^3C(O)N(R^3)_2$，$C(O)NH_2$，$C(O)NHR^3$，

$C(O)N(R^3)_2$，$C(O)NHOH$，$C(O)NHOR^3$，$C(O)NHSO_2R^3$，$C(O)NR^3SO_2R^3$，SO_2NH_2，

SO_2NHR^3，$SO_2N(R^3)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^3$，$C(N)N(R^3)_2$，CNOH，

$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：

R^4，OR^4，SR^4，$S(O)R^4$，SO_2R^4，$C(O)R^4$，$OC(O)OR^4$，NH_2，NHR^4，

$N(R^4)_2$，$NHC(O)R^4$，$NR^4C(O)R^4$，$NHS(O)_2R^4$，$NR^4S(O)_2R^4$，$NHC(O)OR^4$，$NR^4C(O)OR^4$，

$NHC(O)NH_2$，$NHC(O)NHR^4$，$NHC(O)N(R^4)_2$，$NR^4C(O)NHR^4$，$NR^4C(O)N(R^4)_3$，$C(O)NH_2$，

$C(O)NHR^4$，$C(O)N(R^4)_2$，$C(O)NHOH$，$C(O)NHOR^4$，$C(O)NHSO_2R^4$，$C(O)NR^4SO_2R^4$，

SO_2NH_2，SO_3NHR^4，$SO_2N(R^4)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^4$，$C(N)N(R^4)_2$，

CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，和 I。在式 (IA) 的另一个实施方案中，R^2为芳基；其中 R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、F、Cl、和 I。在式 (IA) 的另一个实施方案中，R^2为芳基；其中 R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、和 F。在式 (IA) 的另一个实施方案中，R^2为

苯基；其中 R^2 中的苯基各自任选被一个或多个独立地选自以下的取代基取代：

R^4、OR^4、SO_2R^4、和 F。在式（IA）的另一个实施方案中，R^2 为苯基；其中 R^2 中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和 SO_2R^4。

[0126] 在式（IA）的另一个实施方案中，R^2 为 5-6 元杂芳基；其中 R^2 中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、F、Cl、和 I。在式（IA）的另一个实施方案中，R^2 为 5-6 元杂芳基；其中 R^2 中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、和 F。在式（IA）的另一个实施方案中，R^2 为呋喃基或噻吩基；其中 R^2 中的呋喃基和噻吩基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、和 F。

[0127] 在式（IA）的一个实施方案中，R^4 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^7，OR^7，SR^7，$S(O)R^7$，

SO_2R^7，$C(O)R^7$，$CO(O)R^7$，$OC(O)R^7$，$OC(O)OR^7$，NH_2，NHR^7，$N(R^7)_2$，$NHC(O)R^7$，

$NR^7C(O)R^7$，$NHS(O)_2R^7$，$NR^7S(O)_2R^7$，$NHC(O)OR^7$，$NR^7C(O)OR^7$，$NHC(O)NH_2$，

$NHC(O)NHR^7$，$NHC(O)N(R^7)_2$，$NR^7C(O)NHR^7$，$NR^7C(O)N(R^7)_2$，$C(O)NH_2$，$C(O)NHR^7$，

$C(O)N(R^7)_2$，$C(O)NHOH$，$C(O)NHOR^7$，$C(O)NHSO_2R^7$，$C(O)NR^7SO_2R^7$，SO_2NH_2，

SO_2NHR^7，$SO_2N(R^7)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^7$，$C(N)N(R^7)_2$，CNOH，

$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I。在式（IA）的另一个实施方案中，R^4 在每次出现时为烷基或杂环基。

[0128] 在式（IA）的一个实施方案中，R^4 中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7，OR^7，SR^7，

$S(O)R^7$，SO_2R^7，$C(O)R^7$，$CO(O)R^7$，$OC(O)R^7$，$OC(O)OR^7$，NH_2，NHR^7，$N(R^7)_2$，$NHC(O)R^7$，

$NR^7C(O)R^7$，$NHS(O)_2R^7$，$NR^7S(O)_2R^7$，$NHC(O)OR^7$，$NR^7C(O)OR^7NHC(O)NH_2$，

$NHC(O)NHR^7$，$NHC(O)N(R^7)_2$，$NR^7C(O)NHR^7$，$NR^7C(O)N(R^7)_2$，$C(O)NH_2$，$C(O)NHR^7$，

$C(O)N(R^7)_2$，$C(O)NHOH$，$C(O)NHOR^7$，$C(O)NHSO_2R^7$，$C(O)NR^7SO_2R^7$，SO_2NH_2，

SO_2NHR^7，$SO_2N(R^7)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^7$，$C(N)N(R^7)_2$，CNOH，

$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I。在式（IA）的另一个实施方案中，R^4 中的烷基各自任选被一个 R^7 取代。

[0129] 在式（IA）的一个实施方案中，R^7 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。在式（IA）的另一个实施方案中，R^7 在每次出现时为杂环基。

[0130] 在式（IA）的一个实施方案中，R^4 和 R^7 中的杂环基各自独立地任选被一个或多个独立地选自以下的取代基取代：

R^{10}，OR^{10}，SR^{10}，$S(O)R^{10}$，SO_2R^{10}，$C(O)R^{10}$，$CO(O)R^{10}$，$OC(O)R^{10}$，$OC(O)OR^{10}$，

NH_2，NHR^{10}，$N(R^{10})_2$，$NHC(O)R^{10}$，$NR^{10}C(O)R^{10}$，$NHS(O)_2R^{10}$，$NR^{10}S(O)_2R^{10}$，$NHC(O)OR^{10}$，

$NR^{10}C(O)OR^{10}$，$NHC(O)NH_2$，$NHC(O)NHR^{10}$，$NHC(O)N(R^{10})_2$，$NR^{10}C(O)NHR^{10}$，

$NR^{10}C(O)N(R^{10})_2$，$C(O)NH_2$，$C(O)NHR^{10}$，$C(O)N(R^{10})_2$，$C(O)NHOH$，$C(O)NHOR^{10}$，

$C(O)NHSO_2R^{10}$，$C(O)NR^{10}SO_2R^{10}$，SO_2NH_2，SO_2NHR^{10}，$SO_2N(R^{10})_2$，$C(O)H$，$C(O)OH$，

$C(N)NH_2$，$C(N)NHR^{10}$，$C(N)N(R^{10})_2$，CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br

和 I；R^{10} 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

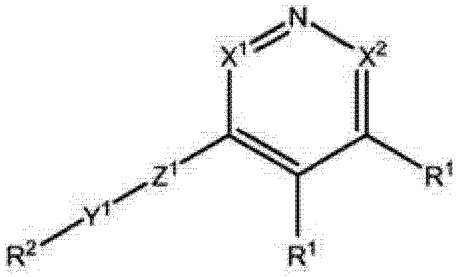
其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$,
$OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{13}$, $NR^{11}S(O)_2R^{11}$,
$NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$,
$NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$,
$C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$,
$C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F,
Cl, Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：

R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12},
$N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$,
$NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$,
$NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$,
$C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$,
$C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br
和 I；R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；
其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0131] 在式（IA）的另一个实施方案中，R^4和 R^7中的杂环基各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、OH、F、Cl、Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl；R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、CF_3、F、和 Cl；R^{12}在每次出现时独立地选自烷基和芳基；和 R^{13}在每次出现时独立地选自烷基和卤代烷基。

[0132] 本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式（IA）



式 (IA);

其中

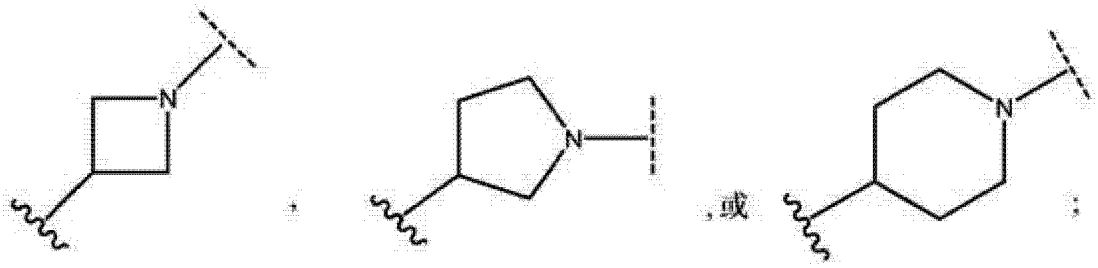
X^1为 N 且 X^2为 CR^1;或

X^1为 CR^1且 X^2为 N;或

X^1为 CR^1且 X^2为 CR^1;

Y^1为 C(O)NH、或 NHC(O);

Z^1为



其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点;

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、Cl、和 F;

R^2为芳基或 5-6 元杂芳基,其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代:R^4、SO_2R^4、OR^4、和 F;

R^4在每次出现时为烷基或杂环基。其中 R^4中的烷基各自任选被 R^7取代;

R^7在每次出现时独立地为杂环基;

其中由 R^4和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代:

R^{10}、C(O)R^{10}、C(O)C(O)R^{10}、CO(O)R^{10}、OH 和 F;

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基;其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代:R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、NHC(O)R^{11}、$NHS(O)_2R^{11}$、OH、NO_2、和 F;其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代:R^{12}、OR^{12}、C(O)R^{12}、OH、CN、CF_3、OCF_3、F、和 Cl;

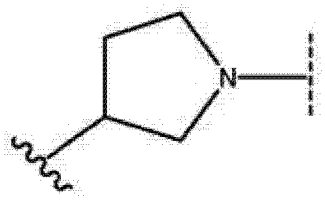
R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基;其中 R^{11}中的烷基各自任选被烷氧基或芳基取代;其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代:R^{13}、C(O)OR^{13}、OCF_3、CF_3、F、和 Cl;

R^{12}在每次出现时独立地选自烷基、和芳基;和

R^{13}在每次出现时独立地选自烷基、卤代烷基、和杂环基;

条件是

当 X^1 为 CR^1 且 X^2 为 CR^1 时；R^1 为氢；Y^1 为 NHC(O)；Z^1 为



；且 R^2 为吡咯基；所述 R^2 中的吡咯基未被两个烷基取代。

[0133] 仍另一个实施方案涉及具有式 (IA) 的化合物，其包括实施例

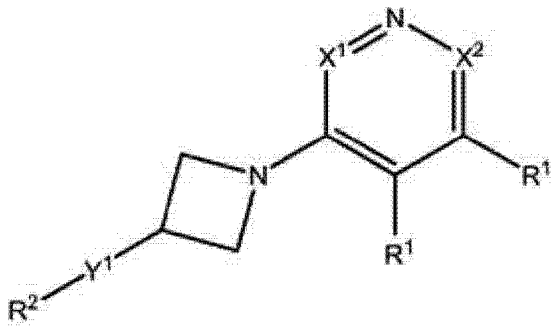
1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,240,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,

634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,及其药学上可接受的盐。

[0134] 仍另一个实施方案涉及式 (1A) 的化合物,其选自实施例 147、310、313、316、317、320、332、333、334、402、433、440、658、681、691、706、707、723、736、795,及其药学上可接受的盐。

[0135] 式 (IIA) 的实施方案

在另一个方面,本发明提供式 (IIA) 的化合物



(IIA);

及其药学上可接受的盐;其中 X^1、X^2、Y^1、R^1、和 R^2如本文对式 (IA) 所描述。

[0136] 本发明的一个实施方案涉及式 (IIA) 的化合物及其药学上可接受的盐;

其中

X^1为 N 且 X^2为 CR^1;或

X^1为 CR^1且 X^2为 N;或

X^1为 CR^1且 X^2为 CR^1;

Y^1为 C(O)NH、或 NHC(O);

R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I;

R^2独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基;其中 R^2中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代:

R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$,

$OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$, $NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$, $NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$, $C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br

和 I；其中 R^2 中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, 和 I；

R^3 在每次出现时独立地选自烷基、烯基、炔基、芳基、环烷基、环烯基、和杂环基；其中 R^3 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^3, $C(O)R^5$, $CO(O)R^5$, $OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, $C(O)NHOH$, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中 R^3 中的芳基、环烷基、环烯基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^5S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^5)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, $C(O)NHOH$, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；

R^4 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_3R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；

R^5 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^5

中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^8，OR^8，SR^8，$S(O)R^8$，SO_2R^8，NHR^8，$N(R^8)_2$，$C(O)R^8$，

$C(O)NH_2$，$C(O)NHR^8$，$C(O)N(R^8)_2$，$NHC(O)R^8$，$NR^8C(O)R^8$，$NHSO_2R^8$，$NHC(O)OR^8$，

SO_2NH_2，SO_2NHR^8，$SO_2N(R^8)_2$，$NHC(O)NH_2$，$NHC(O)NHR^8$，OH，(O)，$C(O)OH$，N_3，CN，

NH_2，F，Cl，Br 和 I；

R^6在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^6 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^9，OR^9，SR^9，$S(O)R^9$，SO_2R^9，NHR^9，$N(R^9)_2$，$C(O)R^9$，

$C(O)NH_2$，$C(O)NHR^9$，$C(O)N(R^9)_2$，$NHC(O)R^9$，$NR^9C(O)R^9$，$NHSO_2R^9$，$NHC(O)OR^9$，

SO_2NH_2，SO_2NHR^9，$SO_2N(R^9)_2$，$NHC(O)NH_2$，$NHC(O)NHR^9$，OH，(O)，$C(O)OH$，N_3，CN，

NH_2，CF_3，CF_2CF_3，F，Cl，Br 和 I；

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^8在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^9在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中由 R^4、R^5、R^6、R^7、R^8、和 R^9表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}，OR^{10}，SR^{10}，$S(O)R^{10}$，SO_2R^{10}，$C(O)R^{10}$，$CO(O)R^{10}$，

$OC(O)R^{10}$，$OC(O)OR^{10}$，$C(O)C(O)R^{10}$，NH_2，NHR^{10}，$N(R^{10})_2$，$NHC(O)R^{10}$，$NR^{10}C(O)R^{10}$，

$NHS(O)_2R^{10}$，$NR^{10}S(O)_2R^{10}$，$NHC(O)OR^{10}$，$NR^{10}C(O)OR^{10}$，$NHC(O)NH_2$，$NHC(O)NHR^{10}$，

$NHC(O)N(R^{10})_2$，$NR^{10}C(O)NHR^{10}$，$NR^{10}C(O)N(R^{10})_2$，$C(O)NH_2$，$C(O)NHR^{10}$，$C(O)N(R^{10})_2$，

$C(O)NHOH$，$C(O)NHOR^{10}$，$C(O)NHSO_2R^{10}$，$C(O)NR^{10}SO_2R^{10}$，SO_2NH_2，SO_2NHR^{10}，

$SO_2N(R^{10})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{10}$，$C(N)N(R^{10})_2$，CNOH，$CNOCH_3$，OH，

CN，N_3，NO_2，F，Cl，Br 和 I；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}，OR^{11}，SR^{11}，$S(O)R^{11}$，SO_2R^{11}，$C(O)R^{11}$，$CO(O)R^{11}$，

$OC(O)R^{11}$，$OC(O)OR^{11}$，NH_2，NHR^{11}，$N(R^{11})_2$，$NHC(O)R^{11}$，$NR^{11}C(O)R^{11}$，$NHS(O)_2R^{11}$，

$NR^{111}S(O)_2R^{11}$，$NHC(O)OR^{11}$，$NR^{11}C(O)OR^{11}$，$NHC(O)NH_2$，$NHC(O)NHR^{11}$，

$NHC(O)N(R^{11})_2$，$NR^{11}C(O)NHR^{11}$，$NR^{11}C(O)N(R^{11})_2$，$C(O)NH_2$，$C(O)NHR^{11}$，$C(O)N(R^{11})_2$，

$C(O)NHOH$，$C(O)NHOR^{11}$，$C(O)NHSO_2R^{11}$，$C(O)NR^{11}SO_2R^{11}$，SO_2NH_2，SO_2NHR^{11}，

$SO_2N(R^{11})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，CNOH，$CNOCH_3$，OH，

(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}，OR^{12}，SR^{12}，$S(O)R^{12}$，SO_2R^{12}，$C(O)R^{12}$，$CO(O)R^{12}$，

$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_2，NHR^{12}，$N(R^{12})_2$，$NHC(O)R^{12}$，$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，

$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，$NHC(O)NH_2$，$NHC(O)NHR^{12}$，

$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，

$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，

$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，CNOH，$CNOCH_3$，OH，

CN，N_3，NO_2，CF_3，OCF_3，F，Cl，Br 和 I；

R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

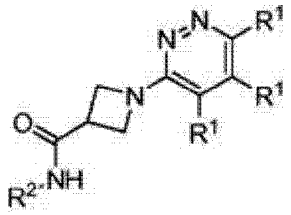
R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0137] 在式（IIA）的一个实施方案中，X^1为 N 且 X^2为 CR^1；或 X^1为 CR^1且 X^2为 N；或 X^1为 CR^1且 X^2为 CR^1。在式（IIA）的另一个实施方案中，X^1为 N 且 X^2为 CR^1。在式（IIA）的另一个实施方案中，X^1为 CR^1且 X^2为 N。在式（IIA）的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1。

[0138] 在式（IIA）的一个实施方案中，Y^1为 C(O)NH、或 NHC(O)。在式（IIA）的另一个实施方案中，Y^1为 C(O)NH。在式（IIA）的另一个实施方案中，Y^1为 NHC(O)。

[0139] 在式（IIA）的一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式（IIA）的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式（IIA）的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式（IIA）的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时为氢。

[0140] 在另一方面，本发明提供式（IIB）的化合物，



式（IIB）

及其药学上可接受的盐；其中 R^1和 R^2如本文对式（IA）的描述。

[0141] 在式（IIA）和（IIB）的一个实施方案中，R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式（IIA）和（IIB）的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式（IIA）和（IIB）的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式（IIA）和（IIB）的另一个实施方案中，R^1在每次出现时为氢。

[0142] 在式（IIA）和（IIB）的一个实施方案中，R^2独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：R^3，OR^3，SR^3，

$S(O)R^3$，SO_2R^3，$C(O)R^3$，$CO(O)R^3$，$OC(O)R^3$，$OC(O)OR^3$，NH_2，NHR^3，$N(R^3)_2$，$NHC(O)R^3$，

$NR^3C(O)R^3$，$NHS(O)_2R^3$，$NR^3S(O)_2R^3$，$NHC(O)OR^3$，$NR^3C(O)OR^3$，$NHC(O)NH_2$，

$NHC(O)NHR^3$，$NHC(O)N(R^3)_2$，$NR^3C(O)NHR^3$，$NR^3C(O)N(R^3)_2$，$C(O)NH_2$，$C(O)NHR^3$，

$C(O)N(R^3)_2$，$C(O)NHOH$，$C(O)NHOR^3$，$C(O)NHSO_2R^3$，$C(O)NR^3SO_2R^3$，SO_2NH_2，

SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH, C(N)NH_2, C(N)NHR^3, C(N)$N(R^3)_2$, CNOH,

$CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I ;其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代 :

R^4, OR^4, SR^4, S(O)R^4, SO_2R^4, C(O)R^4, OC(O)OR^4, NH_2, NHR^4,

$N(R^4)_2$, NHC(O)R^4, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, NHC(O)OR^4, $NR^4C(O)OR^4$,

NHC(O)NH_2, NHC(O)NHR^4, NHC(O)$N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, C(O)NH_2,

C(O)NHR^4, C(O)$N(R^4)_2$, C(O)NHOH, C(O)$NHOR^4$, C(O)$NHSO_2R^4$, C(O)$NR^4SO_2R^4$,

SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, C(N)NH_2, C(N)NHR^4, C(N)$N(R^4)_2$,

CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl,和 I。在式 (IIA) 和 (IIB) 的另一个实施方案中, R^2为芳基 ;其中 R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、OR^4、SO_2R^4、F、Cl、和 I。在式 (IIA) 和 (IIB) 的另一个实施方案中, R^2为芳基 ;其中 R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、OR^4、SO_2R^4、和 F。在式 (IIA) 和 (IIB) 的另一个实施方案中, R^2为苯基 ;其中 R^2中的苯基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、OR^4、SO_2R^4、和 F。在式 (IIA) 和 (IIB) 的另一个实施方案中, R^2为苯基 ;其中 R^2中的苯基各自被独立地选自以下的一个取代基取代 :R^4、OR^4、和 SO_2R^4。

[0143] 在式 (IIA) 和 (IIB) 的另一个实施方案中, R^2为 5-6 元杂芳基 ;其中 R^2中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、OR^4、SO_2R^4、F、Cl、和 I。在式 (IIA) 和 (IIB) 的另一个实施方案中, R^2为 5-6 元杂芳基 ;其中 R^2中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、OR^4、SO_2R^4、和 F。在式 (IIA) 和 (IIB) 的另一个实施方案中, R^2为呋喃基或噻吩基 ;其中 R^2中的呋喃基和噻吩基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、OR^4、SO_2R^4、和 F。

[0144] 在式 (IIA) 和 (IIB) 的一个实施方案中, R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 :

R^7, OR^7, SR^7, S(O)R^7, SO_2R^7, C(O)R^7, CO(O)R^7, OC(O)R^7, OC(O)OR^7, NH_2, NHR^7, $N(R^7)_2$,

NHC(O)R^7, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, NHC(O)OR^7, $NR^7C(O)OR^7$,

NHC(O)NH_2, NHC(O)NHR^7, NHC(O)$N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, C(O)NH_2,

C(O)NHR^7, C(O)$N(R^7)_2$, C(O)NHOH, C(O)$NHOR^7$, C(O)$NHSO_2R^7$, C(O)$NR^7SO_2R^7$,

SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, C(N)NH_2, C(N)NHR^7, C(N)$N(R^7)_2$,

CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (IIA) 和 (IIB) 的另一个实施方案中, R^4在每次出现时为烷基或杂环基。

[0145] 在式 (IIA) 和 (IIB) 的一个实施方案中, R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代 :R^7, OR^7,

SR^7, S(O)R^7, SO_2R^7, C(O)R^7, CO(O)R^7, OC(O)R^7, OC(O)OR^7, NH_2, NHR^7, $N(R^7)_2$,

NHC(O)R^7, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, NHC(O)OR^7, $NR^7C(O)OR^7$,

NHC(O)NH_2, NHC(O)NHR^7, NHC(O)$N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, C(O)NH_2,

C(O)NHR^7, C(O)$N(R^7)_2$, C(O)NHOH, C(O)$NHOR^7$, C(O)$NHSO_2R^7$, C(O)$NR^7SO_2R^7$,

SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, C(N)NH_2, C(N)NHR^7, C(N)$N(R^7)_2$,

CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (I) 的另一个实施方案中, R^4中

的烷基各自任选被一个 R^7 取代。

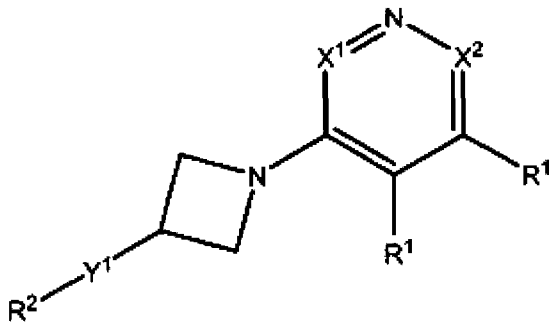
[0146] 在式 (IIA) 和 (IIB) 的一个实施方案中，R^7 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。在式 (IIA) 和 (IIB) 的另一个实施方案中，R^7 在每次出现时为杂环基。

[0147] 在式 (IIA) 和 (IIB) 的一个实施方案中，R^4 和 R^7 中的杂环基各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}，OR^{10}，SR^{10}，$S(O)R^{10}$，SO_2R^{10}，$C(O)R^{10}$，$CO(O)R^{10}$，$OC(O)R^{10}$，$OC(O)OR^{10}$，NH_2，NHR^{10}，$N(R^{10})_2$，$NHC(O)R^{10}$，$NR^{10}C(O)R^{10}$，$NHS(O)_2R^{10}$，$NR^{10}S(O)_2R^{10}$，$NHC(O)OR^{10}$，$NR^{10}C(O)OR^{10}$，$NHC(O)NH_2$，$NHC(O)NHR^{10}$，$NHC(O)N(R^{10})_2$，$NR^{10}C(O)NHR^{10}$，$NR^{10}C(O)N(R^{10})_2$，$C(O)NH_2$，$C(O)NHR^{10}$，$C(O)N(R^{10})_2$，$C(O)NHOH$，$C(O)NHOR^{10}$，$C(O)NHSO_2R^{10}$，$C(O)NR^{10}SO_2R^{10}$，SO_2NH_2，SO_2NHR^{10}，$SO_2N(R^{10})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{10}$，$C(N)N(R^{10})_2$，$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{10} 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10} 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}，OR^{11}，SR^{11}，$S(O)R^{11}$，SO_2R^{11}，$C(O)R^{11}$，$CO(O)R^{11}$，$OC(O)R^{11}$，$OC(O)OR^{11}$，NH_2，NHR^{11}，$N(R^{11})_2$，$NHC(O)R^{11}$，$NR^{11}C(O)R^{11}$，$NHS(O)_2R^{11}$，$NR^{11}S(O)_2R^{11}$，$NHC(O)OR^{11}$，$NR^{11}C(O)OR^{11}$，$NHC(O)NH_2$，$NHC(O)NHR^{11}$，$NHC(O)N(R^{11})_2$，$NR^{11}C(O)NHR^{11}$，$NR^{11}C(O)N(R^{11})_2$，$C(O)NH_2$，$C(O)NHR^{11}$，$C(O)N(R^{11})_2$，$C(O)NHOH$，$C(O)NHOR^{11}$，$C(O)NHSO_2R^{11}$，$C(O)NR^{11}SO_2R^{11}$，SO_2NH_2，SO_2NHR^{11}，$SO_2N(R^{11})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，$CNOH$，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^{10} 中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}，OR^{12}，SR^{12}，$S(O)R^{12}$，SO_2R^{12}，$C(O)R^{12}$，$CO(O)R^{12}$，$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_2，NHR^{12}，$N(R^{12})_2$，$NHC(O)R^{12}$，$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，$NHC(O)NH_2$，$NHC(O)NHR^{12}$，$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，SO_2NH_3，SO_2NHR^{12}，$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{11} 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11} 中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11} 中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；R^{12} 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和 R^{13} 在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0148] 在式 (IIA) 和 (IIB) 的另一个实施方案中，R^4 和 R^7 中的杂环基各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、OH、F、Cl、Br 和 I；R^{10} 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10} 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10} 中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、

F、和 Cl ;R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基 ;其中 R^{11}中的烷基各自任选被烷氧基或芳基取代 ;其中 R^{11}中的芳基和杂环基各自任选被一个或多个独立地选自以下的取代基取代 :R^{13}、CF_3、F、和 Cl ;R^{12}在每次出现时独立地选自烷基和芳基 ;和 R^{13}在每次出现时独立地选自烷基和卤代烷基。

[0149] 本发明的一个实施方案涉及化合物或其药学上可接受的盐,其用作 NAMPT 的抑制剂,所述化合物具有式 (IIA)



式 (IIA):

其中

X^1为 N 且 X^2为 CR^1;或

X^1为 CR^1且 X^2为 N ;或

X^1为 CR^1且 X^2为 CR^1;

Y^1为 C(O)NH、或 NHC(O) ;

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、Cl、和 F ;

R^2为芳基或 5-6 元杂芳基,其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、SO_2R^4、OR^4、和 F ;

R^4在每次出现时为烷基或杂环基。其中 R^4中的烷基各自任选被 R^7取代 ;

R^7在每次出现时独立地为杂环基 ;

其中由 R^4和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代 :

R^{10}、$C(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)R^{10}$、OH 和 F ;

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基 ;其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代 :R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F ;其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代 :R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl ;

R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基 ;其中 R^{11}中的烷基各自任选被烷氧基或芳基取代 ;其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代 :R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl ;

R^{12}在每次出现时独立地选自烷基、和芳基 ;和

R^{13}在每次出现时独立地选自烷基、卤代烷基、和杂环基。

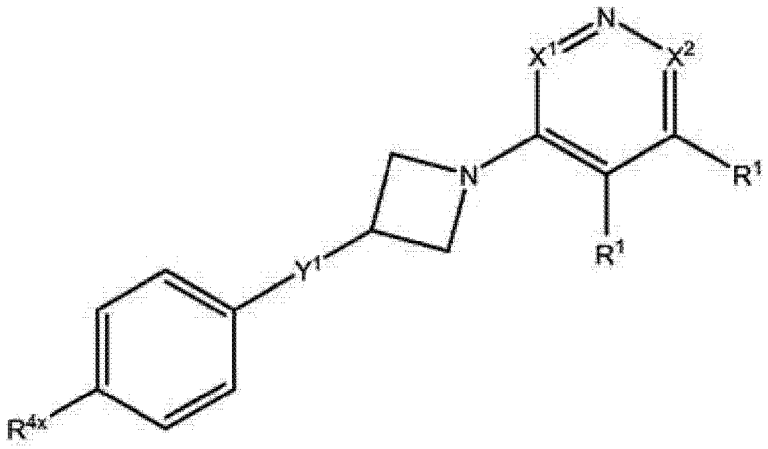
[0150] 仍另一个实施方案涉及具有式 (IIA) 的化合物,其包括实施例

1,2,3,4,5,6,7,10,20,21,22,23,24,25,26,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,

65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,609,610,611,612,613,614,615,616,617,665,666,667,668,737,738,739,740,741,748,750,751,753,784,803,804,805,806,807,809,817,818,819,820,821,822,823,828,829,830,831,832,833,834,835,840,841,842,843,844,845,846,851,852,853,854,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,及其药学上可接受的盐。

[0151] 式(IIIA)的实施方案

在另一方面,本发明提供式(IIIA)的化合物



(IIIA);

及其药学上可接受的盐；其中当式(IA)中的R^2为芳基时，X^1、X^2、R^1、和Y^1如本文式(IA)所描述且R^{4x}如本文对R^2上的取代基所描述。

[0152] 本发明的一个实施方案涉及式(IIIA)的化合物或其药学上可接受的盐；

其中

X^1为N且X^2为CR^1；或

X^1为CR^1且X^2为N；或

X^1为CR^1且X^2为CR^1；

Y^1为C(O)NH、或NHC(O)；

R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br和I；

R^{4X}独立地选自R^4，OR^4，SR^4，$S(O)R^4$，

SO_2R^4，$C(O)R^4$，$OC(O)OR^4$，NH_2，NHR^4，$N(R^4)_2$，$NHC(O)R^4$，$NR^4C(O)R^4$，$NHS(O)_2R^4$，

$NR^4S(O)_2R^4$，$NHC(O)OR^4$，$NR^4C(O)OR^4$，$NHC(O)NH_2$，$NHC(O)NHR^4$，$NHC(O)N(R^4)_2$，

$NR^4C(O)NHR^4$，$NR^4C(O)N(R^4)_2$，$C(O)NH_2$，$C(O)NHR^4$，$C(O)N(R^4)_2$，C(O)NHOH，

$C(O)NHOR^4$，$C(O)NHSO_2R^4$，$C(O)NR^4SO_2R^4$，SO_2NH_2，SO_2NHR^4，$SO_2N(R^4)_2$，C(O)H，

C(O)OH，$C(N)NH_2$，$C(N)NHR^4$，$C(N)N(R^4)_3$，CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，

和I；

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7，OR^7，SR^7，$S(O)R^7$，SO_2R^7，$C(O)R^7$，$CO(O)R^7$，

$OC(O)R^7$，$OC(O)OR^7$，NH_2，NHR^7，$N(R^7)_2$，$NHC(O)R^7$，$NR^7C(O)R^7$，$NHS(O)_2R^7$，

$NR^7S(O)_2R^7$，$NHC(O)OR^7$，$NR^7C(O)OR^7$，$NHC(O)NH_2$，$NHC(O)NHR^7$，$NHC(O)N(R^7)_2$，

$NR^7C(O)NHR^7$，$NR^7C(O)N(R^7)_2$，$C(O)NH_2$，$C(O)NHR^7$，$C(O)N(R^7)_2$，C(O)NHOH，

$C(O)NHOR^7$，$C(O)NHSO_2R^7$，$C(O)NR^7SO_2R^7$，SO_2NH_2，SO_2NHR^7，$SO_2N(R^7)_2$，C(O)H，

C(O)OH，$C(N)NH_2$，$C(N)NHR^7$，$C(N)N(R^7)_2$，CNOH，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，

Cl，Br和I；

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中由R^4和R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取

代：

R^{10}，OR^{10}，SR^{10}，$S(O)R^{10}$，SO_2R^{10}，$C(O)R^{10}$，$CO(O)R^{10}$，$OC(O)R^{10}$，$OC(O)OR^{10}$，$C(O)C(O)R^{10}$，NH_2，NHR^{10}，$N(R^{10})_2$，$NHC(O)R^{10}$，$NR^{10}C(O)R^{10}$，$NHS(O)_2R^{10}$，$NR^{10}S(O)_2R^{10}$，$NHC(O)OR^{10}$，$NR^{10}C(O)OR^{10}$，$NHC(O)NH_2$，$NHC(O)NHR^{10}$，$NHC(O)N(R^{10})_2$，$NR^{10}C(O)NHR^{10}$，$NR^{10}C(O)N(R^{10})_2$，$C(O)NH_2$，$C(O)NHR^{10}$，$C(O)N(R^{10})_2$，$C(O)NHOH$，$C(O)NHOR^{10}$，$C(O)NHSO_2R^{10}$，$C(O)NR^{10}SO_2R^{10}$，SO_2NH_2，SO_2NHR^{10}，$SO_2N(R^{10})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{10}$，$C(N)N(R^{10})_2$，$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}，OR^{11}，SR^{11}，$S(O)R^{11}$，SO_2R^{11}，$C(O)R^{11}$，$CO(O)R^{11}$，$OC(O)R^{11}$，$OC(O)OR^{11}$，NH_2，NHR^{11}，$N(R^{11})_2$，$NHC(O)R^{11}$，$NR^{11}C(O)R^{11}$，$NHS(O)_2R^{11}$，$NR^{11}S(O)_2R^{11}$，$NHC(O)OR^{11}$，$NR^{11}C(O)OR^{11}$，$NHC(O)NH_2$，$NHC(O)NHR^{11}$，$NHC(O)N(R^{11})_2$，$NR^{11}C(O)NHR^{11}$，$NR^{11}C(O)N(R^{11})_2$，$C(O)NH_2$，$C(O)NHR^{11}$，$C(O)N(R^{11})_2$，$C(O)NHOH$，$C(O)NHOR^{11}$，$C(O)NHSO_2R^{11}$，$C(O)NR^{11}SO_2R^{11}$，SO_2NH_2，SO_2NHR^{11}，$SO_2N(R^{11})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，$CNOH$，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}，OR^{12}，SR^{12}，$S(O)R^{12}$，SO_2R^{12}，$C(O)R^{12}$，$CO(O)R^{12}$，$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_3，NHR^{12}，$N(R^{12})_2$，$NHC(O)R^{12}$，$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，$NHC(O)NH_2$，$NHC(O)NHR^{12}$，$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，CF_3，OCF_3，F，Cl，Br 和 I；

R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

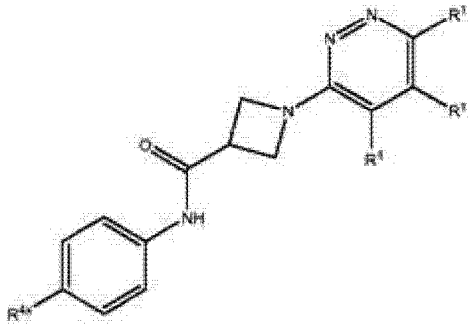
[0153] 在式（IIIA）的一个实施方案中，X^1为 N 且 X^2为 CR^1；或 X^1为 CR^1且 X^2为 N；或 X^1为 CR^1且 X^2为 CR^1。在式（IIIA）的另一个实施方案中，X^1为 N 且 X^2为 CR^1。在式（IIIA）的另一个实施方案中，X^1为 CR^1且 X^2为 N。在式（IIIA）的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1。

[0154] 在式（IIIA）的一个实施方案中，Y^1为 C(O)NH、或 NHC(O)。在式（IIIA）的另一个实施方案中，Y^1为 C(O)NH。在式（IIIA）的另一个实施方案中，Y^1为 NHC(O)。

[0155] 在式（IIIA）的一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地

选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (IIIA) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IIIA) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IIIA) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时为氢。

[0156] 在另一方面，本发明提供式 (IIIB) 的化合物，



式 (IIIB)

及其药学上可接受的盐；其中当式 (IA) 中 R^2为芳基时，R^1如本文对式 (IA) 描述且 R^{4x}如本文对 R^2上的取代基所描述。

[0157] 在式 (IIIA) 和 (IIIB) 的一个实施方案中，R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (IIIA) 和 (IIIB) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IIIA) 和 (IIIB) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IIIA) 和 (IIIB) 的另一个实施方案中，R^1在每次出现时为氢。

[0158] 在式 (IIIA) 和 (IIIB) 的一个实施方案中，R^{4X}独立地选自

R^4, OR^4, SR^4, $S(O)R^4$, SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4,
$N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$, $NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$,
$NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$, $NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$,
$C(O)NHR^4$, $C(O)N(R^4)_2$, $C(O)NHOH$, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$,
SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$,
$CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, 和 I。在式 (IIIA) 和 (IIIB) 的另一个实施方案中，R^{4X}独立地选自 R^4、OR^4、SO_2R^4、F、Cl、和 I。在式 (IIIA) 和 (IIIB) 的另一个实施方案中，R^{4X}独立地选自 R^4、OR^4、SO_2R^4、和 F。

[0159] 在式 (IIIA) 和 (IIIB) 的一个实施方案中，R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$,
$NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$,
$NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$,
$C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$,
SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$,

CNOH，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I。在式 (IIIA) 和 (IIIB) 的另一个实施方案中，R^4在每次出现时为烷基或杂环基。

[0160] 在式 (IIIA) 和 (IIIB) 的一个实施方案中，R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：

R^7，OR^7，SR^7，$S(O)R^7$，SO_2R^7，$C(O)R^7$，$CO(O)R^7$，$OC(O)R^7$，$OC(O)OR^7$，NH_2，NHR^7，$N(R^7)_2$，$NHC(O)R^7$，$NR^7C(O)R^7$，$NHS(O)_2R^7$，$NR^7S(O)_2R^7$，$NHC(O)OR^7$，$NR^7C(O)OR^7$，$NHC(O)NH_2$，$NHC(O)NHR^7$，$NHC(O)N(R^7)_2$，$NR^7C(O)NHR^7$，$NR^7C(O)N(R^7)_2$，$C(O)NH_2$，$C(O)NHR^7$，$C(O)N(R^7)_2$，$C(O)NHOH$，$C(O)NHOR^7$，$C(O)NHSO_2R^7$，$C(O)NR^7SO_2R^7$，SO_2NH_2，SO_2NHR^7，$SO_2N(R^7)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^7$，$C(N)N(R^7)_2$，CNOH，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I。在式 (IIIA) 和 (IIIB) 的另一个实施方案中，R^4中的烷基各自任选被一个 R^7取代。

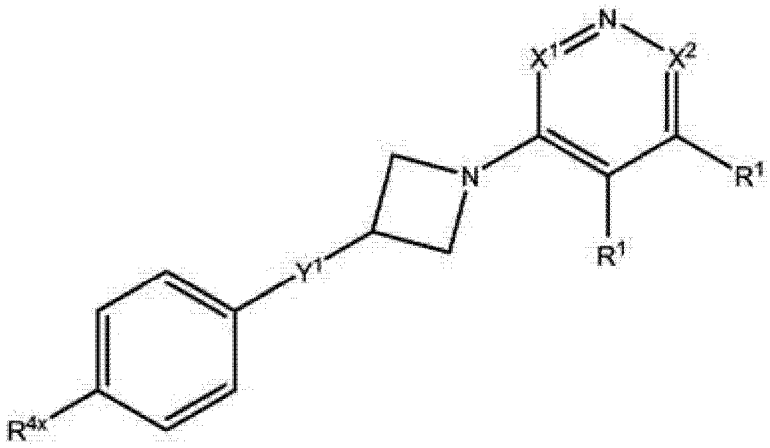
[0161] 在式 (IIIA) 和 (IIIB) 的一个实施方案中，R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。在式 (IIIA) 和 (IIIB) 的另一个实施方案中，R^7在每次出现时为杂环基。

[0162] 在式 (IIIA) 和 (IIIB) 的一个实施方案中，R^4和 R^7中的杂环基各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}，OR^{10}，SR^{10}，$S(O)R^{10}$，SO_2R^{10}，$C(O)R^{10}$，$CO(O)R^{10}$，$OC(O)R^{10}$，$OC(O)OR^{10}$，NH_2，NHR^{10}，$N(R^{10})_2$，$NHC(O)R^{10}$，$NR^{10}C(O)R^{10}$，$NHS(O)_2R^{10}$，$NR^{10}S(O)_2R^{10}$，$NHC(O)OR^{10}$，$NR^{10}C(O)OR^{10}$，$NHC(O)NH_2$，$NHC(O)NHR^{10}$，$NHC(O)N(R^{10})_2$，$NR^{10}C(O)NHR^{10}$，$NR^{10}C(O)N(R^{10})_2$，$C(O)NH_2$，$C(O)NHR^{10}$，$C(O)N(R^{10})_2$，$C(O)NHOH$，$C(O)NHOR^{10}$，$C(O)NHSO_2R^{10}$，$C(O)NR^{10}SO_2R^{10}$，SO_2NH_2，SO_2NHR^{10}，$SO_2N(R^{10})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{10}$，$C(N)N(R^{10})_2$，CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}，OR^{11}，SR^{11}，$S(O)R^{11}$，SO_2R^{11}，$C(O)R^{11}$，$CO(O)R^{11}$，$OC(O)R^{11}$，$OC(O)OR^{11}$，NH_2，NHR^{11}，$N(R^{11})_2$，$NHC(O)R^{11}$，$NR^{11}C(O)R^{11}$，$NHS(O)_2R^{11}$，$NR^{11}S(O)_2R^{11}$，$NHC(O)OR^{11}$，$NR^{11}C(O)OR^{11}$，$NHC(O)NH_2$，$NHC(O)NHR^{11}$，$NHC(O)N(R^{11})_2$，$NR^{11}C(O)NHR^{11}$，$NR^{11}C(O)N(R^{11})_2$，$C(O)NH_2$，$C(O)NHR^{11}$，$C(O)N(R^{11})_2$，$C(O)NHOH$，$C(O)NHOR^{11}$，$C(O)NHSO_2R^{11}$，$C(O)NR^{11}SO_2R^{11}$，SO_2NH_2，SO_2NHR^{11}，$SO_2N(R^{11})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，CNOH，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}，OR^{12}，SR^{12}，$S(O)R^{12}$，SO_2R^{12}，$C(O)R^{12}$，$CO(O)R^{12}$，$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_2，NHR^{12}，$N(R^{12})_2$，$NHC(O)R^{12}$，$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，$NHC(O)NH_2$，$NHC(O)NHR^{12}$，$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自

以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0163] 在式（IIIA）和（IIIB）的另一个实施方案中，R^4和 R^7中的杂环基各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、OH、F、Cl、Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl；R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、CF_3、F、和 Cl；R^{12}在每次出现时独立地选自烷基和芳基；和 R^{13}在每次出现时独立地选自烷基和卤代烷基。

[0164] 本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式（IIIA）



(IIIA);

其中

X^1为 N 且 X^2为 CR^1；或

X^1为 CR^1且 X^2为 N；或

X^1为 CR^1且 X^2为 CR^1；

Y^1为 C(O)NH、或 NHC(O)；

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、Cl、和 F；

R^{4X}独立地选自 R^4、SO_2R^4、OR^4、和 F；

R^4在每次出现时为烷基或杂环基；其中 R^4中的烷基各自任选被 R^7取代；

R^7在每次出现时独立地为杂环基；

其中由 R^4和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)R^{10}$、OH 和 F；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、

$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代：R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl；

R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl；

R^{12}在每次出现时独立地选自烷基、和芳基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、和杂环基。

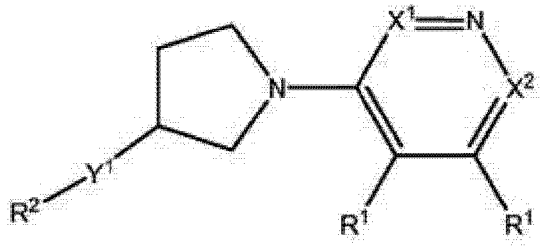
[0165] 仍另一个实施方案涉及具有式 (IIIA) 的化合物，其包括实施例

1,2,3,4,5,6,7,10,20,22,25,26,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,609,610,611,612,613,614,615,616,617,665,666,667,668,737,738,739,740,741,748,750,751,753,784,803,804,805,806,807,809,817,818,819,820,821,

822,823,840,841,842,843,844,845,846,851,852,853,854,857,863,864,865,866,867,及其药学上可接受的盐。

[0166] 式(IVA)的实施方案

在另一方面,本发明提供式(IVA)的化合物



(IVA);

及其药学上可接受的盐;其中 X^1、X^2、Y^1、R^1、和 R^2各自如本文对式(I)所描述。

[0167] 本发明的一个实施方案涉及式(IVA)的化合物及其药学上可接受的盐;

其中

X^1为 N 且 X^2为 CR^1;或

X^1为 CR^1且 X^2为 N;或

X^1为 CR^1且 X^2为 CR^1;

Y^1为 C(O)NH、或 NHC(O);

R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I;

R^2独立地选自 C_4-C_6-烷基、C_4-C_6-烯基、C_4-C_6-炔基、芳基、和 5-6 元杂芳基;其中 R^2中的 C_4-C_6-烷基、C_4-C_6-烯基、和 C_4-C_6-炔基各自被一个或多个独立地选自以下的取代基取代:

R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$,

$OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$,

$NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$,

$NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$,

$C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH,

$C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br

和 I;其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代:R^4, OR^4, SR^4, $S(O)R^4$,

SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$,

$NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$,

$NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH,

$C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H,

C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl,

和 I;

R^3在每次出现时独立地选自烷基、烯基、炔基、芳基、环烷基、环烯基、和杂环基;其中 R^3中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代:

R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$,

$OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$, $NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$, $NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, $C(O)NHOH$, $C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中 R^3 中的芳基、环烷基、环烯基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：

R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$, $NHC(O)R^6$, $NR^6C(O)R^6NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$, $NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^5)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$, $C(O)NHR^6$, $C(O)N(R^6)_2$, $C(O)NHOH$, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$, SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^6$, $C(N)N(R^6)_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；

R^4 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；

R^5 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^5 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$, $C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$, SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O), $C(O)OH$, N_3, CN, NH_2, F, Cl, Br 和 I；

R^6 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^6 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$, $C(O)NH_2$, $C(O)NHR^9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$, SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O), $C(O)OH$, N_3, CN, NH_2, CF_3, CF_2CF_3, F, Cl, Br 和 I；

R^7 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^8 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^9 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中由 R^4、R^5、R^6、R^7、R^8、和 R^9 表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$,

$OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：

R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br 和 I；

R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

条件是

当X^1为CR^1且X^2为CR^1时；R^1为氢；Y^1为NHC(O)；且R^2为吡咯基；所述R^2中的吡咯基未被两个烷基取代。

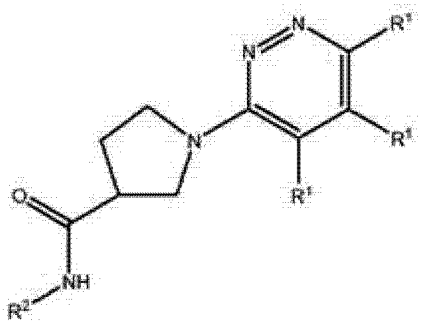
[0168] 在式(IVA)的一个实施方案中，X^1为N且X^2为CR^1；或X^1为CR^1且X^2为N；或X^1为CR^1且X^2为CR^1。在式(IVA)的另一个实施方案中，X^1为N且X^2为CR^1。在式(IVA)的另一个实施方案中，X^1为CR^1且X^2为N。在式(IVA)的另一个实施方案中，X^1为CR^1且X^2为CR^1。

[0169] 在式(IVA)的一个实施方案中，Y^1为C(O)NH、或NHC(O)。在式(IVA)的另一个实施方案中，Y^1为C(O)NH。在式(IVA)的另一个实施方案中，Y^1为NHC(O)。

[0170] 在式(IVA)的一个实施方案中，X^1为CR^1且X^2为CR^1；且R^1在每次出现时独立地

选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (IVA) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IVA) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IVA) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时为氢。

[0171] 在另一方面，本发明提供式 (IVB) 的化合物，



式 (IVB)

及其药学上可接受的盐；其中 R^1和 R^2如本文对式 (IA) 所描述。

[0172] 在式 (IVA) 和 (IVB) 的一个实施方案中，R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (IVA) 和 (IVB) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IVA) 和 (IVB) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IVA) 和 (IVB) 的另一个实施方案中，R^1在每次出现时为氢。

[0173] 在式 (IVA) 和 (IVB) 的一个实施方案中，R^2独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：R^3，OR^3，SR^3，

$S(O)R^3$，SO_2R^3，$C(O)R^3$，$CO(O)R^3$，$OC(O)R^3$，$OC(O)OR^3$，NH_2，NHR^3，$N(R^3)_2$，$NHC(O)R^3$，

$NR^3C(O)R^3$，$NHS(O)_2R^3$，$NR^3S(O)_2R^3$，$NHC(O)OR^3$，$NR^3C(O)OR^3$，$NHC(O)NH_2$，

$NHC(O)NHR^3$，$NHC(O)N(R^3)_2$，$NR^3C(O)NHR^3$，$NR^3C(O)N(R^3)_2$，$C(O)NH_2$，$C(O)NHR^3$，

$C(O)N(R^3)_2$，$C(O)NHOH$，$C(O)NHOR^3$，$C(O)NHSO_2R^3$，$C(O)NR^3SO_2R^3$，SO_2NH_2，

SO_2NHR^3，$SO_2N(R^3)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^3$，$C(N)N(R^3)_2$，CNOH，

$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：

R^4，OR^4，SR^4，$S(O)R^4$，SO_2R^4，$C(O)R^4$，$OC(O)OR^4$，NH_2，NHR^4，

$N(R^4)_2$，$NHC(O)R^4$，$NR^4C(O)R^4$，$NHS(O)_2R^4$，$NR^4S(O)_2R^4$，$NHC(O)OR^4$，$NR^4C(O)OR^4$，

$NHC(O)NH_2$，$NHC(O)NHR^4$，$NHC(O)N(R^4)_2$，$NR^4C(O)NHR^4$，$NR^4C(O)N(R^4)_2$，$C(O)NH_2$，

$C(O)NHR^4$，$C(O)N(R^4)_2$，$C(O)NHOH$，$C(O)NHOR^4$，$C(O)NHSO_2R^4$，$C(O)NR^4SO_2R^4$，

SO_2NH_2，SO_2NHR^4，$SO_2N(R^4)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^4$，$C(N)N(R^4)_2$，

CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，和 I。在式 (IVA) 和 (IVB) 的另一个实施方案中，R^2为芳基；其中 R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、F、Cl、和 I。在式 (IVA) 和 (IVB) 的另一个实施方案中，R^2为芳基；其中 R^2中的芳基

各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、和 F。在式（IVA）和（IVB）的另一个实施方案中，R^2为苯基；其中 R^2中的苯基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、和 F。在式（IVA）和（IVB）的另一个实施方案中，R^2为苯基；其中 R^2中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和 SO_2R^4。

[0174] 在式（IVA）和（IVB）的另一个实施方案中，R^2为 5-6 元杂芳基；其中 R^2中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、F、Cl、和 I。在式（IVA）和（IVB）的另一个实施方案中，R^2为 5-6 元杂芳基；其中 R^2中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、和 F。在式（IVA）和（IVB）的另一个实施方案中，R^2为呋喃基或噻吩基；其中 R^2中的呋喃基和噻吩基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、和 F。

[0175] 在式（IVA）和（IVB）的一个实施方案中，R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式（IVA）和（IVB）的另一个实施方案中，R^4在每次出现时为烷基或杂环基。

[0176] 在式（IVA）和（IVB）的一个实施方案中，R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式（IVA）和（IVB）的另一个实施方案中，R^4中的烷基各自任选被一个 R^7取代。

[0177] 在式（IVA）和（IVB）的一个实施方案中，R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。在式（IVA）和（IVB）的另一个实施方案中，R^7在每次出现时为杂环基。

[0178] 在式（IVA）和（IVB）的一个实施方案中，R^4和 R^7中的杂环基各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH,

CN，N_3，NO_2，F，Cl，Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}，OR^{11}，SR^{11}，$S(O)R^{11}$，

SO_2R^{11}，$C(O)R^{11}$，$CO(O)R^{11}$，$OC(O)R^{11}$，$OC(O)OR^{11}$，NH_2，NHR^{11}，$N(R^{11})_2$，$NHC(O)R^{11}$，

$NR^{11}C(O)R^{11}$，$NHS(O)_2R^{11}$，$NR^{11}S(O)_2R^{11}$，$NHC(O)OR^{11}$，$NR^{11}C(O)OR^{11}$，$NHC(O)NH_2$，

$NHC(O)NHR^{11}$，$NHC(O)N(R^{11})_2$，$NR^{11}C(O)NHR^{11}$，$NR^{11}C(O)N(R^{11})_2$，$C(O)NH_2$，

$C(O)NHR^{11}$，$C(O)N(R^{11})_2$，$C(O)NHOH$，$C(O)NHOR^{11}$，$C(O)NHSO_2R^{11}$，$C(O)NR^{11}SO_2R^{11}$，

SO_2NH_2，SO_2NHR^{11}，$SO_2N(R^{11})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，

$CNOH$，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}，OR^{12}，SR^{12}，$S(O)R^{12}$，SO_2R^{12}，

$C(O)R^{12}$，$CO(O)R^{12}$，$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_2，NHR^{12}，$N(R^{12})_2$，$NHC(O)R^{12}$，

$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，$NHC(O)NH_2$，

$NHC(O)NHR^{12}$，$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，

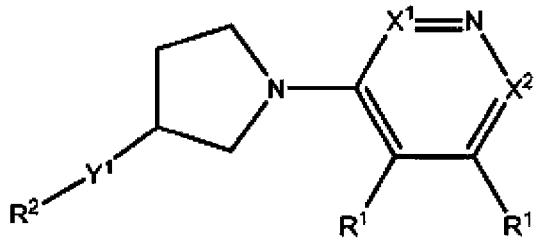
$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，

SO_2NH_2，SO_2NHR^{12}，$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，

$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0179] 在式 (IVA) 和 (IVB) 的另一个实施方案中，R^4和 R^7中的杂环基各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、OH、F、Cl、Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl；R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、CF_3、F、和 Cl；R^{12}在每次出现时独立地选自烷基和芳基；和 R^{13}在每次出现时独立地选自烷基和卤代烷基。

[0180] 本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式 (IVA)



式 (IVA);

其中

X^1为 N 且 X^2为 CR^1;或

X^1为 CR^1且 X^2为 N ;或

X^1为 CR^1且 X^2为 CR^1;

Y^1为 C(O)NH、或 NHC(O) ;

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、Cl、和 F ;

R^2为芳基或 5-6 元杂芳基,其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代 :R^4、SO_2R^4、OR^4、和 F ;

R^4在每次出现时为烷基或杂环基 ;其中 R^4中的烷基各自任选被 R^7取代 ;

R^7在每次出现时独立地为杂环基 ;

其中由 R^4和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代 :

R^{10}、$C(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)R^{10}$、OH 和 F ;

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基 ;其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代 :R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F ;其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代 :R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl ;

R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基 ;其中 R^{11}中的烷基各自任选被烷氧基或芳基取代 ;其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代 :R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl ;

R^{12}在每次出现时独立地选自烷基、和芳基 ;和

R^{13}在每次出现时独立地选自烷基、卤代烷基、和杂环基 ;

条件是

当 X^1为 CR^1且 X^2为 CR^1时 ;R^1为氢 ;Y^1为 NHC(O) ;且 R^2为吡咯基 ;所述 R^2中的吡咯基未被两个烷基取代。

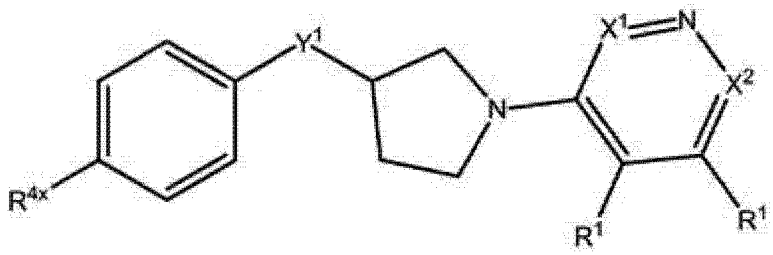
[0181] 仍另一个实施方案涉及具有式 (IVA) 的化合物,其包括实施例

8,9,11,12,13,14,15,16,17,18,19,27,28,141,142,204,310,311,312,313,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,

711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,及其药学上可接受的盐。

[0182] 式 (VA) 的实施方案

在另一方面,本发明提供式 (VA) 的化合物



(VA);

及其药学上可接受的盐;其中当式 (IA) 中的 R^2 为芳基时,X^1、X^2、R^1、和 Y^1 如本文式 (IA) 中所描述且 R^{4x} 如本文对 R^2 上的取代基所描述。

[0183] 本发明的一个实施方案涉及式 (VA) 的化合物或其药学上可接受的盐;

其中

X^1 为 N 且 X^2 为 CR^1;或

X^1 为 CR^1 且 X^2 为 N;或

X^1 为 CR^1 且 X^2 为 CR^1;

Y^1 为 C(O)NH、或 NHC(O);

R^1 在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I;

R^{4X} 独立地选自 R^4, OR^4, SR^4, $S(O)R^4$,

SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$,

$NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$,

$NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH,

$C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H,

C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl,

和 I;

R^4 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基;其中 R^4 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代:

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$,

$OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$,

$NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中由 R^4、和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：

R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_3R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br 和 I；

R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

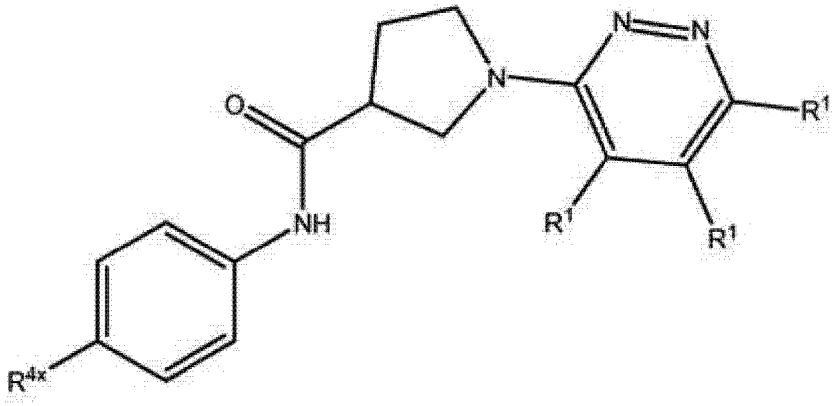
R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0184] 在式 (VA) 的一个实施方案中，X^1为 N 且 X^2为 CR^1；或 X^1为 CR^1且 X^2为 N；或 X^1为 CR^1且 X^2为 CR^1。在式 (VA) 的另一个实施方案中，X^1为 N 且 X^2为 CR^1。在式 (VA) 的另一个实施方案中，X^1为 CR^1且 X^2为 N。在式 (VA) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1。

[0185] 在式 (VA) 的一个实施方案中，Y^1为 C(O)NH、或 NHC(O)。在式 (VA) 的另一个实施方案中，Y^1为 C(O)NH。在式 (VA) 的另一个实施方案中，Y^1为 NHC(O)。

[0186] 在式 (VA) 的一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (VA) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (VA) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (VA) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时为氢。

[0187] 在另一方面，本发明提供式 (VB) 的化合物，



式 (VB)

及其药学上可接受的盐；其中当式 (IA) 中的 R^2为芳基时，R^1如本文对式 (IA) 所描述且 R^{4x}如本文对 R^2上的取代基所描述。

[0188] 在式 (VA) 和 (VB) 的一个实施方案中，R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (VA) 和 (VB) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (VA) 和 (VB) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (VA) 和 (VB) 的另一个实施方案中，R^1在每次出现时为氢。

[0189] 在式 (VA) 和 (VB) 的一个实施方案中，R^{4X}独立地选自

R^4，OR^4，SR^4，$S(O)R^4$，SO_2R^4，$C(O)R^4$，$OC(O)OR^4$，NH_2，NHR^4，

$N(R^4)_2$，$NHC(O)R^4$，$NR^4C(O)R^4$，$NHS(O)_2R^4$，$NR^4S(O)_2R^4$，$NHC(O)OR^4$，$NR^4C(O)OR^4$，

$NHC(O)NH_2$，$NHC(O)NHR^4$，$NHC(O)N(R^4)_2$，$NR^4C(O)NHR^4$，$NR^4C(O)N(R^4)_2$，$C(O)NH_2$，

$C(O)NHR^4$，$C(O)N(R^4)_2$，C(O)NHOH，$C(O)NHOR^4$，$C(O)NHSO_2R^4$，$C(O)NR^4SO_2R^4$，

SO_2NH_2，SO_2NHR^4，$SO_2N(R^4)_2$，C(O)H，C(O)OH，$C(N)NH_2$，$C(N)NHR^4$，$C(N)N(R^4)_2$，

CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，和 I。在式 (VA) 和 (VB) 的另一个实施方案中，R^{4X}独立地选自 R^4、OR^4、SO_2R^4、F、Cl、和 I。在式 (VA) 和 (VB) 的另一个实施方案中，R^{4X}独立地选自 R^4、OR^4、SO_2R^4、和 F。

[0190] 在式 (VA) 和 (VB) 的一个实施方案中，R^4在每次出现时独立地选自烷基、烯基、炔

基、芳基、杂环基、环烷基、和环烯基；其中 R^4 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (VA) 和 (VB) 的另一个实施方案中，R^4 在每次出现时为烷基或杂环基。

[0191] 在式 (VA) 和 (VB) 的一个实施方案中，R^4 中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (I) 的另一个实施方案中，R^4 中的烷基各自任选被一个 R^7 取代。

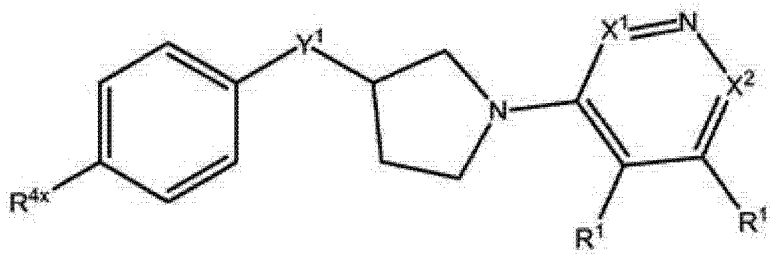
[0192] 在式 (VA) 和 (VB) 的一个实施方案中，R^7 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。在式 (VA) 和 (VB) 的另一个实施方案中，R^7 在每次出现时为杂环基。

[0193] 在式 (VA) 和 (VB) 的一个实施方案中，R^4 和 R^7 中的杂环基各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})^2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；R^{10} 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10} 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中 R^{10} 中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$,

$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，$NHC(O)NH_2$，$NHC(O)NHR^{12}$，$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0194] 在式 (VA) 和 (VB) 的另一个实施方案中，R^4和 R^7中的杂环基各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、OH、F、Cl、Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl；R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、CF_3、F、和 Cl；R^{12}在每次出现时独立地选自烷基和芳基；和 R^{13}在每次出现时独立地选自烷基和卤代烷基。

[0195] 本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式 (VA)



(VA);

其中

X^1为 N 且 X^2为 CR^1；或

X^1为 CR^1且 X^2为 N；或

X^1为 CR^1且 X^2为 CR^1；

Y^1为 $C(O)NH$、或 $NHC(O)$；

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、Cl、和 F；

R^{4X}独立地选自 R^4、SO_2R^4、OR^4、和 F；

R^4在每次出现时为烷基或杂环基；其中 R^4中的烷基各自任选被 R^7取代；

R^7在每次出现时独立地为杂环基；

其中由 R^4和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取

代：

R^{10}、$C(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)R^{10}$、OH 和 F；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代：R^{12}、OR^{12}、$C(O)R^{12}$、OH、CN、CF_3、OCF_3、F、和 Cl；

R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl；

R^{12}在每次出现时独立地选自烷基、和芳基；和

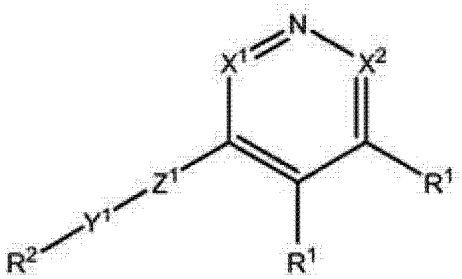
R^{13}在每次出现时独立地选自烷基、卤代烷基、和杂环基。

[0196] 仍另一个实施方案涉及具有式 (VA) 的化合物，其包括实施例

8,9,11,12,13,14,15,16,17,18,19,27,28,141,142,204,310,311,312,313,614,615,616,617,625,626,627,628,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,743,744,745,748,749,750,751,752,753,756,757,759,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872，及其药学上可接受的盐。

[0197] 式 (IC) 的实施方案

因此，本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式 (IC)



式 (IC)；

其中

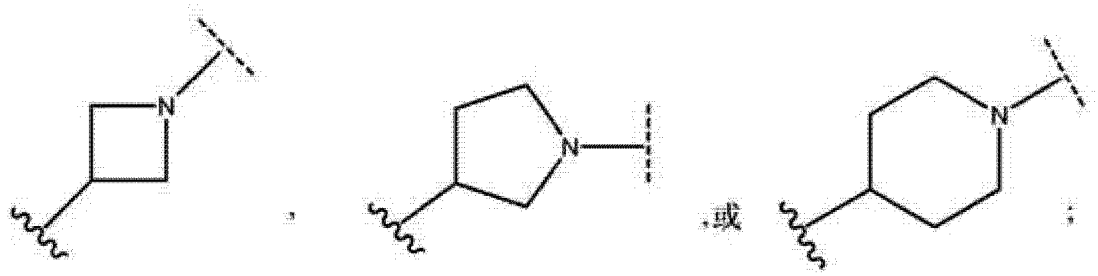
X^1为 N 且 X^2为 CR^1；或

X^1为 CR^1且 X^2为 N；或

X^1为 CR^1且 X^2为 CR^1；

Y^1为 C(O)NH、或 NHC(O)；

Z^1为



其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点；

R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I：

R^2独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：

R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$,

$OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$,

$NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$,

$NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$,

$C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH,

$C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br

和 I；其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4, OR^4, SR^4, $S(O)R^4$,

SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$,

$NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$,

$NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH,

$C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H,

C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl,

和 I；

R^3在每次出现时独立地选自烷基、烯基、炔基、芳基、环烷基、环烯基、和杂环基；其中 R^3中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^5, OR^5, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^5$, $CO(O)R^5$,

$OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$,

$NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$,

$NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)_2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, C(O)NHOH,

$C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, C(O)H,

C(O)OH, $C(N)NH_2$, $C(N)NHR^5$, $C(N)N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F,

Cl, Br 和 I；其中 R^3中的芳基、环烷基、环烯基、和杂环基各自任选被一个或多个独立地

选自以下的取代基取代：

R^6，OR^6，SR^6，$S(O)R^6$，SO_2R^6，$C(O)R^6$，$CO(O)R^6$，$OC(O)R^6$，$OC(O)OR^6$，NH_2，NHR^6，$N(R^6)_2$，$NHC(O)R^6$，$NR^6C(O)R^6$，$NHS(O)_2R^6$，$NR^5S(O)_2R^6$，$NHC(O)OR^6$，$NR^6C(O)OR^6$，$NHC(O)NH_2$，$NHC(O)NHR^6$，$NHC(O)N(R^5)_2$，$NR^6C(O)NHR^6$，$NR^6C(O)N(R^6)_2$，$C(O)NH_2$，$C(O)NHR^6$，$C(O)N(R^6)_2$，$C(O)NHOH$，$C(O)NHOR^6$，$C(O)NHSO_2R^6$，$C(O)NR^6SO_2R^6$，SO_2NH_2，SO_2NHR^6，$SO_2N(R^6)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^6$，$C(N)N(R^6)_2$，$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7，OR^7，SR^7，$S(O)R^7$，SO_2R^7，$C(O)R^7$，$CO(O)R^7$，$OC(O)R^7$，$OC(O)OR^7$，NH_2，NHR^7，$N(R^7)_2$，$NHC(O)R^7$，$NR^7C(O)R^7$，$NHS(O)_2R^7$，$NR^7S(O)_2R^7$，$NHC(O)OR^7$，$NR^7C(O)OR^7$，$NHC(O)NH_2$，$NHC(O)NHR^7$，$NHC(O)N(R^7)_2$，$NR^7C(O)NHR^7$，$NR^7C(O)N(R^7)_2$，$C(O)NH_2$，$C(O)NHR^7$，$C(O)N(R^7)_2$，$C(O)NHOH$，$C(O)NHOR^7$，$C(O)NHSO_2R^7$，$C(O)NR^7SO_2R^7$，SO_2NH_2，SO_2NHR^7，$SO_2N(R^7)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^7$，$C(N)N(R^7)_2$，$CNOH$，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；

R^5在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^5 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^8，OR^8，SR^8，$S(O)R^8$，SO_2R^8，NHR^8，$N(R^8)_2$，$C(O)R^8$，$C(O)NH_2$，$C(O)NHR^8$，$C(O)N(R^8)_2$，$NHC(O)R^8$，$NR^8C(O)R^8$，$NHSO_2R^8$，$NHC(O)OR^8$，SO_2NH_2，SO_2NHR^8，$SO_2N(R^8)_2$，$NHC(O)NH_2$，$NHC(O)NHR^8$，OH，(O)，$C(O)OH$，N_3，CN，NH_2，F，Cl，Br 和 I；

R^6在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^6 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^9，OR^9，SR^9，$S(O)R^9$，SO_2R^9，NHR^9，$N(R^9)_2$，$C(O)R^9$，$C(O)NH_2$，$C(O)NHR^9$，$C(O)N(R^9)_2$，$NHC(O)R^9$，$NR^9C(O)R^9$，$NHSO_2R^9$，$NHC(O)OR^9$，SO_2NH_2，SO_2NHR^9，$SO_2N(R^9)_2$，$NHC(O)NH_2$，$NHC(O)NHR^9$，OH，(O)，$C(O)OH$，N_3，CN，NH_2，CF_3，CF_2CF_3，F，Cl，Br 和 I；

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^8在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^9在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中由 R^4、R^5、R^6、R^7，R^8、和 R^9表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}，OR^{10}，SR^{10}，$S(O)R^{10}$，SO_2R^{10}，$C(O)R^{10}$，$CO(O)R^{10}$，$OC(O)R^{10}$，$OC(O)OR^{10}$，$C(O)C(O)R^{10}$，NH_2，NHR^{10}，$N(R^{10})_2$. $NHC(O)R^{10}$，$NR^{10}C(O)R^{10}$，$NHS(O)_2R^{10}$，$NR^{10}S(O)_2R^{10}$，$NHC(O)OR^{10}$，$NR^{10}C(O)OR^{10}$，$NHC(O)NH_2$，$NHC(O)NHR^{10}$，$NHC(O)N(R^{10})_2$，$NR^{10}C(O)NHR^{10}$，$NR^{10}C(O)N(R^{10})_2$，$C(O)NH_2$，$C(O)NHR^{10}$，$C(O)N(R^{10})_2$，$C(O)NHOH$，$C(O)NHOR^{10}$，$C(O)NHSO_2R^{10}$，$C(O)NR^{10}SO_2R^{10}$，SO_2NH_2，SO_2NHR^{10}，$SO_2N(R^{10})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{10}$，$C(N)N(R^{10})_2$，$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$,

$OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$,

$NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$,

$NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$,

$C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11},

$SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, $CNOH$, $CNOCH_3$, OH,

(O), CN, N_3, NO_2, F, C_1, Br 和 I；其中R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$,

$OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$,

$NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$,

$NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$,

$C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12},

$SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, $CNOH$, $CNOCH_3$, OH,

CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br 和 I；

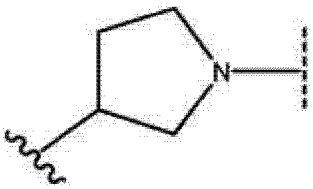
R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

条件是

当X^1为CR^1且X^2为CR^1时；R^1为氢；Y^1为NHC(O)；Z^1为



；且R^2为吡咯基；所述R^2中的吡咯基未被两个烷基取代。

[0198] 在式(IC)的一个实施方案中，X^1为N且X^2为CR^1；或X^1为CR^1且X^2为N；或X^1为CR^1且X^2为CR^1。在式(IC)的另一个实施方案中，X^1为N且X^2为CR^1。在式(IC)的另一个实施方案中，X^1为CR^1且X^2为N。在式(IC)的另一个实施方案中，X^1为CR^1且X^2为CR^1。

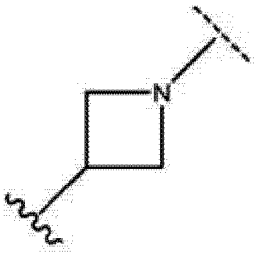
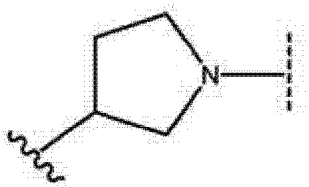
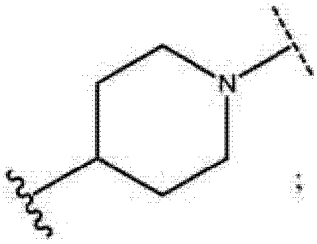
[0199] 在式(IC)的一个实施方案中，R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br和I。在式(IC)的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br和I。在式(IC)的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和Cl。在式(IC)的另一个实施方案中，R^1在每次出现时为氢。

[0200] 在式(IC)的一个实施方案中，X^1为CR^1且X^2为CR^1；且R^1在每次出现时独立地选自

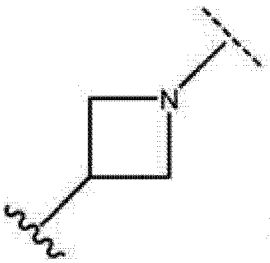
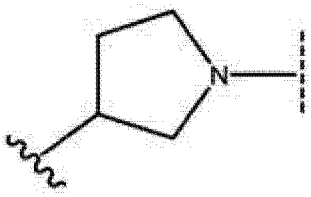
氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (IC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时为氢。

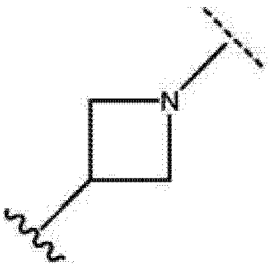
[0201] 在式 (IC) 的一个实施方案中，Y^1为 C(O)NH、或 NHC(O)。在式 (IC) 的另一个实施方案中，Y^1为 C(O)NH。在式 (IC) 的另一个实施方案中，Y^1为 NHC(O)。

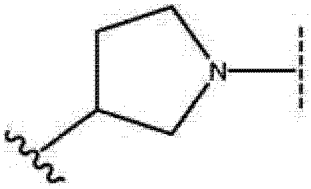
[0202] 在式 (IC) 的一个实施方案中，Z^1为

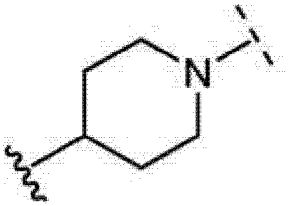

，

，或

；

其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。在式 (IC) 的另一个实施方案中，Z^1为


，或

；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。在式 (IC) 的另一个实施方案中，Z^1为


；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。在式 (IC) 的另一个实施方案中，Z^1为


；其中 表示连接至 Y^1的点且 表示连接至含氮杂芳基的点。在式 (IC) 的另一个实施方案中，Z^1为



；其中 表示连接至 Y^1 的点且 表示连接至含氮杂芳基的点。

[0203] 在式 (IC) 的一个实施方案中，R^2 独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2 中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：R^3，OR^3，SR^3，$S(O)R^3$，

SO_2R^3，$C(O)R^3$，$CO(O)R^3$，$OC(O)R^3$，$OC(O)OR^3$，NH_2，NHR^3，$N(R^3)_2$，$NHC(O)R^3$，

$NR^3C(O)R^3$，$NHS(O)_2R^3$，$NR^3S(O)_2R^3$，$NHC(O)OR^3$，$NR^3C(O)OR^3$，$NHC(O)NH_2$，

$NHC(O)NHR^3$，$NHC(O)N(R^3)_2$，$NR^3C(O)NHR^3$，$NR^3C(O)N(R^3)_2$，$C(O)NH_2$，$C(O)NHR^3$，

$C(O)N(R^3)_2$，$C(O)NHOH$，$C(O)NHOR^3$，$C(O)NHSO_2R^3$，$C(O)NR^3SO_2R^3$，SO_2NH_2，

SO_2NHR^3，$SO_2N(R^3)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^3$，$C(N)N(R^3)_2$，$CNOH$，

$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^2 中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：

R^4，OR^4，SR^4，$S(O)R^4$，SO_2R^4，$C(O)R^4$，$OC(O)OR^4$，NH_2，NHR^4，

$N(R^4)_2$，$NHC(O)R^4$，$NR^4C(O)R^4$，$NHS(O)_2R^4$，$NR^4S(O)_2R^4$，$NHC(O)OR^4$，$NR^4C(O)OR^4$，

$NHC(O)NH_2$，$NHC(O)NHR^4$，$NHC(O)N(R^4)_2$，$NR^4C(O)NHR^4$，$NR^4C(O)N(R^4)_2$，$C(O)NH_2$，

$C(O)NHR^4$，$C(O)N(R^4)_2$，$C(O)NHOH$，$C(O)NHOR^4$，$C(O)NHSO_2R^4$，$C(O)NR^4SO_2R^4$，

SO_2NH_2，SO_2NHR^4，$SO_2N(R^4)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^4$，$C(N)N(R^4)_2$，

$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，和 I。在式 (IC) 的另一个实施方案中，R^2 为芳基；其中 R^2 中的芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、F、Cl、和 I。在式 (IC) 的另一个实施方案中，R^2 为芳基；其中 R^2 中的芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。在式 (IC) 的另一个实施方案中，R^2 为苯基；其中 R^2 中的苯基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。在式 (IC) 的另一个实施方案中，R^2 为苯基；其中 R^2 中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和 SO_2R^4。

[0204] 在式 (IC) 的另一个实施方案中，R^2 为 5-6 元杂芳基；其中 R^2 中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、F、Cl、和 I。在式 (IC) 的另一个实施方案中，R^2 为 5-6 元杂芳基；其中 R^2 中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。在式 (IC) 的另一个实施方案中，R^2 为吡啶基、呋喃基、噻吩基、吡唑、或噻唑基；其中 R^2 中的吡啶基、呋喃基、噻吩基、吡唑、或噻唑基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。

[0205] 在式 (IC) 的一个实施方案中，R^4 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^7，OR^7，SR^7，$S(O)R^7$，

SO_2R^7，$C(O)R^7$，$CO(O)R^7$，$OC(O)R^7$，$OC(O)OR^7$，NH_2，NHR^7，$N(R^7)_2$，$NHC(O)R^7$，

$NR^7C(O)R^7$，$NHS(O)_2R^7$，$NR^7S(O)_2R^7$，$NHC(O)OR^7$，$NR^7C(O)OR^7$，$NHC(O)NH_2$，

$NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (IC) 的另一个实施方案中，R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基。

[0206] 在式 (IC) 的一个实施方案中，R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (IC) 的另一个实施方案中，R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7、OR^7、$N(R^7)_2$、F、Cl、Br 和 I。

[0207] 在式 (IC) 的一个实施方案中，R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。在式 (IC) 的另一个实施方案中，R^7在每次出现时独立地选自烷基、芳基、杂环基、和环烷基。

[0208] 在式 (IC) 的一个实施方案中，R^4和 R^7中的环状基团各自独立地任选被一个或多个独立地选自以下的取代基取代：

R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, SO_2, $N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：

R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$,

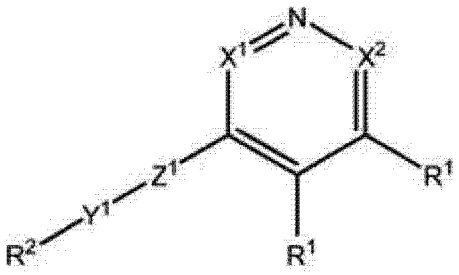
$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，$C(O)NHOH$，$C(O)NHOR^{12}$，

$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，$SO^2N(R^{12})_2$，$C(O)H$，$C(O)OH$，

$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0209] 在式（IC）的另一个实施方案中，R^4和 R^7中的环状基团各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)H$、OH、F、Cl、Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、NH_2、OH、CN、CF_3、OCF_3、F、和 Cl；R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、CF_3、F、和 Cl；R^{12}在每次出现时独立地选自烷基和芳基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、和环烷基。

[0210] 本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式（IC）



式（IC）；

其中

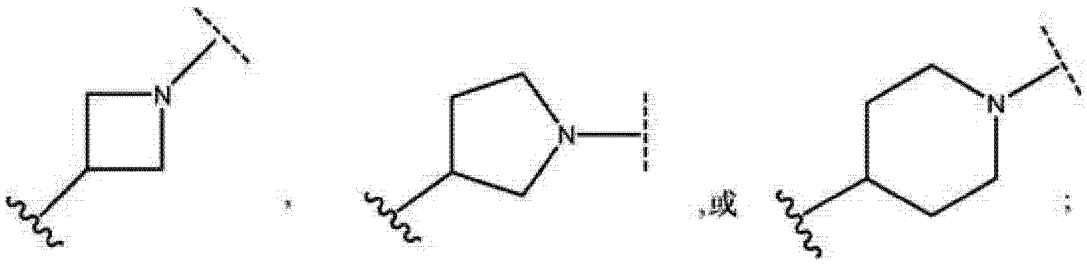
X^1为 N 且 X^2为 CR^1；或

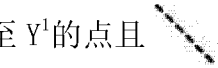
X^1为 CR^1且 X^2为 N；或

X^1为 CR^1且 X^2为 CR^1；

Y^1为 C(O)NH、或 NHC(O)；

Z^1为



其中表示连接至 Y^1的点且  表示连接至含氮杂芳基的点；

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、Cl、和 F；

R^2为芳基或 5-6 元杂芳基，其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、SO_2R^4、OR^4、$C(O)NHR^4$、和 F；

R^4在每次出现时独立地选自烷基、烯基、芳基、杂环基、和环烷基；其中 R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7、OR^7、$N(R^7)_2$、和 F；

R^7在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；

其中由 R^4和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：

R^{10}、$C(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)R^{10}$、$C(O)OH$、OH 和 F；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代：R^{12}、OR^{12}、$C(O)R^{12}$、NH_2、OH、CN、CF_3、OCF_3、F、和 Cl；

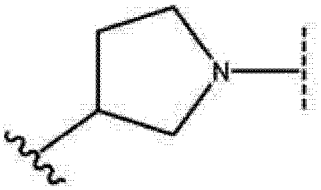
R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl；

R^{12}在每次出现时独立地选自烷基、和芳基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、环烷基、和杂环基；

条件是

当 X^1为 CR^1且 X^2为 CR^1时；R^1为氢；Y^1为 NHC(O)；Z^1为



；且 R^2为吡咯基；所述 R^2中的吡咯基未被两个烷基取代。

[0211] 仍另一个实施方案涉及具有式 (IC) 的化合物，其包括

1-(吡啶 -3- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 氧基} 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 氰基吡啶 -3- 基)-N-{4-[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 苯基} 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 氧基} 苯基)-1-[2-(三氟甲基) 吡啶 -3- 基] 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 氧基} 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(4- 甲基吡啶 -3- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 氧基} 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(4- 氟吡啶 -3- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 氧基} 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-[4-(三氟甲基)吡啶-3-基]氮杂环丁烷-3-甲酰胺；

叔丁基4-[4-({[(3S)-1-(吡啶-3-基)吡咯烷-3-基]羰基}氨基)苯氧基]哌啶-1-甲酸酯；

叔丁基4-[4-({[(3R)-1-(吡啶-3-基)吡咯烷-3-基]羰基}氨基)苯氧基]哌啶-1-甲酸酯；

1-(吡啶-3-基)-N-(4-{1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

(3S)-1-(吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(吡啶-3-基)-N-[4-({1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}氧基)苯基]吡咯烷-3-甲酰胺；

(3S)-1-(吡啶-3-基)-N-[4-({1-[(2R)-四氢呋喃-2-基羰基]哌啶-4-基}氧基)苯基]吡咯烷-3-甲酰胺；

(3S)-1-(吡啶-3-基)-N-(4-{[1-(四氢呋喃-3-基羰基)哌啶-4-基]氧基}苯基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(环丙基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(吡啶-3-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)吡咯烷-3-甲酰胺；

(3S)-N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)吡咯烷-3-甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[1-(吡啶-3-基)氮杂环丁烷-3-基]-4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯甲酰胺；

N-(4-{1-[(2S)-2-甲基丁酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)-N-[1-(吡啶-3-基)氮杂环丁烷-3-基]苯甲酰胺；

4-{[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]氧基}-N-[1-(吡啶-3-基)氮杂环丁烷-3-基]苯甲酰胺；

1-(吡啶-3-基)-N-{4-[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

叔丁基 4-(4-{[(3S)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 氨基甲酰基 } 苯氧基) 哌啶 -1- 甲酸酯 ;

叔丁基 4-(4-{[(3R)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 氨基甲酰基 } 苯氧基) 哌啶 -1- 甲酸酯 ;

N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2S)-2- 甲基丁酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(吡啶 -3- 基)-N-[4-({1-[(2S)- 四氢呋喃 -2- 基羰基] 哌啶 -4- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 戊酰基哌啶 -4- 基) 氧基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2- 甲基环丙基) 羰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(1S,4R)- 双环 [2.2.1] 庚 -2- 基乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(4- 甲基戊酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 甲基戊酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 乙氧基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 丁酰基哌啶 -4- 基) 氧基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(乙氧基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁

烷 -3- 甲酰胺；

N-(4-{[1-(N- 乙酰基 -L- 亮氨酰）哌啶 -4- 基］氧基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 甲氧基乙氧基）乙酰基］哌啶 -4- 基｝氧基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环己基羰基）哌啶 -4- 基］氧基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环己基乙酰基）哌啶 -4- 基］氧基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-(4-{[1-(4,4,4- 三氟丁酰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环戊基羰基）哌啶 -4- 基］氧基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基环己基）羰基］哌啶 -4- 基｝氧基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（呋喃 -3- 基羰基）哌啶 -4- 基］氧基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-(4-{[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 乙酰基哌啶 -4- 基）氧基］苯基｝-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（甲氧基乙酰基）哌啶 -4- 基］氧基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-(4-{[1-（噻吩 -3- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝氧基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（吗啉 -4- 基乙酰基）哌啶 -4- 基］氧基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-(4-{[1-（噻吩 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝氧基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（呋喃 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基 -1H- 吡咯 -2- 基）羰基］哌啶 -4- 基｝氧基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 丙酰基哌啶 -4- 基）氧基］苯基｝-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基环丙基）羰基］哌啶 -4- 基｝氧基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(N，N- 二甲基 - β - 丙氨酰）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-(4-{[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环戊基乙酰基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,3- 二甲基丁酰基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基｝-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基｝-1-(4- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基｝-1-(2- 甲氧基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基甲基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基戊基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 乙基丁基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丁基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 丙基哌啶 -4- 基）氧基］苯基｝-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 环丙基乙基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-(4-{[1-（四氢呋喃 -3- 基甲基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丁基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环己基甲基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,3-二甲基丁基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环戊基甲基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丁基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲基戊基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-丁基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-乙基丁基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-甲基丁基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲基丙基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-丙基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(4-甲氧基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(4-氰基吡啶-3-基)-N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-[4-(1-戊酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-甲基戊酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(1S,4R)-双环[2.2.1]庚-2-基乙酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(吗啉-4-基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(呋喃-3-基羰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-{4-[1-(吡咯烷-1-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(5-氧代-D-脯氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(N,N-二甲基-β-丙氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-{4-[1-(1,3-噻唑-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(1-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(3-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(4-甲基哌嗪-1-基)乙酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(5-氧代-L-脯氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-乙氧基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(4-甲基戊酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(1-甲基环己基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-乙酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环己基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(N-乙酰基-L-亮氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[3-(吗啉-4-基)丙酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-{4-[1-(噻吩-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲

酰胺；

N-(4-{1-[(1- 甲基 -1H- 吡咯 -2- 基）羰基］哌啶 -4- 基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(呋喃 -2- 基羰基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[3-(哌啶 -1- 基）丙酰基］哌啶 -4- 基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(乙氧基乙酰基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁酰基哌啶 -4- 基）苯基］-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(甲氧基乙酰基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环己基羰基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基丁酰基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环戊基羰基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -4- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环戊基乙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -4- 基）吡咯烷 -3- 甲酰胺；

N-(4-{1-[(2S)-2- 甲基丁酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环戊基乙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-{4-[1-(四氢 -2H- 吡喃 -4- 基乙酰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-{4-[1-(四氢 -2H- 吡喃 -4- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲

酰胺；

N-{4-[1-(2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,5-二氯苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(2-甲基吡啶-3-基)-N-(4-{1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

1-(2-甲基吡啶-3-基)-N-{4-[1-(哒嗪-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

1-(2-甲基吡啶-3-基)-N-[4-(1-戊酰基哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-甲基戊酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(1S,4R)-双环[2.2.1]庚-2-基乙酰基]哌啶-4-基}苯基)-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(2-甲基吡啶-3-基)-N-{4-[1-(吗啉-4-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(呋喃-3-基羰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(2-甲基吡啶-3-基)-N-{4-[1-(吡咯烷-1-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(5- 氧代 -D- 脯氨酰) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(N,N- 二甲基 - β - 丙氨酰) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(3- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(4- 甲基哌嗪 -1- 基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(5- 氧代 -L- 脯氨酰) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 乙氧基丙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 甲基环己基) 羰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 乙酰基哌啶 -4- 基) 苯基]-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环己基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(N- 乙酰基 -L- 亮氨酰) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-[4-(1- 丙酰基哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 甲氧基乙氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[3-(吗啉 -4- 基) 丙酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(5- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基)

氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(1- 甲基 -1H- 吡咯 -2- 基) 羰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(呋喃 -2- 基羰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[3-(哌啶 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(乙氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁酰基哌啶 -4- 基) 苯基]-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(甲氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环己基羰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氟苯甲酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[二氟 (苯基) 乙酰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4,4- 二氟环己基) 羰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4- 氟苯基) 乙酰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-[4-({1-[4-(三氟甲基) 苯甲酰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 苯甲酰基氮杂环丁烷 -3- 基）氧基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 羟基 -2- 甲基丙酰基）氮杂环丁烷 -3- 基］氧基} 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基)-N-(4-{[1-（四氢呋喃 -3- 基羰基）氮杂环丁烷 -3- 基］氧基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（呋喃 -3- 基羰基）氮杂环丁烷 -3- 基］氧基} 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 戊酰基氮杂环丁烷 -3- 基）氧基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氯苯甲酰基）哌啶 -4- 基］氧基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 甲基丁酰基］哌啶 -4- 基} 氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基］氧基} 苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-（四氢 -2H- 吡喃 -4- 基羰基）哌啶 -4- 基］氧基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[二氟（苯基）乙酰基］哌啶 -4- 基} 氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4,4- 二氟环己基）羰基］哌啶 -4- 基} 氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基 -2- 苯基丙酰基）哌啶 -4- 基］氧基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-(1,3- 噻唑 -4- 基羰基）哌啶 -4- 基］氧基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基} 氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-{4-[(1-{[4-（三氟甲基）苯基］乙酰基} 哌啶 -4- 基）氧基］苯基} 氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-（四氢呋喃 -2- 基羰基）哌啶 -4- 基］氧基} 苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-[4-({1-[3-（三氟甲基）苯甲酰基］哌啶 -4- 基} 氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{[1-（噻吩 -3- 基羰基）哌啶 -4- 基］氧基} 苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-[4-({1-[3-（三氟甲氧基）苯甲酰基］哌啶 -4- 基} 氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁酰基）哌啶 -4- 基］氧基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁

烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（四氢呋喃 -3- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4- 氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基乙酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,4- 二氟苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-({1-[4-（三氟甲氧基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2,4- 二氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-({1-[4-（三氟甲基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[(1-{[4-（三氟甲氧基）苯基］乙酰基｝哌啶 -4- 基）氧基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[(1-{[3-（三氟甲基）苯基］乙酰基｝哌啶 -4- 基）氧基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（吡啶 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 乙酰基哌啶 -4- 基）氧基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氯苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(甲氧基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2- 氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 氯苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环丙基羰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3,3- 二甲基丁酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环己基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2- 甲基环丙基) 羰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环戊基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环丁基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[1-(四氢呋喃 -2- 基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(4- 甲基戊酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基丙酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂

环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 甲基丁酰基] 氮杂环丁烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(甲氧基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[二氟 (苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4,4- 二氟环己基) 羰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[1-(1,3- 噻唑 -4- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-{4-[(1-{[4-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,4- 二氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-{4-[(1-{[4-(三氟甲氧基) 苯基] 乙酰基 } 哌啶 -4- 基) 氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4- 氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2,4- 二氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氯苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基 -2- 苯基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 乙酰基哌啶 -4- 基) 氧基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[1-(1,3- 噻唑 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-({1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-({1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(3-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-({1-[4-(三氟甲氧基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(3,5-二氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-({1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环丙基乙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(吡啶-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(四氢呋喃-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3,5-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2,2-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环丙基羰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(四氢呋喃-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(噻吩-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁

烷 -3- 甲酰胺；

N-[4-({1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-{4-[(1-{[3-（三氟甲基）苯基］乙酰基｝哌啶 -4- 基）氧基］苯基｝氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（四氢 -2H- 吡喃 -4- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 甲基丁酰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基］-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

5-[1-(2- 甲基丙基）-1H- 吡唑 -4- 基］-N-[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］呋喃 -2- 甲酰胺；

(3S)-N-{4-[1-(2- 甲基丙酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-（哒嗪 -3- 基）-N-{4-[1-（四氢 -2H- 吡喃 -4- 基乙酰基）哌啶 -4- 基］苯基｝吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

叔丁基 4-(4-{[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］氨基甲酰基｝苯基）哌啶 -1- 甲酸酯；

5-[1-(2- 甲基丙基）-1H- 吡唑 -4- 基］-N-[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］噻吩 -2- 甲酰胺；

N-[4-(1- 乙酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 戊酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基丁酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基丁酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 己酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基戊酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基戊酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 甲基戊酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丁酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁

烷 -3- 甲酰胺；

N-{4-[1-(2,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 乙基丁酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 庚酰基哌啶 -4- 基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（丁 -3- 烯酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（戊 -4- 烯酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（甲氧基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[（甲基巯基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 甲氧基乙氧基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 硝基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[3-（甲基巯基）丙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（戊 -4- 炔酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环己基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环己基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 羟基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 羟基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲氧基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁

烷 -3- 甲酰胺；

N-{4-[1-(3- 甲氧基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 甲氧基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氰基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 氰基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{1-[3-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{1-[4-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{1-[3-（三氟甲氧基）苯甲酰基］哌啶 -4- 基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,3- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,4- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,5- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,4- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,4- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,5- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,4- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 氟苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3- 氟苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 氟苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 氯苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 氯苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-[4-(1-{[4-（三氟甲基）苯基］乙酰基} 哌啶 -4- 基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,5- 二甲基苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,5- 二氟苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,4- 二氯苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（呋喃 -3- 基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-{4-[1-（噻吩 -2- 基羰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(5- 甲基吡嗪 -2- 基）羰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环丙基）羰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 乙氧基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 苯基环丙基）羰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-(4-{1-[（嘧啶 -2- 基巯基）乙酰基］哌啶 -4- 基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 乙酰基哌啶 -4- 基）羰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁

烷 -3- 甲酰胺；

N-{4-[1-(N- 乙酰基 -L- 亮氨酰）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（二苯基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(5- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氟 -4- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,3- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[4-（丙烷 -2- 基）苯甲酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 叔丁基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[2- 氟 -5-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[2- 氯 -5-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(4- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环戊基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基苯氧基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2S)-2- 苯基丁酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-(1-{[3-（三氟甲基）苯基］乙酰基｝哌啶 -4- 基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3- 氯苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,4- 二氯苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（萘 -1- 基羰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2R)-2- 甲氧基 -2- 苯基乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[N-（呋喃 -2- 基羰基）甘氨酰］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[（苄基氧基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（萘 -1- 基乙酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环丙基羰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[1-（四氢呋喃 -2- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N- 苯甲酰基甘氨酰）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[1-（四氢呋喃 -3- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{1-[4-（噻吩 -2- 基）丁酰基］哌啶 -4- 基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,5- 二氟苯甲酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环丁基羰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1-{N-[(4- 甲基苯基）磺酰基］甘氨酰｝哌啶 -4- 基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,3- 二氟苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2S)-2- 甲氧基 -2- 苯基乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（萘 -2- 基乙酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 苯基丙酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,6- 二氯苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁

烷 -3- 甲酰胺；

N-(4-{1-[3-(苯基磺酰基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,5- 二甲基呋喃 -3- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环丙基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(1,3- 噻唑 -4- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(1,3- 噻唑 -5- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(乙氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(6- 甲基吡啶 -3- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(呋喃 -2- 基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环己基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氧代丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环戊基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丙酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氯苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-(1,3- 噻唑 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(环丙基乙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(2S)-2-甲基丁酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(四氢-2H-吡喃-4-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-{[4-(三氟甲氧基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(噻吩-3-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(4-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(3,5-二氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(3,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(3-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-({(3R)-1-[3-(三氟甲基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(2,4-二氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-{[4-(三氟甲基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(1,3-噻唑-4-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(四氢呋喃-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(5-甲基噻吩-2-基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(2-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(环丙基羰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(四氢呋喃-3-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-({(3R)-1-[3-(三氟甲氧基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(吡啶-2-基羰基)吡咯烷-3-基]氧基}苯基)

氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氯苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(4- 氯苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基 -2- 苯基丙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-（甲氧基乙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-（噻吩 -2- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-{[3-（三氟甲基）苯基］乙酰基｝吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基丙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丁酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3,5- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({(3R)-1-[4-（三氟甲基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({(3R)-1-[4-（三氟甲氧基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 甲基丁酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-(3,3,3- 三氟丙酰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[二氟（苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(4,4- 二氟环己基）羰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氯苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(1,3- 噻唑 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(环丙基乙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(2S)-2- 甲基丁酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(四氢 -2H- 吡喃 -4- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-{[4-(三氟甲氧基) 苯基] 乙酰基 } 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(4- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(噻吩 -3- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(4- 氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(3,5- 二氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(3,4- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(3- 氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-[4-({(3R)-1-[3-(三氟甲基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(2,4- 二氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-{[4-(三氟甲基) 苯基] 乙酰基 } 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(1,3- 噻唑 -4- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(四氢呋喃 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(5- 甲基噻吩 -2- 基) 羰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(2- 氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(环丙基羰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂

环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(四氢呋喃 -3- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-[4-({(3R)-1-[3-(三氟甲氧基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(吡啶 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氯苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(4- 氯苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基 -2- 苯基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(甲氧基乙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(噻吩 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-{[3-(三氟甲基) 苯基] 乙酰基 } 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丁酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3,5- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-[4-({(3R)-1-[4-(三氟甲基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-[4-({(3R)-1-[4-(三氟甲氧基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 甲基丁酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(3,3,3- 三氟丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[二氟(苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(2,2-二甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({(3R)-1-[(4,4-二氟环己基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(1,3-噻唑-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环丙基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(4-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(3,5-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,4-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(3-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-(4-{1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2,4-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(1,3-噻唑-4-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰

胺；

1-(哒嗪-4-基)-N-{4-[1-(四氢呋喃-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(吡啶-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲基-2-苯基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,4-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(噻吩-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-[4-(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-(4-{1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-(4-{1-[4-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{1-[二氟(苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(4,4-二氟环己基)羰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-[4-(1-{[4-(三氟甲氧基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-(1-{[4-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-叔丁基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-甲氧基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环己基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环丙基乙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲氧基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(2S)-2-苯基丁酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[4-(丙烷-2-基)苯甲酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-苯甲酰基哌啶-4-基)磺酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(4,4,4-三氟丁酰基)哌啶-4-基]磺酰基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2,5-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(4-氟苯基)乙酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环

丁烷 -3- 甲酰胺；

N-(4-{[1-(2,3- 二甲基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 氟苯基）乙酰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-[4-({1-[3-（三氟甲基）苯甲酰基］哌啶 -4- 基｝磺酰基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-[4-({1-[4-（三氟甲基）苯甲酰基］哌啶 -4- 基｝磺酰基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,3- 二氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氯苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（萘 -1- 基羰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基羰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲氧基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环戊基羰基）哌啶 -4- 基］磺酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(苯基乙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(1-苯基环丙基)羰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-甲基丙氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3R)-1-(吡啶-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3R)-1-(哒嗪-4-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3R)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-4-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(吡啶-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

叔丁基 4-(2-甲基-1-氧代-1-{4-[4-({[1-(吡啶-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]哌啶-1-基}丙烷-2-基)哌嗪-1-甲酸酯;

N-(4-{1-[2-甲基-2-(哌嗪-1-基)丙酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-甲基戊酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(2-氟苯基)乙酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-苯甲酰基哌啶-4-基)磺酰基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环戊基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[(3R)-1-(5,6-二氯哒嗪-4-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-2-甲酰胺;

N-[(3R)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]

噻吩 -2- 甲酰胺；

N-[(3S)-1-(5,6- 二氯哒嗪 -4- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -2- 甲酰胺；

N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -2- 甲酰胺；

N-[(3R)-1-(5,6- 二氯哒嗪 -4- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -3- 甲酰胺；

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -3- 甲酰胺；

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -4- 基) 吡咯烷 -3- 基] 噻吩 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 哌啶 -4- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 哌啶 -4- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 哌啶 -4- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 哌啶 -4- 甲酰胺；

N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(1,3- 噻唑 -5- 基羰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2S)-2- 苯基丁酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2S)-2- 甲氧基 -2- 苯基乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2R)-2- 甲氧基 -2- 苯基乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(乙氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(4- 甲基苯氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(四氢呋喃 -3- 基羰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(萘 -1- 基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2,6- 二氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(萘 -1- 基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-1-(哒嗪 -3- 基)-N-(4-{1-[4-(噻吩 -2- 基) 丁酰基] 哌啶 -4- 基 } 苯基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(环丙基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,5- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(萘 -2- 基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[3-(苯基磺酰基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-1-(哒嗪 -3- 基)-N-[4-(1-{[3-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 苯基] 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(呋喃 -2- 基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(N- 苯甲酰基甘氨酰) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(2,4- 二氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(1- 甲基环己基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(6- 甲基吡啶 -3- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(3- 氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 丙酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(环戊基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-氟-5-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-氟吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-氟-6-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

(3S)-N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,4-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-庚酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,4-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(4-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,3-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-己酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(3-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯

烷 -3- 甲酰胺；

(3S)-N-[4-(1- 丁酰基哌啶 -4- 基）苯基]-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 甲基戊酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(3,5- 二甲基苯基）乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,5- 二氯苯甲酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(4- 氯苯基）乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(呋喃 -3- 基羰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,4- 二甲基苯甲酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 氟苯甲酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[2- 氯 -5-(三氟甲基）苯甲酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 乙酰基哌啶 -4- 基）苯基]-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,5- 二甲基苯甲酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 乙氧基丙酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,5- 二氯苯甲酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,5- 二甲基苯甲酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(5- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(二苯基乙酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-(4-{1-[4-(三氟甲基）苯甲酰基] 哌啶 -4- 基 } 苯基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(戊 -4- 烯酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{1-[(1-苯基环丙基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{1-[2-氟-5-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(环己基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(4-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(2-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(2-乙基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(4-叔丁基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{1-[(2-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{1-[(1-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(戊-4-炔酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{1-[(3-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{1-[3-(甲基巯基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{1-[(1-乙酰基哌啶-4-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(丁-3-烯酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(2,2-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(3-氟-4-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(3-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯

烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2- 氯苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2- 甲氧基乙氧基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(N- 乙酰基 -L- 亮氨酰）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 氰基苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 甲氧基苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,3- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[4-(丙烷 -2- 基）苯甲酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环己基羰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(噻吩 -2- 基羰基）哌啶 -4- 基］苯基｝吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 羟基苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氰基苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基］苯基｝吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(甲氧基乙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 甲基丁酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(2- 氰基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(4- 氰基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(6- 氟 -4- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

2-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-1,3-噻唑-5-甲酰胺；

(3S)-N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-甲基吡啶-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(2-甲基吡啶-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

N-[(3S)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]呋喃-2-甲酰胺；

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]呋喃-2-甲酰胺；

N-(4-{1-[(4-甲基四氢-2H-吡喃-4-基)甲基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[(3S)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-4-[1-(2-甲基丙酰基)哌啶-4-基]苯甲酰胺；

N-(4-{1-[2-(哌嗪-1-基)乙基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

4-[1-(2-甲基丙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]苯甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

5-[1-(3-氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺；

5-[1-(4-氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺；

(3S)-N-(4-{1-[(4-甲基四氢-2H-吡喃-4-基)甲基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-羟基-2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(四氢-2H-吡喃-4-基羰基)哌啶-4-基]噻吩-2-甲酰胺；

(3S)-N-{4-[1-(2,2-二甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯

烷 -3- 甲酰胺；

5-[1-(2- 甲基丙酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

5-{1-[(2- 甲基环丙基) 羰基] 哌啶 -4- 基 }-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

5-[1-(2- 氟苯甲酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

5-(1- 苯甲酰基哌啶 -4- 基)-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(四氢呋喃 -3- 基羰基) 哌啶 -4- 基] 噻吩 -2- 甲酰胺；

N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基]-5-{1-[(2R)- 四氢呋喃 -2- 基羰基] 哌啶 -4- 基 } 噻吩 -2- 甲酰胺；

5-{1-[(1- 甲基哌啶 -4- 基) 乙酰基] 哌啶 -4- 基 }-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺；

N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(1,3- 噻唑 -4- 基羰基) 哌啶 -4- 基] 噻吩 -2- 甲酰胺；

(3S)-N-{4-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(丙烷 -2- 基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环丙基甲基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(四氢 -2H- 吡喃 -2- 基甲基)-1H- 吡唑 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 叔丁基 -1H- 吡唑 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1- 苯甲酰基吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(2- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(3- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(4- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(3,5- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(2-甲基苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[(3R)-1-(2,2-二甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-[4-({(3R)-1-[(4,4-二氟环己基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-1-(哒嗪-3-基)-N-(4-{[(3R)-1-(4,4,4-三氟丁酰基)吡咯烷-3-基]氧基}苯基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[(3R)-1-(2,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

N-[4-(5-丙基-1,2,4-氧杂二唑-3-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

(3S)-N-{4-[1-(2-氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(3-氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(4-氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-[4-(1-苯甲酰基氮杂环丁烷-3-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(2,2-二甲基丙酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(3,5-二氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(2-甲基苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(2,4-二氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3R)-N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3R)-N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3R)-N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[1-(环己基羰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[1-(3-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[(1-苯甲酰基哌啶-4-基)氧基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[1-(4-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-[4-({1-[(2-甲基环丙基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

N-{4-[5-(2,2-二甲基丙基)-1,3,4-氧杂二唑-2-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,2-二甲基丙基)-1H-咪唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(3-环丙基-1-甲基-1H-吡唑-5-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[5-(2,2-二甲基丙基)-1,2,4-氧杂二唑-3-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[3-环丙基-1-(2-甲氧基乙基)-1H-吡唑-5-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

叔丁基4-(5-{[1-(哒嗪-3-基)氮杂环丁烷-3-基]氨基甲酰基}噻吩-2-基)哌啶-1-甲酸酯;

叔丁基4-氟-4-[4-({[1-(哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]哌啶-1-甲酸酯;

5-(1-苯甲酰基哌啶-4-基)-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺;

5-[1-(2-氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺;

5-[1-(2-甲基苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺;

5-[1-(2,4-二氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺;

5-[1-(3-氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺;

5-[1-(4-氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺;

5-[1-(3,5-二氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺;

N-{4-[3-环丙基-1-(2-羟基乙基)-1H-吡唑-5-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰

胺；

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(6-氟哒嗪-3-基)-N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-乙基丁酰基)哌啶-4-基]苯基}-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

(3S)-N-(4-{[(3S)-1-苯甲酰基吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3S)-1-(2-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3S)-1-(3,5-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3S)-1-(2,2-二甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

N-{2-氟-4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)-2-氟苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{2-氟-4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{2-氟-4-[1-(2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{2-氟-4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,4-二氟苯甲酰基)哌啶-4-基]-2-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,5-二氟苯甲酰基)哌啶-4-基]-2-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]-2-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

(3S)-N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(6-甲基哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[(1-苯甲酰基哌啶-4-基)氧基]苯基}-1-(6-甲基哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(2,2- 二甲基丙酰基)哌啶 -4- 基]氧基}苯基)-1-(6- 甲基哒嗪 -3- 基)吡咯烷 -3- 甲酰胺;

(3S)-N-(4-{[1-(环己基羰基)哌啶 -4- 基]氧基}苯基)-1-(6- 甲基哒嗪 -3- 基)吡咯烷 -3- 甲酰胺;

N-{4-[8-(2- 甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基]苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺;

1-(哒嗪 -3- 基)-N-{4-[8-(4,4,4- 三氟丁酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基]苯基}氮杂环丁烷 -3- 甲酰胺;

N-[4-(8- 苯甲酰基 -8- 氮杂双环 [3.2.1] 辛 -3- 基)苯基]-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺;

N-{4-[8-(2- 氟苯甲酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基]苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺;

N-{4-[8-(2,2- 二甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基]苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺;

N-(4-{8-[(1- 甲基环丙基)羰基]-8- 氮杂双环 [3.2.1] 辛 -3- 基}苯基)-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺;

N-{4-[1-(2- 甲氧基乙基)-3-(2- 甲基丙基)-1H- 吡唑 -5- 基]苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺;

5-[1-(2,2- 二甲基丙酰基)哌啶 -4- 基]-N-[1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基]噻吩 -2- 甲酰胺;

5-{1-[(1- 甲基环丙基)羰基]哌啶 -4- 基}-N-[1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基]噻吩 -2- 甲酰胺;

N-[1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基]-5-[1-(3,3,3- 三氟丙酰基)哌啶 -4- 基]噻吩 -2- 甲酰胺;

5-[1-(2,2- 二甲基丁酰基)哌啶 -4- 基]-N-[1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基]噻吩 -2- 甲酰胺;

N-{4-[1-(2- 氟苯甲酰基)哌啶 -4- 基]苯基}-1-(6- 甲基哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺;

N-{4-[1-(2,2- 二甲基丙酰基)哌啶 -4- 基]苯基}-1-(6- 甲基哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺;

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基)氮杂环丁烷 -3- 基]羰基}氨基)苯基]-4- 氟哌啶 -1- 甲酸酯;

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基)氮杂环丁烷 -3- 基]羰基}氨基)苯基]-4- 羟基哌啶 -1- 甲酸酯;

N-[1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基]-5-[1-(4,4,4- 三氟丁酰基)哌啶 -4- 基]噻吩 -2- 甲酰胺;

5-[1-(环丙基羰基)哌啶 -4- 基]-N-[1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基]噻吩 -2- 甲酰胺;

N-{4-[4- 氟 -1-(2- 氟苯甲酰基)哌啶 -4- 基]苯基}-1-(哒嗪 -3- 基)氮杂环丁

烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］-2- 氟苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环丙基羰基）哌啶 -4- 基]-2- 氟苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(2- 氟 -4-{1-[(1- 甲基环丙基）羰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环丙基乙酰基）哌啶 -4- 基］-2- 氟苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基 -4- 氟哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）-4- 氟哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[3- 叔丁基 -1-(2- 甲氧基乙基）-1H- 吡唑 -5- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁基 -3- 叔丁基 -1H- 吡唑 -5- 基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[3- 叔丁基 -1-（四氢 -2H- 吡喃 -4- 基甲基）-1H- 吡唑 -5- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）-2- 氟苯基］-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］-2- 氟苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］-2- 氟苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(4,4,4- 三氟丁酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基哌啶 -4- 基）甲基］-1H- 吡唑 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1- 甲基 -3-（三氟甲基）-1H- 吡唑 -5- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(6- 氯哒嗪 -3- 基）-N-{4-[1-(2,2- 二甲基丙基）-1H- 吡唑 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-(6- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-3- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基)-3- 氟苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基]-3- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环丙基乙酰基) 哌啶 -4- 基]-3- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 氟苯甲酰基)-4- 羟基哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基)-4- 羟基哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(6- 甲基哒嗪 -3- 基)-N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

N-{4-[(1- 苯甲酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁

烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 乙基丁酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-(4,4,4- 三氟丁酰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 乙酰基哌啶 -4- 基）甲基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 甲基丁酰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基环丙基）羰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1-{[4- 甲基 -1-（氧杂环丁烷 -3- 基）哌啶 -4- 基］甲基｝-1H- 吡唑 -4- 基）苯基］-1-(6- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-(4- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

5-[1-(2- 氟苯甲酰基）哌啶 -4- 基］-N-[(3S)-1-（哒嗪 -3- 基）吡咯烷 -3- 基］呋喃 -2- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基］-1-(3- 甲基哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基｝-1-(3- 甲基哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 氨基吡啶 -3- 基）羰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1- 甲基 -5-[4-({[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］羰基｝氨基）苯基］-1H- 吡唑 -3- 甲酸；

乙基 1- 甲基 -5-[4-({[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］羰基｝氨基）苯基］-1H- 吡唑 -3- 甲酸酯；

乙基 1- 苯基 -5-[4-({[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基］羰基｝氨基）苯基］-1H- 吡唑 -3- 甲酸酯；

N-{6-[1-(2- 氟苯甲酰基）哌啶 -4- 基］吡啶 -3- 基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 甲基丁酰基）吡咯烷 -3- 基］氧基｝苯基）-1-(6- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基丙酰基)吡咯烷-3- 基]氧基}苯基)-1-(6- 甲基哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基)吡咯烷-3- 基]氧基}苯基)-1-(6- 甲基哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

1-(6- 甲基哒嗪-3- 基)-N-(4-{[(3R)-1-(1,3- 噻唑-4- 基羰基)吡咯烷-3- 基]氧基}苯基)氮杂环丁烷-3- 甲酰胺;

1-(哒嗪-3- 基)-N-{6-[1-(4,4,4- 三氟丁酰基)哌啶-4- 基]吡啶-3- 基}氮杂环丁烷-3- 甲酰胺;

N-{6-[1-(3,3- 二甲基丁酰基)哌啶-4- 基]吡啶-3- 基}-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

(3S)-N-[4-(1- 苯甲酰基哌啶-4- 基)苯基]-1-(4- 甲基哒嗪-3- 基)吡咯烷-3- 甲酰胺;

(3S)-N-{4-[1-(2,2- 二甲基丙酰基)哌啶-4- 基]苯基}-1-(4- 甲基哒嗪-3- 基)吡咯烷-3- 甲酰胺;

N-{4-[1- 苯基-3-(三氟甲基)-1H- 吡唑-5- 基]苯基}-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-{6-[1-(2,2- 二甲基丙基)-1H- 吡唑-4- 基]吡啶-3- 基}-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

叔丁基 4-[4-({[1-(哒嗪-3- 基)氮杂环丁烷-3- 基]羰基}氨基)-1H- 吡唑-1- 基]哌啶-1- 甲酸酯;

N-(6-{1-[(4- 甲基哌啶-4- 基)甲基]-1H- 吡唑-4- 基}吡啶-3- 基)-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

1-(哒嗪-3- 基)-N-(4-{[1-(1,3- 噻唑-5- 基羰基)哌啶-4- 基]甲基}苯基)氮杂环丁烷-3- 甲酰胺;

N-(4-{[1-(环戊基羰基)哌啶-4- 基]甲基}苯基)-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-(4-{[1-(1H- 吡唑-4- 基羰基)哌啶-4- 基]甲基}苯基)-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-(4-{[1-(2,2- 二甲基丁酰基)哌啶-4- 基]甲基}苯基)-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-[4-({1-[(2- 甲基环丙基)羰基]哌啶-4- 基}甲基)苯基]-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-[4-({1-[(甲基巯基)乙酰基]哌啶-4- 基}甲基)苯基]-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-[4-({1-[(1S,4R)- 双环[2.2.1]庚-2- 基乙酰基]哌啶-4- 基}甲基)苯基]-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-(4-{[1-(2- 甲基戊酰基)哌啶-4- 基]甲基}苯基)-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-(4-{[1-(4- 甲基戊酰基)哌啶-4- 基]甲基}苯基)-1-(哒嗪-3- 基)氮杂环丁

烷 -3- 甲酰胺；

N-[4-({1-[3-(甲基巯基) 丙酰基] 哌啶 -4- 基 } 甲基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(1,3- 噻唑 -4- 基羰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(1H- 吡唑 -5- 基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(6- 甲基吡啶 -3- 基) 羰基] 哌啶 -4- 基 } 甲基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 甲基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(戊 -4- 炔酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(甲氧基乙酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(四氢呋喃 -2- 基羰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 甲氧基乙氧基) 乙酰基] 哌啶 -4- 基 } 甲基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(乙氧基乙酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 己酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基 -1H- 吡咯 -2- 基) 羰基] 哌啶 -4- 基 } 甲基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(丁 -3- 烯酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(1,3- 噻唑 -2- 基羰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(呋喃 -2- 基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(1,2- 唑 -5- 基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(吡啶 -2- 基羰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(呋喃-3-基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环丙基乙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基丁酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-丙酰基哌啶-4-基)甲基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-丁酰基哌啶-4-基)甲基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环丁基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-戊酰基哌啶-4-基)甲基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环戊基乙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基苯甲酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基戊酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环己基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环丙基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(4-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{1-[1-(3,3-二甲基丁酰基)哌啶-4-基]-1H-吡唑-4-基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{1-[1-(2-氟苯甲酰基)哌啶-4-基]-1H-吡唑-4-基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(苯基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(2,2-二甲基丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(3-甲氧基-2,2-二甲基丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(2- 环丙基乙基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[2-(2- 乙基哌啶 -1- 基）乙基］氨基甲酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[（环丁基甲基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2S)- 丁烷 -2- 基氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（丁基氨基甲酰基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2,2- 二甲基四氢 -2H- 吡喃 -4- 基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(1S)-1- 环丙基乙基］氨基甲酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({2-[甲基（苯基）氨基］乙基｝氨基甲酰基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1,1'- 双（环丙基）-1- 基氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-（噻吩 -3- 基氨基甲酰基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(1R)-1- 环丙基乙基］氨基甲酰基｝苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 甲基哌啶 -4- 基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2R)- 丁烷 -2- 基氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 氮杂双环 [2.2.2] 辛 -3- 基氨基甲酰基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[（四氢呋喃 -3- 基甲基）氨基甲酰基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-{4-[（氧杂环丁烷 -3- 基甲基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2- 甲基环丙基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（环丁基氨基甲酰基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 甲基环丙基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2- 甲氧基 -2- 甲基丙基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[（环丙基甲基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(2R)- 四氢呋喃 -2- 基甲基］氨基甲酰基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-3-基)-N-{4-[(3,3,3-三氟丙基)氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[(1-甲基哌啶-3-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3-甲基氧杂环丁烷-3-基)甲基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(2S)-四氢呋喃-2-基甲基]氨基甲酰基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[(四氢-2H-吡喃-4-基甲基)氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-(四氢-2H-吡喃-4-基氨基甲酰基)苯基]氮杂环丁烷-3-甲酰胺;

N-(4-{[(1-甲基哌啶-3-基)甲基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(环丙基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(环戊基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(苄基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(3-氟苯基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(丙基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(4-氟苯基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(2-氟苯基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-甲基环丁基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(丙-2-烯-1-基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

5-[1-(2,2-二甲基丙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(3,3-二甲基丁酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(2,2-二甲基丁酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-{1-[(1-甲基环丙基)羰基]哌啶-4-基}-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(3,3,3-三氟丙酰基)哌啶-4-基]噻吩-2-甲酰胺;

5-[1-(环丙基乙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(双环[2.2.1]庚-2-基乙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

1-(哒嗪-3-基)-N-{4-[(3S)-四氢呋喃-3-基氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺;

N-[4-({4-[2-(二甲基氨基)乙基]苯基}氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[(3R)-四氢呋喃-3-基氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[(2-甲氧基乙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-氨基-2,2-二甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[2,2-二甲基-3-(哌嗪-1-基)丙基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[2-甲基-2-(哌嗪-1-基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;及其药学上可接受的盐。

[0212] 仍另一个实施方案涉及式(1A)的化合物,其选自

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

(3S)-N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

N-[4-(1-乙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-丁酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(甲基巯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

(3S)-N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-[4-(1-丁酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-[4-(1-乙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(2-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(2-乙基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

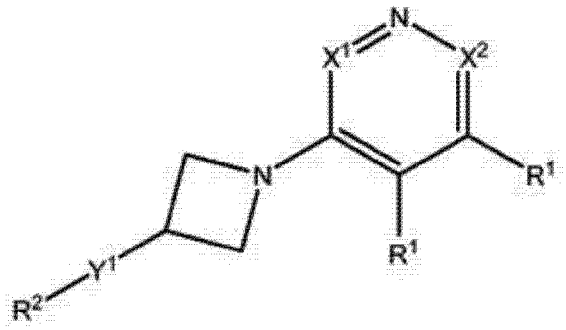
(3S)-N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3R)-N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;及其药学上可接受的盐。

[0213] 式(IIC)的实施方案

在另一方面,本发明提供式(IIC)的化合物



(IIC);

及其药学上可接受的盐;其中 X^1、X^2、Y^1、R^1、和 R^2如本文对式(IC)所描述。

[0214] 本发明的一个实施方案涉及式(IIC)的化合物及其药学上可接受的盐;

其中

X^1为N且X^2为CR^1;或

X^1为CR^1且X^2为N;或

X^1为CR^1且X^2为CR^1;

Y^1为C(O)NH、或NHC(O);

R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br和I;

R^2独立地选自C_4-C_6-烷基、C_4-C_6-烯基、C_4-C_6-炔基、芳基、和5-6元杂芳基;其中R^2中的C_4-C_6-烷基、C_4-C_6-烯基、和C_4-C_6-炔基各自被一个或多个独立地选自以下的取代基取代:

R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$,
$OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$,
$NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$,
$NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, $C(O)NHOH$, $C(O)NHOR^3$,
$C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, $C(O)H$, $C(O)OH$,
$C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br
和I;其中R^2中的芳基和5-6元杂芳基各自任选被一个或多个独立地选自以下的取代

基取代：R^4，OR^4，SR^4，$S(O)R^4$，

SO_2R^4，$C(O)R^4$，$OC(O)OR^4$，NH_2，NHR^4，$N(R^4)_2$，$NHC(O)R^4$，$NR^4C(O)R^4$，$NHS(O)_2R^4$，

$NR^4S(O)_2R^4$，$NHC(O)OR^4$，$NR^4C(O)OR^4$，$NHC(O)NH_2$，$NHC(O)NHR^4$，$NHC(O)N(R^4)_2$，

$NR^4C(O)NHR^4$，$NR^4C(O)N(R^4)_2$，$C(O)NH_2$，$C(O)NHR^4$，$C(O)N(R^4)_2$，$C(O)NHOH$，

$C(O)NHOR^4$，$C(O)NHSO_2R^4$，$C(O)NR^4SO_2R^4$，SO_2NH_2，SO_2NHR^4，$SO_2N(R^4)_2$，$C(O)H$，

$C(O)OH$，$C(N)NH_2$，$C(N)NHR^4$，$C(N)N(R^4)_2$，$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，

和 I；

R^3在每次出现时独立地选自烷基、烯基、炔基、芳基、环烷基、环烯基、和杂环基；其中 R^3 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^5，OR^5，SR^5，$S(O)R^5$，SO_2R^5，$C(O)R^5$，$CO(O)R^5$，

$OC(O)R^5$，$OC(O)OR^5$，NH_2，NHR^5，$N(R^5)_2$，$NHC(O)R^5$，$NR^5C(O)R^5$，$NHS(O)_2R^5$，

$NR^5S(O)_2R^5$，$NHC(O)OR^5$，$NR^5C(O)OR^5$，$NHC(O)NH_2$，$NHC(O)NHR^5$，$NHC(O)N(R^5)_2$，

$NR^5C(O)NHR^5$，$NR^5C(O)N(R^5)_2$，$C(O)NH_2$，$C(O)NHR^5$，$C(O)N(R^5)_2$，$C(O)NHOH$，

$C(O)NHOR^5$，$C(O)NHSO_2R^5$，$C(O)NR^5SO_2R^5$，SO_2NH_2，SO_2NHR^5，$SO_2N(R^5)_2$，$C(O)H$，

$C(O)OH$，$C(N)NH_2$，$C(N)NHR^5$，$C(N)N(R^5)_2$，$CNOH$，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，

Cl，Br 和 I；其中 R^3 中的芳基、环烷基、环烯基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：

R^6，OR^6，SR^6，$S(O)R^6$，SO_2R^6，$C(O)R^6$，$CO(O)R^6$，$OC(O)R^6$，$OC(O)OR^6$，NH_2，NHR^6，$N(R^6)_2$，

$NHC(O)R^6$，$NR^6C(O)R^6$，$NHS(O)_2R^6$，$NR^5S(O)_2R^6$，$NHC(O)OR^6$，$NR^6C(O)OR^6$，

$NHC(O)NH_2$，$NHC(O)NHR^6$，$NHC(O)N(R^5)_2$，$NR^6C(O)NHR^6$，$NR^6C(O)N(R^6)_2$，$C(O)NH_2$，

$C(O)NHR^6$，$C(O)N(R^6)_2$，$C(O)NHOH$，$C(O)NHOR^6$，$C(O)NHSO_2R^6$，$C(O)NR^6SO_2R^6$，

SO_2NH_2，SO_2NHR^6，$SO_2N(R^6)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^6$，$C(N)N(R^6)_2$，

$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7，OR^7，SR^7，$S(O)R^7$，SO_2R^7，$C(O)R^7$，$CO(O)R^7$，

$OC(O)R^7$，$OC(O)OR^7$，NH_2，$NHR^7N(R^7)_2$，$NHC(O)R^7$，$NR^7C(O)R^7$，$NHS(O)_2R^7$，

$NR^7S(O)_2R^7$，$NHC(O)OR^7$，$NR^7C(O)OR^7$，$NHC(O)NH_2$，$NHC(O)NHR^7$，$NHC(O)N(R^7)_2$，

$NR^7C(O)NHR^7$，$NR^7C(O)N(R^7)_2$，$C(O)NH_2$，$C(O)NHR^7$，$C(O)N(R^7)_2$，$C(O)NHOH$，

$C(O)NHOR^7$，$C(O)NHSO_2R^7$，$C(O)NR^7SO_2R^7$，SO_2NH_2，SO_2NHR^7，$SO_2N(R^7)_2$，$C(O)H$，

$C(O)OH$，$C(N)NH_2$，$C(N)NHR^7$，$C(N)N(R^7)_2$，$CNOH$，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，

Cl，Br 和 I；

R^5在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^5 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^8，OR^8，SR^8，$S(O)R^8$，SO_2R^8，NHR^8，$N(R^8)_2$，$C(O)R^8$，

$C(O)NH_2$，$C(O)NHR^8$，$C(O)N(R^8)_2$，$NHC(O)R^8$，$NR^8C(O)R^8$，$NHSO_2R^8$，$NHC(O)OR^8$，

SO_2NH_2，SO_2NHR^8，$SO_2N(R^8)_2$，$NHC(O)NH_2$，$NHC(O)NHR^8$，OH，(O)，$C(O)OH$，N_3，CN，

NH_2，F，Cl，Br 和 I；

R^6在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^6

中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^9，OR^9，SR^9，$S(O)R^9$，SO_2R^9，NHR^8，$N(R^9)_2$，$C(O)R^9$，

$C(O)NH_2$，$C(O)NHR^9$，$C(O)N(R^9)_2$，$NHC(O)R^9$，$NR^9C(O)R^9$，$NHSO_2R^9$，$NHC(O)OR^9$，

SO_2NH_2，SO_2NHR^9，$SO_2N(R^9)_2$，$NHC(O)NH_2$，$NHC(O)NHR^9$，OH，(O)，$C(O)OH$，N_3，CN，

NH_2，CF_3，CF_2CF_3，F，Cl，Br 和 I；

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^8在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^9在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中由 R^4、R^5、R^6、R^7、R^8、和 R^9表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}，OR^{10}，SR^{10}，$S(O)R^{10}$，SO_2R^{10}，$C(O)R^{10}$，$CO(O)R^{10}$，

$OC(O)R^{10}$，$OC(O)OR^{10}$，$C(O)C(O)R^{10}$，NH_2，NHR^{10}，$N(R^{10})_2$，$NHC(O)R^{10}$，$NR^{10}C(O)R^{10}$，

$NHS(O)_2R^{10}$，$NR^{10}S(O)_2R^{10}$，$NHC(O)OR^{10}$，$NR^{10}C(O)OR^{10}$，$NHC(O)NH_2$，$NHC(O)NHR^{10}$，

$NHC(O)N(R^{10})_2$，$NR^{10}C(O)NHR^{10}$，$NR^{10}C(O)N(R^{10})_2$，$C(O)NH_2$，$C(O)NHR^{10}$，$C(O)N(R^{10})_2$，

$C(O)NHOH$，$C(O)NHOR^{10}$，$C(O)NHSO_2R^{10}$，$C(O)NR^{10}SO_2R^{10}$，SO_2NH_2，SO_2NHR^{10}，

$SO_2N(R^{10})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{10}$，$C(N)N(R^{10})_2$，CNOH，$CNOCH_3$，OH，

CN，N_3，NO_2，F，Cl，Br 和 I；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}，OR^{11}，SR^{11}，$S(O)R^{11}$，SO_2R^{11}，$C(O)R^{11}$，$CO(O)R^{11}$，

$OC(O)R^{11}$，$OC(O)OR^{11}$，NH_2，NHR^{11}，$N(R^{11})_2$，$NHC(O)R^{11}$，$NR^{11}C(O)R^{11}$，$NHS(O)_2R^{11}$，

$NR^{11}S(O)_2R^{11}$，$NHC(O)OR^{11}$，$NR^{11}C(O)OR^{11}$，$NHC(O)NH_2$，$NHC(O)NHR^{11}$，

$NHC(O)N(R^{11})_2$，$NR^{11}C(O)NHR^{11}$，$NR^{11}C(O)N(R^{11})_2$，$C(O)NH_2$，$C(O)NHR^{11}$，$C(O)N(R^{11})_2$，

$C(O)NHOH$，$C(O)NHOR^{11}$，$C(O)NHSO_2R^{11}$，$C(O)NR^{11}SO_2R^{11}$，SO_2NH_2，SO_2NHR^{11}，

$SO_2N(R^{11})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，CNOH，$CNOCH_3$，OH，

(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}，OR^{12}，SR^{12}，$S(O)R^{12}$，SO_2R^{12}，$C(O)R^{12}$，$CO(O)R^{12}$，

$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_2，NHR^{12}，$N(R^{12})_2$，$NHC(O)R^{12}$，$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，

$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，$NHC(O)NH_2$，$NHC(O)NHR^{12}$，

$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，

$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，

$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，CNOH，$CNOCH_3$，OH，

CN，N_3，NO_2，CF_3，OCF_3，F，Cl，Br 和 I；

R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基各自、烯基、和炔基任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯

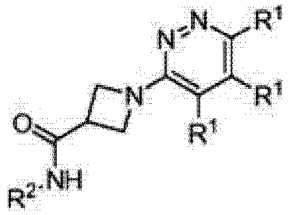
基。

[0215] 在式 (IIC) 的一个实施方案中，X^1为 N 且 X^2为 CR^1；或 X^1为 CR^1且 X^2为 N；或 X^1为 CR^1且 X^2为 CR^1。在式 (IIC) 的另一个实施方案中，X^1为 N 且 X^2为 CR^1。在式 (IIC) 的另一个实施方案中，X^1为 CR^1且 X^2为 N。在式 (IIC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1。

[0216] 在式 (IIC) 的一个实施方案中，Y^1为 C(O)NH、或 NHC(O)。在式 (IIC) 的另一个实施方案中，Y^1为 C(O)NH。在式 (IIC) 的另一个实施方案中，Y^1为 NHC(O)。

[0217] 在式 (IIC) 的一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (IIC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IIC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IIC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时为氢。

[0218] 在另一方面，本发明提供式 (IID) 的化合物，



式 (IID)

及其药学上可接受的盐；其中 R^1和 R^2如本文对式 (IC) 所描述。

[0219] 在式 (IIC) 和 (IID) 的一个实施方案中，R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (IIC) 和 (IID) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IIC) 和 (IID) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IIC) 和 (IID) 的另一个实施方案中，R^1在每次出现时为氢。

[0220] 在式 (IIC) 和 (IID) 的一个实施方案中，R^2独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：R^3，OR^3，SR^3，

$S(O)R^3$，SO_2R^3，$C(O)R^3$，$CO(O)R^3$，$OC(O)R^3$，$OC(O)OR^3$，NH_2，NHR^3，$N(R^3)_2$，$NHC(O)R^3$，

$NR^3C(O)R^3$，$NHS(O)_2R^3$，$NR^3S(O)_2R^3$，$NHC(O)OR^3$，$NR^3C(O)OR^3$，$NHC(O)NH_2$，

$NHC(O)NHR^3$，$NHC(O)N(R^3)_2$，$NR^3C(O)NHR^3$，$NR^3C(O)N(R^3)_2$，$C(O)NH_2$，$C(O)NHR^3$，

$C(O)N(R^3)_2$，C(O)NHOH，$C(O)NHOR^3$，$C(O)NHSO_2R^3$，$C(O)NR^3SO_2R^3$，SO_2NH_2，

SO_2NHR^3，$SO_2N(R^3)_2$，C(O)H，C(O)OH，C(N)NH_2，C(N)NHR^3，C(N)$N(R^3)_2$，CNOH，

$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：

R^4，OR^4，SR^4，$S(O)R^4$，SO_2R^4，$C(O)R^4$，$OC(O)OR^4$，NH_2，NHR^4，

$N(R^4)_2$，$NHC(O)R^4$，$NR^4C(O)R^4$，$NHS(O)_2R^4$，$NR^4S(O)_2R^2$，$NHC(O)OR^4$，$NR^4C(O)OR^4$，

$NHC(O)NH_2$，$NHC(O)NHR^4$，$NHC(O)N(R^4)_2$，$NR^4C(O)NHR^4$，$NR^4C(O)N(R^4)_2$，$C(O)NH_2$，

$C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$,

SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$,

$CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, 和 I。在式 (IIC) 和 (IID) 的另一个实施方案中，R^2为芳基；其中 R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、F、Cl、和 I。在式 (IIC) 和 (IID) 的另一个实施方案中，R^2为芳基；其中 R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。在式 (IIC) 和 (IID) 的另一个实施方案中，R^2为苯基；其中 R^2中的苯基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。在式 (IIC) 和 (IID) 的另一个实施方案中，R^2为苯基；其中 R^2中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和 SO_2R^4。

[0221] 在式 (IIC) 和 (IID) 的另一个实施方案中，R^2为 5-6 元杂芳基；其中 R^2中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、F、Cl、和 I。在式 (IIC) 和 (IID) 的另一个实施方案中，R^2为 5-6 元杂芳基；其中 R^2中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。在式 (IIC) 和 (IID) 的另一个实施方案中，R^2为吡啶基、呋喃基、噻吩基、吡唑、或噻唑基；其中 R^2中的吡啶基、呋喃基、噻吩基、吡唑、和噻唑基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。

[0222] 在式 (IIC) 和 (IID) 的一个实施方案中，R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$,

$NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$,

$NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$,

$C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$,

SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$,

$CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (IIC) 和 (IID) 的另一个实施方案中，R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基。

[0223] 在式 (IIC) 和 (IID) 的一个实施方案中，R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7, OR^7,

SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$,

NHCCO)R^7, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O))OR^7$,

$NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C((O)NH_2$,

$C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$,

SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$,

$CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (IIC) 和 (IID) 的另一个实施方案中，R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7、OR^7、$N(R^7)_2$、F、Cl、Br 和 I。

[0224] 在式 (IIC) 和 (IID) 的一个实施方案中，R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。在式 (IIC) 和 (IID) 的另一个实施方案中，R^7在每

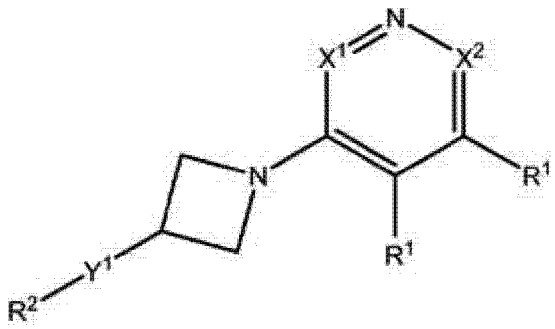
次出现时独立地选自烷基、芳基、杂环基、和环烷基。

[0225] 在式 (IIC) 和 (IID) 的一个实施方案中，R^4和 R^7中的环状基团各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}，OR^{10}，SR^{10}，$S(O)R^{10}$，SO_2R^{10}，$C(O)R^{10}$，$CO(O)R^{10}$，$OC(O)R^{10}$，$OC(O)OR^{10}$，NH_2，NHR^{10}，$N(R^{10})_2$，$NHC(O)R^{10}$，$NR^{10}C(O)R^{10}$，$NHS(O)_2R^{10}$，$NR^{10}S(O)_2R^{10}$，$NHC(O)OR^{10}$，$NR^{10}C(O)OR^{10}$，$NHC(O)NH_2$，$NHC(O)NHR^{10}$，$NHC(O)N(R^{10})_2$，$NR^{10}C(O)NHR^{10}$，$NR^{10}C(O)N(R^{10})_2$，$C(O)NH_2$，$C(O)NHR^{10}$，$C(O)N(R^{10})_2$，$C(O)NHOH$，$C(O)NHOR^{10}$，$C(O)NHSO_2R^{10}$，$C(O)NR^{10}SO_2R^{10}$，SO_2NH_2，SO_2NHR^{10}，$SO_2N(R^{10})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{10}$，$C(N)N(R^{10})_2$，CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}，OR^{11}，SR^{11}，$S(O)R^{11}$，SO_2R^{11}，$C(O)R^{11}$，$CO(O)R^{11}$，$OC(O)R^{11}$，$OC(O)OR^{11}$，NH_2，NHR^{11}，$N(R^{11})_2$，$NHC(O)R^{11}$，$NR^{11}C(O)R^{11}$，$NHS(O)_2R^{11}$，$NR^{11}S(O)_2R^{11}$，$NHC(O)OR^{11}$，$NR^{11}C(O)OR^{11}$，$NHC(O)NH_2$，$NHC(O)NHR^{11}$，$NHC(O)N(R^{11})_2$，$NR^{11}C(O)NHR^{11}$，$NR^{11}C(O)N(R^{11})_2$，$C(O)NH_2$，$C(O)NHR^{17}$，$C(O)N(R^{11})_2$，$C(O)NHOH$，$C(O)NHOR^{11}$，$C(O)NHSO_2R^{11}$，$C(O)NR^{11}SO_2R^{11}$，SO_2NH_2，SO_2NHR^{11}，$SO_2N(R^{11})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，CNOH，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}，OR^{12}，SR^{12}，$S(O)R^{12}$，SO_2R^{12}，$C(O)R^{12}$，$CO(O)R^{12}$，$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_2，NHR^{12}，$N(R^{12})_2$，$NHC(O)R^{12}$，$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，$NHC(O)NH_2$，$NHC(O)NHR^{12}$，$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0226] 在式 (IIC) 和 (IID) 的另一个实施方案中，R^4和 R^7中的环状基团各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)H$、OH、F、Cl、Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、NH_2、OH、CN、CF_3、OCF_3、F、和 Cl；R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、CF_3、F、和 Cl；R^{12}在每次出现时独立地选自烷基和芳

基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、和环烷基。

[0227] 本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式 (IIC)



式 (IIC);

其中

X^1为 N 且 X^2为 CR^1；或

X^1为 CR^1且 X^2为 N；或

X^1为 CR^1且 X^2为 CR^1；

Y^1为 C(O)NH、或 NHC(O)；

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、Cl、和 F；

R^2为芳基或 5-6 元杂芳基，其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、SO_2R^4、OR^4、$C(O)NHR^4$、和 F；

R^4在每次出现时独立地选自烷基、烯基、芳基、杂环基、和环烷基；其中 R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7、OR^7、$N(R^7)_2$、和 F；

R^7在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；

其中由 R^4和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：

R^{10}、$C(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)R^{10}$、C(O)OH、OH 和 F；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代：R^{12}、OR^{12}、$C(O)R^{12}$、NH_2、OH、CN、CF_3、OCF_3、F、和 Cl；

R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl；

R^{12}在每次出现时独立地选自烷基、和芳基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、环烷基、和杂环基。

[0228] 仍另一个实施方案涉及具有式 (IIC) 的化合物，其包括

1-(吡啶 -3- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 氧基} 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 氰基吡啶 -3- 基)-N-{4-[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 苯基} 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-[2-(三氟甲基)吡啶-3-基]氮杂环丁烷-3-甲酰胺；

1-(2-甲基吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(4-甲基吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(4-氟吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-[4-(三氟甲基)吡啶-3-基]氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-(4-{1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[1-(吡啶-3-基)氮杂环丁烷-3-基]-4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯甲酰胺；

N-(4-{1-[(2S)-2-甲基丁酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)-N-[1-(吡啶-3-基)氮杂环丁烷-3-基]苯甲酰胺；

4-{[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]氧基}-N-[1-(吡啶-3-基)氮杂环丁烷-3-基]苯甲酰胺；

1-(吡啶-3-基)-N-{4-[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-[4-({1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺；

N-{4-[(1-戊酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2-甲基环丙基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(1S,4R)-双环[2.2.1]庚-2-基乙酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-甲基戊酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基戊酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-乙氧基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,2-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3,3-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-丁酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(乙氧基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(N-乙酰基-L-亮氨酰)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环己基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环己基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-(4-{[1-(4,4,4-三氟丁酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环戊基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(1-甲基环己基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(呋喃-3-基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)氮杂环

丁烷 -3- 甲酰胺；

N-{4-[(1- 乙酰基哌啶 -4- 基）氧基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（甲氧基乙酰基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基)-N-(4-{[1-（噻吩 -3- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝氧基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（吗啉 -4- 基乙酰基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基)-N-(4-{[1-（噻吩 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝氧基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（呋喃 -2- 基羰基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基 -1H- 吡咯 -2- 基）羰基］哌啶 -4- 基｝氧基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 丙酰基哌啶 -4- 基）氧基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基环丙基）羰基］哌啶 -4- 基｝氧基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(N，N- 二甲基 -β- 丙氨酰）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基)-N-(4-{[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环戊基乙酰基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,3- 二甲基丁酰基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(4- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(2- 甲氧基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基甲基）哌啶 -4- 基］氧基｝苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基戊基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基丙基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 甲基丁基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 乙基丁基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丙基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基丁基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 丙基哌啶 -4- 基) 氧基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 环丙基乙基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(吡啶 -3- 基)-N-(4-{[1-(四氢呋喃 -3- 基甲基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丁基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环己基甲基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环戊基甲基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丁基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基戊基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丁基哌啶 -4- 基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 乙基丁基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基丁基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基丙基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丙基哌啶 -4- 基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(4-甲氧基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(4-氰基吡啶-3-基)-N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-[4-(1-戊酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-甲基戊酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(1S,4R)-双环[2.2.1]庚-2-基乙酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(吗啉-4-基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(呋喃-3-基羰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-{4-[1-(吡咯烷-1-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(5-氧代-D-脯氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(N,N-二甲基-β-丙氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-{4-[1-(1,3-噻唑-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(1-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(3-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(4-甲基哌嗪-1-基)乙酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(5-氧代-L-脯氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-乙氧基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 甲基环己基) 羰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 乙酰基哌啶 -4- 基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环己基乙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(N- 乙酰基 -L- 亮氨酰) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丙酰基哌啶 -4- 基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(吡啶 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 甲氧基乙氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[3-(吗啉 -4- 基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(5- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(吡啶 -3- 基)-N-{4-[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 甲基 -1H- 吡咯 -2- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(呋喃 -2- 基羰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[3-(哌啶 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(乙氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丁酰基哌啶 -4- 基) 苯基]-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(甲氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环己基羰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环戊基羰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2S)-2- 甲基丁酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-{4-[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-{4-[1-(四氢 -2H- 吡喃 -4- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,5- 二氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[4-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(哒嗪 -3- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁

烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-[4-(1- 戊酰基哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1S,4R)- 双环 [2.2.1] 庚 -2- 基乙酰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(吗啉 -4- 基乙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(呋喃 -3- 基羰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(吡咯烷 -1- 基乙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(5- 氧代 -D- 脯氨酰) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N,N- 二甲基 -β- 丙氨酰) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(3- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基哌嗪 -1- 基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(5- 氧代 -L- 脯氨酰) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 乙氧基丙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环己基) 羰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 乙酰基哌啶 -4- 基) 苯基]-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环己基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(N- 乙酰基 -L- 亮氨酰) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-[4-(1- 丙酰基哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 甲氧基乙氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[3-(吗啉 -4- 基) 丙酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(5- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(1- 甲基 -1H- 吡咯 -2- 基) 羰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(呋喃 -2- 基羰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[3-(哌啶 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(乙氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丁酰基哌啶 -4- 基) 苯基]-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(甲氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环己基羰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁

烷 -3- 甲酰胺；

N-{4-[1-(2,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基）氮杂环丁烷 -3- 基］氧基} 苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氟苯甲酰基）氮杂环丁烷 -3- 基］氧基} 苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[二氟 (苯基）乙酰基］氮杂环丁烷 -3- 基} 氧基）苯基]-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4,4- 二氟环己基）羰基］氮杂环丁烷 -3- 基} 氧基）苯基]-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4- 氟苯基）乙酰基］氮杂环丁烷 -3- 基} 氧基）苯基]-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-[4-({1-[4-(三氟甲基）苯甲酰基］氮杂环丁烷 -3- 基} 氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 苯甲酰基氮杂环丁烷 -3- 基）氧基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 羟基 -2- 甲基丙酰基）氮杂环丁烷 -3- 基］氧基} 苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[1-(四氢呋喃 -3- 基羰基）氮杂环丁烷 -3- 基］氧基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(呋喃 -3- 基羰基）氮杂环丁烷 -3- 基］氧基} 苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 戊酰基氮杂环丁烷 -3- 基）氧基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氯苯甲酰基）哌啶 -4- 基］氧基} 苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 甲基丁酰基］哌啶 -4- 基} 氧基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基］氧基} 苯基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基羰基）哌啶 -4- 基］氧基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[二氟 (苯基）乙酰基］哌啶 -4- 基} 氧基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4,4- 二氟环己基）羰基］哌啶 -4- 基} 氧基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基 -2- 苯基丙酰基）哌啶 -4- 基］氧基} 苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-3-基)-N-(4-{[1-(1,3-噻唑-4-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[(1-{[4-(三氟甲基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(四氢呋喃-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-({1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(噻吩-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-({1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(四氢呋喃-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(3-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2,4-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(4-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环丙基乙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3,4-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-({1-[4-(三氟甲氧基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(2,4-二氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-({1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}氧基)苯基]

氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[(1-{[4-(三氟甲氧基) 苯基] 乙酰基 } 哌啶 -4- 基) 氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3,5- 二氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[(1-{[3-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(吡啶 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 乙酰基哌啶 -4- 基) 氧基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氯苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(甲氧基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氯苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(环丙基羰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,3- 二甲基丁酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(环己基羰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 氮杂环丁烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2-甲基环丙基)羰基]氮杂环丁烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-(4-{[1-(3,3,3-三氟丙酰基)氮杂环丁烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环戊基羰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3,3-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环丁基羰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-(4-{[1-(四氢呋喃-2-基羰基)氮杂环丁烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-甲基戊酰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基丙酰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2S)-2-甲基丁酰基]氮杂环丁烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(甲氧基乙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[二氟(苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(4,4-二氟环己基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-(4-{[1-(1,3-噻唑-4-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[(1-{[4-(三氟甲基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3,4-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[(1-{[4-(三氟甲氧基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(4-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂

环丁烷 -3- 甲酰胺；

N-[4-({1-[(2,4- 二氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（噻吩 -3- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氯苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基 -2- 苯基丙酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 乙酰基哌啶 -4- 基）氧基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({1-[3-（三氟甲基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({1-[4-（三氟甲基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氟苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({1-[4-（三氟甲氧基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({1-[3-（三氟甲氧基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基乙酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氯苯甲酰基）哌啶 -4- 基］氧基｝苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-4-基)-N-(4-{[1-(吡啶-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(四氢呋喃-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3,5-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2,2-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环丙基羰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(四氢呋喃-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(噻吩-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[1-(四氢-2H-吡喃-4-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(2-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]呋喃-2-甲酰胺;

叔丁基4-(4-{[1-(哒嗪-3-基)氮杂环丁烷-3-基]氨基甲酰基}苯基)哌啶-1-甲酸酯;

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺;

N-[4-(1-乙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-丁酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-戊酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1- 己酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 乙基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 庚酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(丁 -3- 烯酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(戊 -4- 烯酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(甲氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(甲基巯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 甲氧基乙氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 硝基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[3-(甲基巯基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(戊 -4- 炔酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环己基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环己基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲

酰胺；

N-{4-[1-(2-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,3-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,4-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,5-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,4-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,5- 二甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,4- 二氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,5- 二氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,4- 二氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,5- 二氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 氟苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(3- 氟苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(4- 氟苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(4- 氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-[4-(1-{[4-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(3,5- 二甲基苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2,5- 二氟苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(3,4- 二氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(呋喃 -3- 基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(5- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(5- 甲基吡嗪 -2- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 乙氧基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲

酰胺；

N-(4-{1-[(1- 苯基环丙基）羰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{1-[（嘧啶 -2- 基巯基）乙酰基］哌啶 -4- 基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 乙酰基哌啶 -4- 基）羰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N- 乙酰基 -L- 亮氨酰）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（二苯基乙酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(5- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氟 -4- 甲基苯甲酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,3- 二氟苯甲酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[4-（丙烷 -2- 基）苯甲酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 叔丁基苯甲酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[2- 氟 -5-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[2- 氯 -5-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(4- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环戊基乙酰基）哌啶 -4- 基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基苯氧基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2S)-2- 苯基丁酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-(1-{[3-（三氟甲基）苯基］乙酰基} 哌啶 -4- 基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3- 氯苯基）乙酰基］哌啶 -4- 基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,4- 二氯苯基）乙酰基］哌啶 -4- 基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（萘 -1- 基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2R)-2- 甲氧基 -2- 苯基乙酰基］哌啶 -4- 基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[N-（呋喃 -2- 基羰基）甘氨酰］哌啶 -4- 基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[（苄基氧基）乙酰基］哌啶 -4- 基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（萘 -1- 基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环丙基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[1-（四氢呋喃 -2- 基羰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N- 苯甲酰基甘氨酰）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[1-（四氢呋喃 -3- 基羰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{1-[4-（噻吩 -2- 基）丁酰基］哌啶 -4- 基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,5- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环丁基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1-{N-[(4- 甲基苯基）磺酰基］甘氨酰} 哌啶 -4- 基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,3- 二氟苯基）乙酰基］哌啶 -4- 基} 苯基）-1-（哒嗪 -3- 基）氮杂环丁

烷 -3- 甲酰胺；

N-(4-{1-[(2S)-2- 甲氧基 -2- 苯基乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(萘 -2- 基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 苯基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,6- 二氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[3-(苯基磺酰基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,5- 二甲基呋喃 -3- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环丙基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(1,3- 噻唑 -4- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(1,3- 噻唑 -5- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(乙氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(6- 甲基吡啶 -3- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(呋喃 -2- 基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环己基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氧代丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环戊基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰

胺；

N-[4-(1- 丙酰基哌啶 -4- 基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 甲基苯甲酰基）哌啶 -4- 基] 苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氯苯甲酰基）吡咯烷 -3- 基] 氧基 } 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-(1,3- 噻唑 -2- 基羰基）吡咯烷 -3- 基] 氧基 } 苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-（环丙基乙酰基）吡咯烷 -3- 基] 氧基 } 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2S)-2- 甲基丁酰基] 吡咯烷 -3- 基 } 氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-（四氢 -2H- 吡喃 -4- 基羰基）吡咯烷 -3- 基] 氧基 } 苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-{[4-（三氟甲氧基）苯基] 乙酰基 } 吡咯烷 -3- 基] 氧基 } 苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-（噻吩 -3- 基羰基）吡咯烷 -3- 基] 氧基 } 苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(4- 氟苯基）乙酰基] 吡咯烷 -3- 基 } 氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(3,5- 二氟苯基）乙酰基] 吡咯烷 -3- 基 } 氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3,4- 二氟苯甲酰基）吡咯烷 -3- 基] 氧基 } 苯基)-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(3- 氟苯基）乙酰基] 吡咯烷 -3- 基 } 氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({(3R)-1-[3-（三氟甲基）苯甲酰基] 吡咯烷 -3- 基 } 氧基）苯基] 氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2,4- 二氟苯基）乙酰基] 吡咯烷 -3- 基 } 氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-{[4-（三氟甲基）苯基] 乙酰基 } 吡咯烷 -3- 基] 氧基 } 苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-(1,3- 噻唑 -4- 基羰基）吡咯烷 -3- 基] 氧基 } 苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-（四氢呋喃 -2- 基羰基）吡咯烷 -3- 基] 氧基 } 苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(5- 甲基噻吩 -2- 基）羰基] 吡咯烷 -3- 基 } 氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2- 氟苯基）乙酰基] 吡咯烷 -3- 基 } 氧基）苯基]-1-（哒嗪 -4- 基）

氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(环丙基羰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-(四氢呋喃 -3- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-[4-({(3R)-1-[3-(三氟甲氧基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-(吡啶 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氯苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(4- 氯苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基 -2- 苯基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(甲氧基乙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-(噻吩 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-{[3-(三氟甲基) 苯基] 乙酰基 } 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丁酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3,5- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-[4-({(3R)-1-[4-(三氟甲基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-[4-({(3R)-1-[4-(三氟甲氧基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 甲基丁酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(3,3,3-三氟丙酰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[二氟(苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(2,2-二甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(4,4-二氟环己基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(2-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-(1,3-噻唑-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(环丙基乙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(2S)-2-甲基丁酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-(四氢-2H-吡喃-4-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-{[4-(三氟甲氧基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(4-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-(噻吩-3-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(4-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(3,5-二氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(3,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(3-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-({(3R)-1-[3-(三氟甲基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(2,4-二氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-{[4-(三氟甲基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(3R)-1-(1,3-噻唑-4-基羰基)吡咯烷-3-基]氧基}苯

基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-（四氢呋喃 -2- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(5- 甲基噻吩 -2- 基）羰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2- 氟苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-（环丙基羰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-（四氢呋喃 -3- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-({(3R)-1-[3-（三氟甲氧基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-（吡啶 -2- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氯苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(4- 氯苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基 -2- 苯基丙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-（甲氧基乙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-（噻吩 -2- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-{[3-（三氟甲基）苯基］乙酰基｝吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基丙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丁酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3,5- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-({(3R)-1-[4-（三氟甲基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-[4-({(3R)-1-[4-(三氟甲氧基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 甲基丁酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(3,3,3- 三氟丙酰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[二氟（苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丙酰基）吡咯烷 -3- 基］氧基｝苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(4,4- 二氟环己基）羰基］吡咯烷 -3- 基｝氧基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-{4-[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环丙基乙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-{4-[1-(噻吩 -3- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 氟苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,4- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3- 氟苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{1-[3-(三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,4- 二氟苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-{4-[1-(1,3- 噻唑 -4- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁

烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-{4-[1-(四氢呋喃 -2- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(5- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 氟苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环丙基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-{4-[1-(四氢呋喃 -3- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-{4-[1-(吡啶 -2- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基 -2- 苯基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(甲氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-{4-[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-[4-(1-{[3-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{1-[4-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{1-[4-(三氟甲氧基) 苯甲酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-(4-{1-[二氟(苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(4,4-二氟环己基)羰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-(1-{[4-(三氟甲氧基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-(1-{[4-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-叔丁基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-甲氧基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环己基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环丙基乙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲氧基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(2S)-2-苯基丁酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[4-(丙烷-2-基)苯甲酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(4-氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-苯甲酰基哌啶-4-基)磺酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(4,4,4-三氟丁酰基)哌啶-4-基]磺酰基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2,5-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂

环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4- 氟苯基）乙酰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,3- 二甲基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 氟苯基）乙酰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-({1-[3-（三氟甲基）苯甲酰基］哌啶 -4- 基｝磺酰基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-({1-[4-（三氟甲基）苯甲酰基］哌啶 -4- 基｝磺酰基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,3- 二氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氯苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（萘 -1- 基羰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基羰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲氧基苯甲酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 甲基丁酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环戊基羰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(苯基乙酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(1- 苯基环丙基) 羰基] 哌啶 -4- 基 } 磺酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基丙氨酰) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

叔丁基 4-(2- 甲基 -1- 氧代 -1-{4-[4-({[1-(吡啶 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基] 哌啶 -1- 基 } 丙烷 -2- 基) 哌嗪 -1- 甲酸酯 ;

N-(4-{1-[2- 甲基 -2-(哌嗪 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 氯苯甲酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(4- 甲基戊酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2- 氟苯基) 乙酰基] 哌啶 -4- 基 } 磺酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 苯甲酰基哌啶 -4- 基) 磺酰基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环戊基羰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 氟 -5- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(5- 氟吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(2- 氟 -6- 甲基吡啶 -3- 基) 氮杂环丁

烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(2- 氰基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(4- 氰基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(6- 氟 -4- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(5- 氰基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(5- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基）甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[2-(哌嗪 -1- 基）乙基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(5- 丙基 -1,2,4- 氧杂二唑 -3- 基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[5-(2,2- 二甲基丙基)-1,3,4- 氧杂二唑 -2- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙基)-1H- 咪唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(3- 环丙基 -1- 甲基 -1H- 吡唑 -5- 基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[5-(2,2- 二甲基丙基)-1,2,4- 氧杂二唑 -3- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[3- 环丙基 -1-(2- 甲氧基乙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

叔丁基 4- 氟 -4-[4-({[1-(哒嗪 -3- 基）氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基] 哌啶 -1- 甲酸酯；

N-{4-[3- 环丙基 -1-(2- 羟基乙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(6- 氟哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(6- 氟哒嗪 -3- 基)-N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 乙基丁酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基)-2- 氟苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(2- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[8-(2- 甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[8-(4,4,4- 三氟丁酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(8- 苯甲酰基 -8- 氮杂双环 [3.2.1] 辛 -3- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[8-(2- 氟苯甲酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[8-(2,2- 二甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{8-[(1- 甲基环丙基) 羰基]-8- 氮杂双环 [3.2.1] 辛 -3- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲氧基乙基)-3-(2- 甲基丙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁

烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基 }-1-(6- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基）氮杂环丁烷 -3- 基］羰基 } 氨基）苯基]-4- 氟哌啶 -1- 甲酸酯；

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基）氮杂环丁烷 -3- 基］羰基 } 氨基）苯基]-4- 羟基哌啶 -1- 甲酸酯；

N-{4-[4- 氟 -1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(2- 甲基丙酰基）哌啶 -4- 基］苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环丙基羰基）哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(2- 氟 -4-{1-[(1- 甲基环丙基）羰基］哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环丙基乙酰基）哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基 -4- 氟哌啶 -4- 基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基)-4- 氟哌啶 -4- 基］苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[3- 叔丁基 -1-(2- 甲氧基乙基)-1H- 吡唑 -5- 基］苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁基 -3- 叔丁基 -1H- 吡唑 -5- 基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[3- 叔丁基 -1-(四氢 -2H- 吡喃 -4- 基甲基)-1H- 吡唑 -5- 基］苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基 }-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基)-2- 氟苯基]-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(4,4,4- 三氟丁酰基）哌啶 -4- 基］苯基 }-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1- 甲基 -3-(三氟甲基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(6- 氯哒嗪 -3- 基)-N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-3- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基)-3- 氟苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基]-3- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{3- 氟 -4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环丙基乙酰基) 哌啶 -4- 基]-3- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 氟苯甲酰基)-4- 羟基哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基)-4- 羟基哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(6- 甲基哒嗪 -3- 基)-N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 苯甲酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲

酰胺；

N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3,3-二甲基丁酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-乙基丁酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{[1-(4,4,4-三氟丁酰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-乙酰基哌啶-4-基)甲基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(1-甲基环丙基)羰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-{[4-甲基-1-(氧杂环丁烷-3-基)哌啶-4-基]甲基}-1H-吡唑-4-基)苯基]-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(4-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(3-甲基哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(3-甲基哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2-氨基吡啶-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-甲基-5-[4-({[1-(哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]-1H-吡唑-3-甲酸；

乙基 1-甲基-5-[4-({[1-(哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]-1H-吡唑-3-甲酸酯；

乙基 1-苯基-5-[4-({[1-(哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]-1H-吡唑-3-甲酸酯；

N-{6-[1-(2-氟苯甲酰基)哌啶-4-基]吡啶-3-基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(3-甲基丁酰基)吡咯烷-3-基]氧基}苯基)-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[(3R)-1-(2- 甲基丙酰基)吡咯烷-3- 基]氧基}苯基)-1-(6- 甲基哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基)吡咯烷-3- 基]氧基}苯基)-1-(6- 甲基哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

1-(6- 甲基哒嗪-3- 基)-N-(4-{[(3R)-1-(1,3- 噻唑-4- 基羰基)吡咯烷-3- 基]氧基}苯基)氮杂环丁烷-3- 甲酰胺;

1-(哒嗪-3- 基)-N-{6-[1-(4,4,4- 三氟丁酰基)哌啶-4- 基]吡啶-3- 基}氮杂环丁烷-3- 甲酰胺;

N-{6-[1-(3,3- 二甲基丁酰基)哌啶-4- 基]吡啶-3- 基}-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-{4-[1- 苯基-3-(三氟甲基)-1H- 吡唑-5- 基]苯基}-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-{6-[1-(2,2- 二甲基丙基)-1H- 吡唑-4- 基]吡啶-3- 基}-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

叔丁基 4-[4-({[1-(哒嗪-3- 基)氮杂环丁烷-3- 基]羰基}氨基)-1H- 吡唑-1- 基]哌啶-1- 甲酸酯;

N-(6-{1-[(4- 甲基哌啶-4- 基)甲基]-1H- 吡唑-4- 基}吡啶-3- 基)-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

1-(哒嗪-3- 基)-N-(4-{[1-(1,3- 噻唑-5- 基羰基)哌啶-4- 基]甲基}苯基)氮杂环丁烷-3- 甲酰胺;

N-(4-{[1-(环戊基羰基)哌啶-4- 基]甲基}苯基)-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-(4-{[1-(1H- 吡唑-4- 基羰基)哌啶-4- 基]甲基}苯基)-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-(4-{[1-(2,2- 二甲基丁酰基)哌啶-4- 基]甲基}苯基)-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-[4-({1-[(2- 甲基环丙基)羰基]哌啶-4- 基}甲基)苯基]-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-[4-({1-[(甲基巯基)乙酰基]哌啶-4- 基}甲基)苯基]-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-[4-({1-[(1S,4R)- 双环[2.2.1]庚-2- 基乙酰基]哌啶-4- 基}甲基)苯基]-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-(4-{[1-(2- 甲基戊酰基)哌啶-4- 基]甲基}苯基)-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-(4-{[1-(4- 甲基戊酰基)哌啶-4- 基]甲基}苯基)-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

N-[4-({1-[3-(甲基巯基)丙酰基]哌啶-4- 基}甲基)苯基]-1-(哒嗪-3- 基)氮杂环丁烷-3- 甲酰胺;

1-(哒嗪-3- 基)-N-(4-{[1-(1,3- 噻唑-4- 基羰基)哌啶-4- 基]甲基}苯基)氮杂

环丁烷 -3- 甲酰胺；

N-(4-{[1-(1H- 吡唑 -5- 基羰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(6- 甲基吡啶 -3- 基）羰基］哌啶 -4- 基｝甲基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝甲基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（戊 -4- 炔酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（噻吩 -3- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（甲氧基乙酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（四氢呋喃 -2- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 甲氧基乙氧基）乙酰基］哌啶 -4- 基｝甲基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（乙氧基乙酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（噻吩 -2- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 己酰基哌啶 -4- 基）甲基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基 -1H- 吡咯 -2- 基）羰基］哌啶 -4- 基｝甲基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（丁 -3- 烯酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（呋喃 -2- 基羰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(1,2- 唑 -5- 基羰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（吡啶 -2- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（呋喃 -3- 基羰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基乙酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丁酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 丙酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 丁酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环丁基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 戊酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环戊基乙酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基苯甲酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 甲基戊酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环己基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 甲基丁酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环丙基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(4- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{1-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-1H- 吡唑 -4- 基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{1-[1-(2- 氟苯甲酰基) 哌啶 -4- 基]-1H- 吡唑 -4- 基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(苯基氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(2,2- 二甲基丙基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(3- 甲氧基 -2,2- 二甲基丙基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(2- 环丙基乙基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[2-(2- 乙基哌啶 -1- 基) 乙基] 氨基甲酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(环丁基甲基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(2S)-丁烷-2-基氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(丁基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(2,2-二甲基四氢-2H-吡喃-4-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(1S)-1-环丙基乙基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({2-[甲基(苯基)氨基]乙基}氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1,1′-双(环丙基)-1-基氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-[4-(噻吩-3-基氨基甲酰基)苯基]氮杂环丁烷-3-甲酰胺;

N-(4-{[(1R)-1-环丙基乙基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-甲基哌啶-4-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(2R)-丁烷-2-基氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-氮杂双环[2.2.2]辛-3-基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[(四氢呋喃-3-基甲基)氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[(氧杂环丁烷-3-基甲基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(2-甲基环丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(环丁基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-甲基环丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(2-甲氧基-2-甲基丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(环丙基甲基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[(2R)-四氢呋喃-2-基甲基]氨基甲酰基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-{4-[(3,3,3-三氟丙基)氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[(1-甲基哌啶-3-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3- 甲基氧杂环丁烷 -3- 基) 甲基] 氨基甲酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[(2S)- 四氢呋喃 -2- 基甲基] 氨基甲酰基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[(四氢 -2H- 吡喃 -4- 基甲基) 氨基甲酰基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-[4-(四氢 -2H- 吡喃 -4- 基氨基甲酰基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(1- 甲基哌啶 -3- 基) 甲基] 氨基甲酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(环丙基氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(环戊基氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(苄基氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(3- 氟苯基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(丙基氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(4- 氟苯基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(2- 氟苯基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 甲基环丁基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(丙 -2- 烯 -1- 基氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[(3S)- 四氢呋喃 -3- 基氨基甲酰基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({4-[2-(二甲基氨基) 乙基] 苯基 } 氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[(3R)- 四氢呋喃 -3- 基氨基甲酰基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(2- 甲氧基乙基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 氨基 -2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

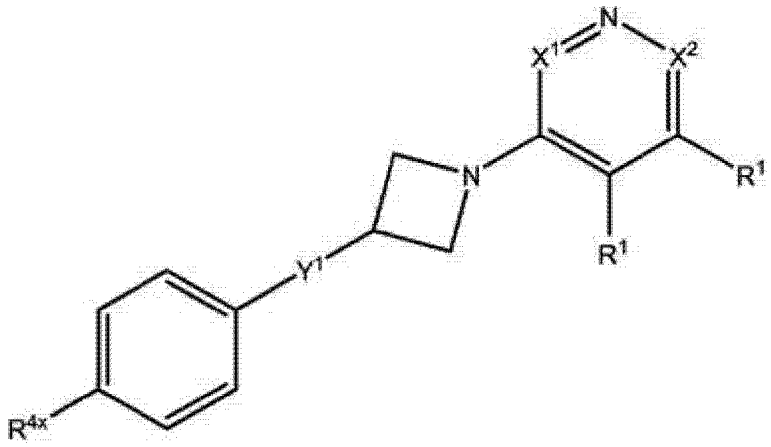
N-(4-{1-[2,2- 二甲基 -3-(哌嗪 -1- 基) 丙基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[2- 甲基 -2-(哌嗪 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

及其药学上可接受的盐。

[0229] 式 (IIIC) 的实施方案

在另一方面,本发明提供式 (IIIC) 的化合物



(IIIC);

及其药学上可接受的盐；其中当式 (IC) 中的 R^2 为芳基时，X^1、X^2、R^1、和 Y^1 如本文式 (IC) 中所描述且 R^{4x} 如本文对 R^2 上的取代基所描述。

[0230] 本发明的一个实施方案涉及式 (IIIC) 的化合物或其药学上可接受的盐；

其中

X^1 为 N 且 X^2 为 CR^1；或

X^1 为 CR^1 且 X^2 为 N；或

X^1 为 CR^1 且 X^2 为 CR^1；

Y^1 为 C(O)NH、或 NHC(O)；

R^1 在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I；

R^{4X} 独立地选自 R^4，OR^4，SR^4，$S(O)R^4$，

SO_2R^4，$C(O)R^4$，$OC(O)OR^4$，NH_2，NHR^4，$N(R^4)_2$，$NHC(O)R^4$，$NR^4C(O)R^4$，$NHS(O)_2R^4$，

$NR^4S(O)_2R^4$，$NHC(O)OR^4$，$NR^4C(O)OR^4$，$NHC(O)NH_2$，$NHC(O)NHR^4$，$NHC(O)N(R^4)_2$，

$NR^4C(O)NHR^4$，$NR^4C(O)N(R^4)_2$，$C(O)NH_2$，$C(O)NHR^4$，$C(O)N(R^4)_2$，C(O)NHOH，

$C(O)NHOR^4$，$C(O)NHSO_2R^4$，$C(O)NR^4SO_2R^4$，SO_2NH_2，SO_2NHR^4，$SO_2N(R^4)_2$，C(O)H，

C(O)OH，$C(N)NH_2$，$C(N)NHR^4$，$C(N)N(R^4)_2$，CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，

和 I；

R^4 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中

R^4 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7，OR^7，SR^7，$S(O)R^7$，SO_2R^7，$C(O)R^7$，$CO(O)R^7$，

$OC(O)R^7$，$OC(O)OR^7$，NH_2，NHR^7，$N(R^7)_2$，$NHC(O)R^7$，$NR^7C(O)R^7$，$NHS(O)_2R^7$，

$NR^7S(O)_2R^7$，$NHC(O)OR^7$，$NR^7C(O)OR^7$，$NHC(O)NH_2$，$NHC(O)NHR^7$，$NHC(O)N(R^7)_2$，

$NR^7C(O)NHR^7$，$NR^7C(O)N(R^7)_2$，$C(O)NH_2$，$C(O)NHR_7$，$C(O)N(R^7)_2$，C(O)NHOH，

$C(O)NHOR^7$，$C(O)NHSO_2R^7$，$C(O)NR^7SO_2R^7$，SO_2NH_2，SO_2NHR^7，$SO_2N(R^7)_2$，C(O)H，

C(O)OH，$C(N)NH_2$，$C(N)NHR^7$，$C(N)N(R^7)_2$，CNOH，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，

Cl，Br 和 I；

R^7 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中由 R^4 和 R^7 表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：

R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, $C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, CF_3, OCF_3, F, Cl, Br 和 I；

R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

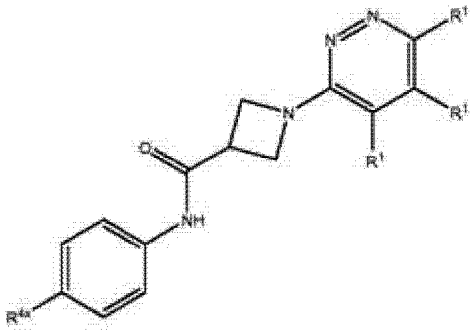
[0231] 在式 (IIIC) 的一个实施方案中，X^1为 N 且 X^2为 CR^1；或 X^1为 CR^1且 X^2为 N；或 X^1为 CR^1且 X^2为 CR^1。在式 (IIIC) 的另一个实施方案中，X^1为 N 且 X^2为 CR^1。在式 (IIIC) 的另一个实施方案中，X^1为 CR^1且 X^2为 N。在式 (IIIC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1。

[0232] 在式 (IIIC) 的一个实施方案中，Y^1为 C(O)NH、或 NHC(O)。在式 (IIIC) 的另一个实施方案中，Y^1为 C(O)NH。在式 (IIIC) 的另一个实施方案中，Y^1为 NHC(O)。

[0233] 在式 (IIIC) 的一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式

(IIIC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IIIC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IIIC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时为氢。

[0234] 在另一方面，本发明提供式 (IIID) 的化合物，



式 (IIID)

及其药学上可接受的盐；其中当式 (IC) 中 R^2的为芳基时，R^1如本文对式 (IC) 所描述且 R^{4x}如本文对 R^2上的取代基所描述。

[0235] 在式 (IIIC) 和 (IIID) 的一个实施方案中，R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (IIIC) 和 (IIID) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IIIC) 和 (IIID) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IIIC) 和 (IIID) 的另一个实施方案中，R^1在每次出现时为氢。

[0236] 在式 (IIIC) 和 (IIID) 的一个实施方案中，R^{4X}独立地选自 R^4，OR^4，SR^4，$S(O)R^4$，SO_2R^4，$C(O)R^4$，$OC(O)OR^4$，NH_2，NHR^4，

$N(R^4)_2$，$NHC(O)R^4$，$NR^4C(O)R^4$，$NHS(O)_2R^4$，$NR^4S(O)_2R^4$，$NHC(O)OR^4$，$NR^4C(O)OR^4$，

$NHC(O)NH_2$，$NHC(O)NHR^4$，$NHC(O)N(R^4)_2$，$NR^4C(O)NHR^4$，$NR^4C(O)N(R^4)_2$，$C(O)NH_2$，

$C(O)NHR^4$，$C(O)N(R^4)_2$，$C(O)NHOH$，$C(O)NHOR^4$，$C(O)NHSO_2R^4$，$C(O)NR^4SO_2R^4$，

SO_2NH_2，SO_2NHR^4，$SO_2N(R^4)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^4$，$C(N)N(R^4)_2$，

CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，和 I。在式 (IIIC) 和 (IIID) 的另一个实施方案中，R^{4X}独立地选自 R^4、OR^4、SO_2R^4、$C(O)NHR^4$、F、Cl、和 I。在式 (IIIC) 和 (IIID) 的另一个实施方案中，R^{4X}独立地选自 R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。

[0237] 在式 (IIIC) 和 (IIID) 的一个实施方案中，R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7，OR^7，SR^7，$S(O)R^7$，SO_2R^7，$C(O)R^7$，$CO(O)R^7$，$OC(O)R^7$，$OC(O)OR^7$，NH_2，NHR^7，$N(R^7)_2$，

$NHC(O)R^7$，$NR^7C(O)R^7$，$NHS(O)_2R^7$，$NR^7S(O)_2R^7$，$NHC(O)OR^7$，$NR^7C(O)OR^7$，

$NHC(O)NH_2$，$NHC(O)NHR^7$，$NHC(O)N(R^7)_2$，$NR^7C(O)NHR^7$，$NR^7C(O)N(R^7)_2$，$C(O)NH_2$，

$C(O)NHR^7$，$C(O)N(R^7)_2$，$C(O)NHOH$，$C(O)NHOR^7$，$C(O)NHSO_2R^7$，$C(O)NR^7SO_2R^7$，

SO_2NH_2，SO_2NHR^7，$SO_2N(R^7)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^7$，$C(N)N(R^7)_2$，

CNOH，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I。在式 (IIIC) 和 (IIID) 的另一个实

施方案中，

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基。

[0238] 在式（IIIC）和（IIID）的一个实施方案中，R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH,)O), CN, N_3, NO_2, F, Cl, Br 和 I。在式（IIIC）和（IIID）的另一个实施方案中，

R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7、OR^7、$N(R^7)_2$、F、Cl、Br 和 I。

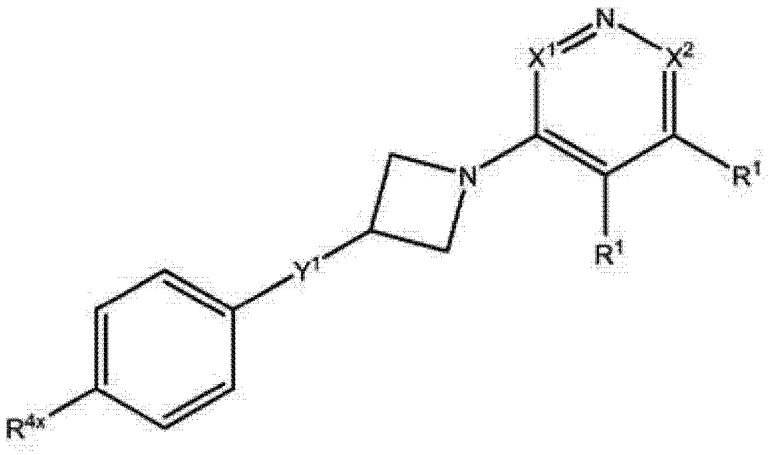
[0239] 在式（IIIC）和（IIID）的一个实施方案中，R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。在式（IIIC）和（IIID）的另一个实施方案中，R^7在每次出现时独立地选自烷基、芳基、杂环基、和环烷基。

[0240] 在式（IIIC）和（IIID）的一个实施方案中，R^4和 R^7中的环状基团各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2$, $C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$,

CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0241] 在式（IIIC）和（IIID）的另一个实施方案中，R^4和 R^7中的环状基团各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)H$、OH、F、Cl、Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、NH_2、OH、CN、CF_3、OCF_3、F、和 Cl；R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、CF_3、F、和 Cl；R^{12}在每次出现时独立地选自烷基和芳基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、和环烷基。

[0242] 本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式（IIIC）



(IIIC);

其中

X^1为 N 且 X^2为 CR^1；或

X^1为 CR^1且 X^2为 N；或

X^1为 CR^1且 X^2为 CR^1；

Y^1为 $C(O)NH$、或 $NHC(O)$；

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、Cl、和 F；

R^{4X}独立地选自 R^4、SO_2R^4、OR^4、和 F；

R^4在每次出现时独立地选自烷基、烯基、芳基、杂环基、和环烷基；其中 R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7、OR^7、$N(R^7)_2$、和 F；

R^7在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；

其中由 R^4和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：

R^{10}、C(O)R^{10}、C(O)C(O)R^{10}、CO(O)R^{10}、C(O)OH、OH 和 F；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、NHC(O)R^{11}、NHS(O)$_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代：R^{12}、OR^{12}、C(O)R^{12}、NH_2、OH、CN、CF_3、OCF_3、F、和 Cl；

R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、C(O)OR^{13}、OCF_3、CF_3、F、和 Cl；

R^{12}在每次出现时独立地选自烷基、和芳基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、环烷基、和杂环基。

[0243] 仍另一个实施方案涉及具有式 (IIIC) 的化合物，其包括

1-(吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(2-氰基吡啶-3-基)-N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-[2-(三氟甲基)吡啶-3-基]氮杂环丁烷-3-甲酰胺；

1-(2-甲基吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(4-甲基吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

1-(4-氟吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-[4-(三氟甲基)吡啶-3-基]氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-(4-{1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2S)-2-甲基丁酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-{4-[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲

酰胺；

N-(4-{[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

1-(吡啶-3-基)-N-[4-({1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺；

N-{4-[(1-戊酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2-甲基环丙基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(1S,4R)-双环[2.2.1]庚-2-基乙酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-甲基戊酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基戊酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-乙氧基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,2-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3,3-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-丁酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(乙氧基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(N-乙酰基-L-亮氨酰)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环己基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环己基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-(4-{[1-(4,4,4-三氟丁酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环戊基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(1-甲基环己基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(呋喃-3-基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-乙酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(甲氧基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-(4-{[1-(噻吩-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(3-甲基噻吩-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(吗啉-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-(4-{[1-(噻吩-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(呋喃-2-基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(1-甲基-1H-吡咯-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-丙酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-({1-[(1-甲基环丙基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(N,N-二甲基-β-丙氨酰)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

1-(吡啶-3-基)-N-(4-{[1-(1,3-噻唑-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环戊基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁

烷 -3- 甲酰胺；

N-(4-{[1-(2,3- 二甲基丁酰基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(4- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(2- 甲氧基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(环丙基甲基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基戊基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 乙基丁基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丁基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 丙基哌啶 -4- 基）氧基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 环丙基乙基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(吡啶 -3- 基)-N-(4-{[1-(四氢呋喃 -3- 基甲基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丁基）哌啶 -4- 基］氧基｝苯基)-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环己基甲基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环戊基甲基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丁基）哌啶 -4- 基］苯基}-1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲

酰胺；

N-{4-[1-(2- 甲基戊基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁基哌啶 -4- 基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 乙基丁基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基丁基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基丙基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丙基哌啶 -4- 基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-(4- 甲氧基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(4- 氰基吡啶 -3- 基）-N-{4-[1-(2- 羟基 -2- 甲基丙酰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 戊酰基哌啶 -4- 基）苯基]-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基戊酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1S,4R)- 双环 [2.2.1] 庚 -2- 基乙酰基］哌啶 -4- 基} 苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环戊基乙酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 甲基环丙基）羰基］哌啶 -4- 基} 苯基)-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（吗啉 -4- 基乙酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（呋喃 -3- 基羰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-{4-[1-（吡咯烷 -1- 基乙酰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(5- 氧代 -D- 脯氨酰）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N, N- 二甲基 -β- 丙氨酰）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-{4-[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-{4-[1-（噻吩 -3- 基羰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环丙基）羰基］哌啶 -4- 基} 苯基)-1-（吡啶 -3- 基）氮杂环丁

烷 -3- 甲酰胺；

N-(4-{1-[(3- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-{4-[1-(4,4,4- 三氟丁酰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基哌嗪 -1- 基）乙酰基］哌啶 -4- 基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(5- 氧代 -L- 脯氨酰）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 乙氧基丙酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 甲基戊酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环己基）羰基］哌啶 -4- 基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 乙酰基哌啶 -4- 基）苯基］-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环己基乙酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N- 乙酰基 -L- 亮氨酰）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丙酰基哌啶 -4- 基）苯基］-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-{4-[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 甲氧基乙氧基）乙酰基］哌啶 -4- 基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[3-（吗啉 -4- 基）丙酰基］哌啶 -4- 基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（吡啶 -3- 基）-N-{4-[1-（噻吩 -2- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基 -1H- 吡咯 -2- 基）羰基］哌啶 -4- 基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（呋喃 -2- 基羰基）哌啶 -4- 基］苯基}-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[3-（哌啶 -1- 基）丙酰基］哌啶 -4- 基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(乙氧基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,2-二甲基丁酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-丁酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环己基羰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环戊基羰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2S)-2-甲基丁酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(四氢-2H-吡喃-4-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,5- 二氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[4-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(哒嗪 -3- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-[4-(1- 戊酰基哌啶 -4- 基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1S,4R)- 双环 [2.2.1] 庚 -2- 基乙酰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(吗啉 -4- 基乙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(呋喃 -3- 基羰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(吡咯烷 -1- 基乙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(5- 氧代 -D- 脯氨酰) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(N,N- 二甲基 -β- 丙氨酰) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(2- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(3- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 氮杂环

丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基哌嗪 -1- 基）乙酰基］哌啶 -4- 基} 苯基)-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(5- 氧代 -L- 脯氨酰）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 乙氧基丙酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 甲基戊酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(1- 甲基环己基）羰基］哌啶 -4- 基} 苯基)-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 乙酰基哌啶 -4- 基）苯基］-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环己基乙酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(N- 乙酰基 -L- 亮氨酰）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-[4-(1- 丙酰基哌啶 -4- 基）苯基］氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 甲氧基乙氧基）乙酰基］哌啶 -4- 基} 苯基)-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[3-(吗啉 -4- 基）丙酰基］哌啶 -4- 基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基} 苯基）氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(噻吩 -2- 基羰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[(1- 甲基 -1H- 吡咯 -2- 基）羰基］哌啶 -4- 基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(呋喃 -2- 基羰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(2- 甲基吡啶 -3- 基)-N-(4-{1-[3-(哌啶 -1- 基）丙酰基］哌啶 -4- 基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(乙氧基乙酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁酰基哌啶 -4- 基）苯基］-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(甲氧基乙酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环己基羰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3- 甲基丁酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-(2- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基）氮杂环丁烷 -3- 基］氧基} 苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氟苯甲酰基）氮杂环丁烷 -3- 基］氧基} 苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[二氟（苯基）乙酰基］氮杂环丁烷 -3- 基} 氧基）苯基]-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4,4- 二氟环己基）羰基］氮杂环丁烷 -3- 基} 氧基）苯基]-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4- 氟苯基）乙酰基］氮杂环丁烷 -3- 基} 氧基）苯基]-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-[4-({1-[4-(三氟甲基）苯甲酰基］氮杂环丁烷 -3- 基} 氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 苯甲酰基氮杂环丁烷 -3- 基）氧基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 羟基 -2- 甲基丙酰基）氮杂环丁烷 -3- 基］氧基} 苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -4- 基)-N-(4-{[1-(四氢呋喃 -3- 基羰基）氮杂环丁烷 -3- 基］氧基} 苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(呋喃 -3- 基羰基）氮杂环丁烷 -3- 基］氧基} 苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 戊酰基氮杂环丁烷 -3- 基）氧基］苯基}-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氯苯甲酰基）哌啶 -4- 基］氧基} 苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 甲基丁酰基］哌啶 -4- 基} 氧基）苯基]-1-(哒嗪 -3- 基）氮杂

环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(1,3- 噻唑 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[二氟 (苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4,4- 二氟环己基) 羰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基 -2- 苯基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(1,3- 噻唑 -4- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(5- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[(1-{[4-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(四氢呋喃 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-[4-({1-[3-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-[4-({1-[3-(三氟甲氧基) 苯甲酰基] 哌啶 -4- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(四氢呋喃 -3- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4- 氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环丙基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3,4- 二氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-[4-({1-[4-(三氟甲氧基) 苯甲酰基] 哌啶 -4- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2,4- 二氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-[4-({1-[4-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[(1-{[4-(三氟甲氧基) 苯基] 乙酰基 } 哌啶 -4- 基) 氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(3,5- 二氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[(1-{[3-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(吡啶 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 乙酰基哌啶 -4- 基) 氧基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(4- 氯苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(甲氧基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2- 氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 氯苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环丙基羰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁

烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,3- 二甲基丁酰基）氮杂环丁烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环己基羰基）氮杂环丁烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（四氢 -2H- 吡喃 -4- 基乙酰基）氮杂环丁烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 甲基环丙基）羰基］氮杂环丁烷 -3- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-(3,3,3- 三氟丙酰基）氮杂环丁烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环戊基羰基）氮杂环丁烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丁基羰基）氮杂环丁烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（四氢呋喃 -2- 基羰基）氮杂环丁烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 甲基戊酰基）氮杂环丁烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基）氮杂环丁烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 甲基丁酰基］氮杂环丁烷 -3- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（甲氧基乙酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[二氟（苯基）乙酰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(4,4- 二氟环己基）羰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[1-(1,3- 噻唑 -4- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-{4-[(1-{[4-(三氟甲基) 苯基] 乙酰基 } 哌啶 -4- 基) 氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3,4- 二氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-{4-[(1-{[4-(三氟甲氧基) 苯基] 乙酰基 } 哌啶 -4- 基) 氧基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(4- 氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2,4- 二氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[1-(噻吩 -3- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 氯苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 甲基 -2- 苯基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 乙酰基哌啶 -4- 基) 氧基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[1-(1,3- 噻唑 -2- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-[4-({1-[3-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-[4-({1-[4-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(3- 氟苯基) 乙酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-[4-({1-[4-(三氟甲氧基) 苯甲酰基] 哌啶 -4- 基 } 氧基) 苯基]

氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({1-[3-（三氟甲氧基）苯甲酰基］哌啶 -4- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基乙酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 氯苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（吡啶 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氯苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（四氢呋喃 -3- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丁酰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环丙基羰基）哌啶 -4- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（四氢呋喃 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（噻吩 -2- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-{4-[(1-{[3-（三氟甲基）苯基］乙酰基｝哌啶 -4- 基）氧基］苯基｝氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[1-（四氢 -2H- 吡喃 -4- 基羰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2S)-2- 甲基丁酰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 氟苯基）乙酰基］哌啶 -4- 基｝氧基）苯基]-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 乙酰基哌啶 -4- 基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁酰基哌啶 -4- 基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 戊酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 己酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 乙基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 庚酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(丁 -3- 烯酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(戊 -4- 烯酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(甲氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(甲基巯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 甲氧基乙氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 硝基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[3-(甲基巯基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(戊 -4- 炔酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环己基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环己基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,3-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,4-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁

烷 -3- 甲酰胺；

N-{4-[1-(2,5- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,4- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,4- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,5- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,4- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 氟苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3- 氟苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 氟苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2- 氯苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 氯苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-(1-{[4-（三氟甲基）苯基］乙酰基} 哌啶 -4- 基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,5- 二甲基苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(2,5- 二氟苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,4- 二氯苯基）乙酰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（呋喃 -3- 基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[1-（噻吩 -2- 基羰基）哌啶 -4- 基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(5- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(5- 甲基吡嗪 -2- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 乙氧基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 苯基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{1-[(嘧啶 -2- 基巯基) 乙酰基] 哌啶 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(1- 乙酰基哌啶 -4- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(3,5- 二氟苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(N- 乙酰基 -L- 亮氨酰) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(二苯基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 氟 -2- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(5- 氟 -2- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3- 氟 -4- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,3- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[4-(丙烷 -2- 基) 苯甲酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 叔丁基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[2- 氟 -5-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[2- 氯 -5-(三氟甲基) 苯甲酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(4- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲

酰胺；

N-(4-{1-[(4-甲基苯氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2S)-2-苯基丁酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-[4-(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(3-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2,4-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(萘-1-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2R)-2-甲氧基-2-苯基乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[N-(呋喃-2-基羰基)甘氨酰]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(苄基氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(萘-1-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(N-苯甲酰基甘氨酰)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{1-[4-(噻吩-2-基)丁酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环丁基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-{N-[(4-甲基苯基)磺酰基]甘氨酰}哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2,3-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2S)-2-甲氧基-2-苯基乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(萘-2-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-苯基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2,6-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[3-(苯基磺酰基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(2,5-二甲基呋喃-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(环丙基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[1-(1,3-噻唑-4-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[1-(1,3-噻唑-5-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-{4-[1-(乙氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(6-甲基吡啶-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(呋喃-2-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(1- 甲基环己基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 氧代丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环戊基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丙酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(4- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(2- 氯苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-(1,3- 噻唑 -2- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(环丙基乙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(2S)-2- 甲基丁酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-(四氢 -2H- 吡喃 -4- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-{[4-(三氟甲氧基) 苯基] 乙酰基 } 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-(噻吩 -3- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(4- 氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(3,5- 二氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(3,4- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(3- 氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-[4-({(3R)-1-[3-(三氟甲基) 苯甲酰基] 吡咯烷 -3- 基 } 氧基) 苯基] 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({(3R)-1-[(2,4- 二氟苯基) 乙酰基] 吡咯烷 -3- 基 } 氧基) 苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-{[4-(三氟甲基) 苯基] 乙酰基 } 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -4- 基)-N-(4-{[(3R)-1-(1,3- 噻唑 -4- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(四氢呋喃-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(5-甲基噻吩-2-基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-[4-({(3R)-1-[(2-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(环丙基羰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(四氢呋喃-3-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-({(3R)-1-[3-(三氟甲氧基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(吡啶-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(3-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(4-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(2-甲基-2-苯基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(2,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(甲氧基乙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-(噻吩-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{[(3R)-1-{[3-(三氟甲基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(2-甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(2-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(2,2-二甲基丁酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(3,5-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-({(3R)-1-[4-(三氟甲基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺;

N-(4-{[(3R)-1-(3-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮

杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-[4-({(3R)-1-[4-（三氟甲氧基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 甲基丁酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-(4-{[(3R)-1-(3,3,3- 三氟丙酰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[二氟（苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基］-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(4,4- 二氟环己基）羰基］吡咯烷 -3- 基｝氧基）苯基］-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氯苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-(1,3- 噻唑 -2- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-（环丙基乙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2S)-2- 甲基丁酰基］吡咯烷 -3- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-（四氢 -2H- 吡喃 -4- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-{[4-（三氟甲氧基）苯基］乙酰基｝吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(4- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-（噻吩 -3- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(4- 氟苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(3,5- 二氟苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3,4- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(3- 氟苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-({(3R)-1-[3-（三氟甲基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2,4- 二氟苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-{[4-（三氟甲基）苯基］乙酰基｝吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-(1,3- 噻唑 -4- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-（四氢呋喃 -2- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(5- 甲基噻吩 -2- 基）羰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(2- 氟苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-（环丙基羰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-（四氢呋喃 -3- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-({(3R)-1-[3-（三氟甲氧基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-（吡啶 -2- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氯苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(4- 氯苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基 -2- 苯基丙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-（甲氧基乙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-（噻吩 -2- 基羰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-{[3-（三氟甲基）苯基］乙酰基｝吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 甲基丙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丁酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）

氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3,5- 二氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-({(3R)-1-[4-（三氟甲基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 氟苯甲酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-({(3R)-1-[4-（三氟甲氧基）苯甲酰基］吡咯烷 -3- 基｝氧基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(3- 甲基丁酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(3R)-1-(3,3,3- 三氟丙酰基）吡咯烷 -3- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[二氟（苯基）乙酰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3R)-1-(2,2- 二甲基丙酰基）吡咯烷 -3- 基］氧基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({(3R)-1-[(4,4- 二氟环己基）羰基］吡咯烷 -3- 基｝氧基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-{4-[1-(1,3- 噻唑 -2- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-（环丙基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -4- 基）-N-{4-[1-（噻吩 -3- 基羰基）哌啶 -4- 基］苯基｝氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 氟苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3,5- 二氟苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,4- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(3- 氟苯基）乙酰基］哌啶 -4- 基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪-4-基)-N-(4-{1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2,4-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(1,3-噻唑-4-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[(2-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(四氢呋喃-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(吡啶-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-甲基-2-苯基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,4-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-{4-[1-(噻吩-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-[4-(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-4-基)-N-(4-{1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲

酰胺；

1-(哒嗪-4-基)-N-(4-{1-[4-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺；

N-(4-{1-[二氟(苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(4,4-二氟环己基)羰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-[4-(1-{[4-(三氟甲氧基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-(4-{1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-4-基)-N-[4-(1-{[4-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-叔丁基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-甲氧基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环己基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环丙基乙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲氧基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(2S)-2-苯基丁酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[4-(丙烷-2-基)苯甲酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[(1-苯甲酰基哌啶-4-基)磺酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-(4-{[1-(4,4,4-三氟丁酰基)哌啶-4-基]磺酰基}苯基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,5-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(4-氟苯基)乙酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,3-二甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(3-氟苯基)乙酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3-氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-[4-({1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}磺酰基)苯基]氮杂环丁烷-3-甲酰胺；

N-[4-({1-[(3,5-二氟苯基)乙酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,4-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-[4-({1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}磺酰基)苯基]氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(4-氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,3-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(2,4-二氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(萘-1-基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环丙基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(3,5-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂

环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,3- 二甲基丁酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲氧基苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3- 甲基丁酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环戊基羰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（苯基乙酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 苯基环丙基）羰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲基丙氨酰）哌啶 -4- 基］苯基｝-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

叔丁基 4-(2- 甲基 -1- 氧代 -1-{4-[4-({[1-（吡啶 -3- 基）氮杂环丁烷 -3- 基］羰基｝氨基）苯基］哌啶 -1- 基｝丙烷 -2- 基）哌嗪 -1- 甲酸酯；

N-(4-{1-[2- 甲基 -2-（哌嗪 -1- 基）丙酰基］哌啶 -4- 基｝苯基）-1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氯苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 甲基戊酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 氟苯基）乙酰基］哌啶 -4- 基｝磺酰基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 苯甲酰基哌啶 -4- 基）磺酰基］苯基}-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（环戊基羰基）哌啶 -4- 基］磺酰基｝苯基）-1-（哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(6- 氟 -5- 甲基吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-氟吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-氟-6-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(4-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-氟-4-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[(4-甲基四氢-2H-吡喃-4-基)甲基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{1-[2-(哌嗪-1-基)乙基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(5-丙基-1,2,4-氧杂二唑-3-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[5-(2,2-二甲基丙基)-1,3,4-氧杂二唑-2-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙基)-1H-咪唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(3-环丙基-1-甲基-1H-吡唑-5-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[5-(2,2-二甲基丙基)-1,2,4-氧杂二唑-3-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[3-环丙基-1-(2-甲氧基乙基)-1H-吡唑-5-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

叔丁基4-氟-4-[4-({[1-(哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]哌啶-1-甲酸酯；

N-{4-[3-环丙基-1-(2-羟基乙基)-1H-吡唑-5-基]苯基}-1-(哒嗪-3-基)氮杂

环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(6- 氟哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基）哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(6- 氟哒嗪 -3- 基)-N-{4-[1-(2- 甲基丙酰基）哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 乙基丁酰基）哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 氟苯甲酰基）哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[8-(2- 甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[8-(4,4,4- 三氟丁酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-[4-(8- 苯甲酰基 -8- 氮杂双环 [3.2.1] 辛 -3- 基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[8-(2- 氟苯甲酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺 ;N-{4-[8-(2,2- 二甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{8-[(1- 甲基环丙基）羰基]-8- 氮杂双环 [3.2.1] 辛 -3- 基 } 苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲氧基乙基)-3-(2- 甲基丙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基）哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基）氮杂环丁烷 -3- 基] 羰基 } 氨基）苯基]-4- 氟哌啶 -1- 甲酸酯；

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基）氮杂环丁烷 -3- 基] 羰基 } 氨基）苯基]-4- 羟基哌啶 -1- 甲酸酯；

N-{4-[4- 氟 -1-(2- 氟苯甲酰基）哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基 -4- 氟哌啶 -4- 基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基)-4- 氟哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基）氮杂环丁

烷 -3- 甲酰胺；

N-{4-[3- 叔丁基 -1-(2- 甲氧基乙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁基 -3- 叔丁基 -1H- 吡唑 -5- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[3- 叔丁基 -1-(四氢 -2H- 吡喃 -4- 基甲基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1- 甲基 -3-(三氟甲基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(6- 氯哒嗪 -3- 基)-N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基)-4- 羟基哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基)-4- 羟基哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(6- 甲基哒嗪 -3- 基)-N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 苯甲酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 乙基丁酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-(4-{[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 乙酰基哌啶 -4- 基) 甲基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(2S)-2- 甲基丁酰基] 哌啶 -4- 基 } 甲基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-({1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 甲基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1-{[4- 甲基 -1-(氧杂环丁烷 -3- 基) 哌啶 -4- 基] 甲基 }-1H- 吡唑 -4- 基) 苯基]-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(4- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(3- 甲基哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(3- 甲基哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{1-[(2- 氨基吡啶 -3- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1- 甲基 -5-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基]-1H- 吡唑 -3- 甲酸 ;

乙基 1- 甲基 -5-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基]-1H- 吡唑 -3- 甲酸酯 ;

乙基 1- 苯基 -5-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基]-1H- 吡唑 -3- 甲酸酯 ;

N-(4-{[(3R)-1-(3- 甲基丁酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(2- 甲基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(6- 甲基哒嗪 -3- 基)-N-(4-{[(3R)-1-(1,3- 噻唑 -4- 基羰基) 吡咯烷 -3- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1- 苯基 -3-(三氟甲基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-(4-{[1-(1,3- 噻唑 -5- 基羰基) 哌啶 -4- 基] 甲基 } 苯基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环戊基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(1H- 吡唑 -4- 基羰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基] 甲基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环

丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 甲基环丙基）羰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[（甲基巯基）乙酰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1S,4R)- 双环 [2.2.1] 庚 -2- 基乙酰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(2- 甲基戊酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(4- 甲基戊酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[3-（甲基巯基）丙酰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-(1,3- 噻唑 -4- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(1H- 吡唑 -5- 基羰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(6- 甲基吡啶 -3- 基）羰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(3- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（戊 -4- 炔酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（噻吩 -3- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（甲氧基乙酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（四氢呋喃 -2- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(2- 甲氧基乙氧基）乙酰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-（乙氧基乙酰基）哌啶 -4- 基］甲基｝苯基）-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[1-（噻吩 -2- 基羰基）哌啶 -4- 基］甲基｝苯基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 己酰基哌啶 -4- 基）甲基］苯基｝-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-({1-[(1- 甲基 -1H- 吡咯 -2- 基）羰基］哌啶 -4- 基｝甲基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[1-(丁-3-烯酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(1,3-噻唑-2-基羰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(呋喃-2-基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(1,2-唑-5-基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(吡啶-2-基羰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(呋喃-3-基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环丙基乙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲基丁酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-丙酰基哌啶-4-基)甲基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-丁酰基哌啶-4-基)甲基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环丁基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[(1-戊酰基哌啶-4-基)甲基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环戊基乙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(2-甲基苯甲酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-甲基戊酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环己基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{[1-(环丙基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(哒嗪-3-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(4-甲基哒嗪-3-基)氮杂环

丁烷 -3- 甲酰胺；

N-[4-(苯基氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2,2- 二甲基丙基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(3- 甲氧基 -2,2- 二甲基丙基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2- 环丙基乙基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[2-(2- 乙基哌啶 -1- 基) 乙基] 氨基甲酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(环丁基甲基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2S)- 丁烷 -2- 基氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(丁基氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2,2- 二甲基四氢 -2H- 吡喃 -4- 基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(1S)-1- 环丙基乙基] 氨基甲酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-({2-[甲基 (苯基) 氨基] 乙基 } 氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1,1′ - 双 (环丙基)-1- 基氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-[4-(噻吩 -3- 基氨基甲酰基) 苯基] 氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(1R)-1- 环丙基乙基] 氨基甲酰基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 甲基哌啶 -4- 基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2R)- 丁烷 -2- 基氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 氮杂双环 [2.2.2] 辛 -3- 基氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(哒嗪 -3- 基)-N-{4-[(四氢呋喃 -3- 基甲基) 氨基甲酰基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(氧杂环丁烷 -3- 基甲基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2- 甲基环丙基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(环丁基氨基甲酰基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 甲基环丙基) 氨基甲酰基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰

胺；

N-{4-[(2- 甲氧基 -2- 甲基丙基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[（环丙基甲基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(2R)- 四氢呋喃 -2- 基甲基］氨基甲酰基} 苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[(3,3,3- 三氟丙基）氨基甲酰基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 甲基哌啶 -3- 基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(3- 甲基氧杂环丁烷 -3- 基）甲基］氨基甲酰基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-(4-{[(2S)- 四氢呋喃 -2- 基甲基］氨基甲酰基} 苯基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[（四氢 -2H- 吡喃 -4- 基甲基）氨基甲酰基］苯基} 氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-[4-（四氢 -2H- 吡喃 -4- 基氨基甲酰基）苯基］氮杂环丁烷 -3- 甲酰胺；

N-(4-{[(1- 甲基哌啶 -3- 基）甲基］氨基甲酰基} 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（环丙基氨基甲酰基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（环戊基氨基甲酰基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（苄基氨基甲酰基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(3- 氟苯基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（丙基氨基甲酰基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(4- 氟苯基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2- 氟苯基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 甲基环丁基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-[4-（丙 -2- 烯 -1- 基氨基甲酰基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[(3S)- 四氢呋喃 -3- 基氨基甲酰基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-[4-({4-[2-（二甲基氨基）乙基］苯基} 氨基甲酰基）苯基］-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基）-N-{4-[(3R)- 四氢呋喃 -3- 基氨基甲酰基］苯基} 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(2- 甲氧基乙基）氨基甲酰基］苯基}-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3-氨基-2,2-二甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

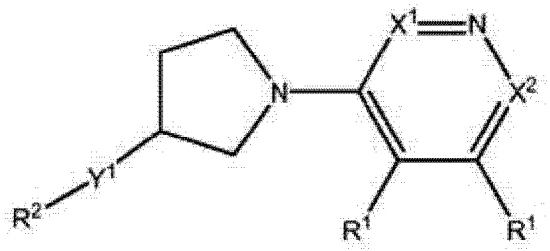
N-(4-{1-[2,2-二甲基-3-(哌嗪-1-基)丙基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-(4-{1-[2-甲基-2-(哌嗪-1-基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

及其药学上可接受的盐。

[0244] 式(IVC)的实施方案

在另一方面,本发明提供式(IVC)的化合物



(IVC);

及其药学上可接受的盐;其中 X^1、X^2、Y^1、R^1、和 R^2各自如本文对式(I)所描述。

[0245] 本发明的一个实施方案涉及式(IVC)的化合物及其药学上可接受的盐;

其中

X^1为N且X^2为CR^1;或

X^1为CR^1且X^2为N;或

X^1为CR^1且X^2为CR^1;

Y^1为C(O)NH、或NHC(O);

R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br和I;

R^2独立地选自C_4-C_6-烷基、C_4-C_6-烯基、C_4-C_6-炔基、芳基、和5-6元杂芳基;其中R^2中的C_4-C_6-烷基、C_4-C_6-烯基、和C_4-C_6-炔基各自被一个或多个独立地选自以下的取代基取代:

R^3, OR^3, SR^3, $S(O)R^3$, SO_2R^3, $C(O)R^3$, $CO(O)R^3$, $OC(O)R^3$,

$OC(O)OR^3$, NH_2, NHR^3, $N(R^3)_2$, $NHC(O)R^3$, $NR^3C(O)R^3$, $NHS(O)_2R^3$, $NR^3S(O)_2R^3$,

$NHC(O)OR^3$, $NR^3C(O)OR^3$, $NHC(O)NH_2$, $NHC(O)NHR^3$, $NHC(O)N(R^3)_2$, $NR^3C(O)NHR^3$,

$NR^3C(O)N(R^3)_2$, $C(O)NH_2$, $C(O)NHR^3$, $C(O)N(R^3)_2$, C(O)NHOH, $C(O)NHOR^3$,

$C(O)NHSO_2R^3$, $C(O)NR^3SO_2R^3$, SO_2NH_2, SO_2NHR^3, $SO_2N(R^3)_2$, C(O)H, C(O)OH,

$C(N)NH_2$, $C(N)NHR^3$, $C(N)N(R^3)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br

和I;其中R^2中的芳基和5-6元杂芳基各自任选被一个或多个独立地选自以下的取代基取代:R^4, OR^4, SR^4, $S(O)R^4$,

SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$,

$NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$,

$NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH,

$C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H,
C(O)OH, C(N)NH_2, C(N)NHR^4, C(N)$N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl,
和 I ;

R^3在每次出现时独立地选自烷基、烯基、炔基、芳基、环烷基、环烯基、和杂环基 ;其中 R^3中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 :

R^4, OR^3, SR^5, $S(O)R^5$, SO_2R^5, $C(O)R^4$, $CO(O)R^5$,
$OC(O)R^5$, $OC(O)OR^5$, NH_2, NHR^5, $N(R^5)_2$, $NHC(O)R^5$, $NR^5C(O)R^5$, $NHS(O)_2R^5$,
$NR^5S(O)_2R^5$, $NHC(O)OR^5$, $NR^5C(O)OR^5$, $NHC(O)NH_2$, $NHC(O)NHR^5$, $NHC(O)N(R^5)_2$,
$NR^5C(O)NHR^5$, $NR^5C(O)N(R^5)2$, $C(O)NH_2$, $C(O)NHR^5$, $C(O)N(R^5)_2$, C(O)NHOH,
$C(O)NHOR^5$, $C(O)NHSO_2R^5$, $C(O)NR^5SO_2R^5$, SO_2NH_2, SO_2NHR^5, $SO_2N(R^5)_2$, C(O)H,
C(O)OH, C(N)NH_2, C(N)NHR^5, C(N)$N(R^5)_2$, CNOH, $CNOCH_3$, OH, (O) , CN, N_3, NO_2, F,
Cl, Br 和 I ;其中 R^3中的芳基、环烷基、环烯基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代 :

R^6, OR^6, SR^6, $S(O)R^6$, SO_2R^6, $C(O)R^6$, $CO(O)R^6$, $OC(O)R^6$, $OC(O)OR^6$, NH_2, NHR^6, $N(R^6)_2$,
$NHC(O)R^6$, $NR^6C(O)R^6$, $NHS(O)_2R^6$, $NR^6S(O)_2R^6$, $NHC(O)OR^6$, $NR^6C(O)OR^6$,
$NHC(O)NH_2$, $NHC(O)NHR^6$, $NHC(O)N(R^5)_2$, $NR^6C(O)NHR^6$, $NR^6C(O)N(R^6)_2$, $C(O)NH_2$,
$C(O)NHR^6$, $C(O)N(R^6)_2$, C(O)NHOH, $C(O)NHOR^6$, $C(O)NHSO_2R^6$, $C(O)NR^6SO_2R^6$,
SO_2NH_2, SO_2NHR^6, $SO_2N(R^6)_2$, C(O)H, C(O)OH, C(N)NH_2, C(N)NHR^6, C(N)$N(R^6)_2$,
CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I ;

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 :

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$,
$OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$,
$NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$,
$NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH,
$C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H,
C(O)OH, C(N)NH_2, C(N)NHR^7, C(N)$N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O) , CN, N_3, NO_2, F,
Cl, Br 和 I ;

R^5在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^5中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 :

R^8, OR^8, SR^8, $S(O)R^8$, SO_2R^8, NHR^8, $N(R^8)_2$, $C(O)R^8$,
$C(O)NH_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, $NHC(O)R^8$, $NR^8C(O)R^8$, $NHSO_2R^8$, $NHC(O)OR^8$,
SO_2NH_2, SO_2NHR^8, $SO_2N(R^8)_2$, $NHC(O)NH_2$, $NHC(O)NHR^8$, OH, (O) , $C(O)OH$, N_3, CN,
NH_2, F, Cl, Br 和 I ;

R^6在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基 ;其中 R^6中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代 :

R^9, OR^9, SR^9, $S(O)R^9$, SO_2R^9, NHR^9, $N(R^9)_2$, $C(O)R^9$,
$C(O)NH_2$, $C(O)NHR_9$, $C(O)N(R^9)_2$, $NHC(O)R^9$, $NR^9C(O)R^9$, $NHSO_2R^9$, $NHC(O)OR^9$,
SO_2NH_2, SO_2NHR^9, $SO_2N(R^9)_2$, $NHC(O)NH_2$, $NHC(O)NHR^9$, OH, (O) , $C(O)OH$, N_3, CN,

NH_2，CF_3，CF_2CF_3，F，Cl，Br 和 I；

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^8在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

R^9在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

其中由 R^4、R^5、R^6、R^7、R^8、和 R^9表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}，OR^{20}，SR^{10}，$S(O)R^{10}$，SO_2R^{10}，$C(O)R^{10}$，$CO(O)R^{10}$，

$OC(O)R^{10}$，$OC(O)OR^{10}$，$C(O)C(O)R^{10}$，NH_2，NHR^{10}，$N(R^{10})_2$，$NHC(O)R^{10}$，$NR^{10}C(O)R^{10}$，

$NHS(O)_2R^{10}$，$NR^{10}S(O)_2R^{10}$，$NHC(O)OR^{10}$，$NR^{10}C(O)OR^{10}$，$NHC(O)NH_2$，$NHC(O)NHR^{10}$，

$NHC(O)N(R^{10})_2$，$NR^{10}C(O)NHR^{10}$，$NR^{10}C(O)N(R^{10})_2$，$C(O)NH_2$，$C(O)NHR^{10}$，$C(O)N(R^{10})_2$，

$C(O)NHOH$，$C(O)NHOR^{10}$，$C(O)NHSO_2R^{10}$，$C(O)NR^{10}SO_2R^{10}$，SO_2NH_2，SO_2NHR^{10}，

$SO_2N(R^{10})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{10}$，$C(N)N(R^{10})_2$，CNOH，$CNOCH_3$，OH，

CN，N_3，NO_2，F，Cl，Br 和 I；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中

R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^{11}，OR^{11}，SR^{11}，$S(O)R^{11}$，SO_2R^{11}，$C(O)R^{11}$，$CO(O)R^{11}$，

$OC(O)R^{11}$，$OC(O)OR^{11}$，NH_2，NHR^{11}，$N(R^{11})_2$，$NHC(O)R^{11}$，$NR^{11}C(O)R^{11}$，$NHS(O)_2R^{11}$，

$NR^{11}S(O)_2R^{11}$，$NHC(O)OR^{11}$，$NR^{11}C(O)OR^{11}$，$NHC(O)NH_2$，$NHC(O)NHR^{11}$，

$NHC(O)N(R^{11})_2$，$NR^{11}C(O)NHR^{11}$，$NR^{11}C(O)N(R^{11})_2$，$C(O)NH_2$，$C(O)NHR^{11}$，$C(O)N(R^{11})_2$，

$C(O)NHOH$，$C(O)NHOR^{11}$，$C(O)NHSO_2R^{11}$，$C(O)NR^{11}SO_2R^{11}$，SO_2NH_2，SO_2NHR^{11}，

$SO_2N(R^{11})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，CNOH，$CNOCH_3$，OH，

(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}，OR^{12}，SR^{12}，$S(O)R^{12}$，SO_2R^{12}，$C(O)R^{12}$，$CO(O)R^{12}$，$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_2，NHR^{12}，$N(R^{12})_2$，$NHC(O)R^{12}$，$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，

$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，$NHC(O)NH_2$，$NHC(O)NHR^{12}$，

$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，

$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，

$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，CNOH，$CNOCH_3$，OH，

CN，N_3，NO_2，CF_3，OCF_3，F，Cl，Br 和 I；

R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中

R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；

条件是

当 X^1为 CR^1且 X^2为 CR^1时；R^1为氢；Y^1为 NHC(O)；且 R^2为吡咯基；所述 R^2中的吡咯基未被两个烷基取代。

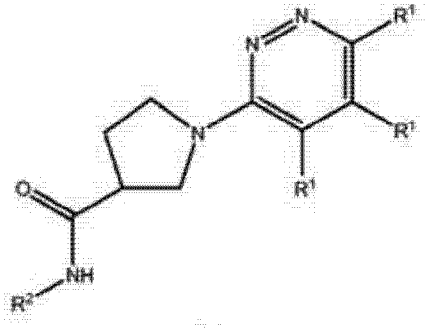
[0246] 在式 (IVC) 的一个实施方案中，X^1为 N 且 X^2为 CR^1；或 X^1为 CR^1且 X^2为 N；或 X^1为

CR^1且 X^2为 CR^1。在式 (IVC) 的另一个实施方案中，X^1为 N 且 X^2为 CR^1。在式 (IVC) 的另一个实施方案中，X^1为 CR^1且 X^2为 N。在式 (IVC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1。

[0247] 在式 (IVC) 的一个实施方案中，Y^1为 C(O)NH、或 NHC(O)。在式 (IVC) 的另一个实施方案中，Y^1为 C(O)NH。在式 (IVC) 的另一个实施方案中，Y^1为 NHC(O)。

[0248] 在式 (IVC) 的一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (IVC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IVC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IVC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时为氢。

[0249] 在另一方面，本发明提供式 (IVD) 的化合物，



式 (IVD)

及其药学上可接受的盐；其中 R^1和 R^2如本文对式 (IC) 所描述。

[0250] 在式 (IVC) 和 (IVD) 的一个实施方案中，R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (IVC) 和 (IVD) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (IVC) 和 (IVD) 的另一个实施方案中，R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (IVC) 和 (IVD) 的另一个实施方案中，R^1在每次出现时为氢。

[0251] 在式 (IVC) 和 (IVD) 的一个实施方案中，R^2独立地选自 C_4-C_6- 烷基、C_4-C_6- 烯基、C_4-C_6- 炔基、芳基、和 5-6 元杂芳基；其中 R^2中的 C_4-C_6- 烷基、C_4-C_6- 烯基、和 C_4-C_6- 炔基各自被一个或多个独立地选自以下的取代基取代：R^3，OR^3，S R^3，

S(O)R^3，SO_2R^3，C(O)R^3，CO(O)R^3，OC(O)R^3，OC(O)OR^3，NH_2，NHR^3，N(R^3)$_2$，NHC(O)R^3，

NR^3C(O)R^3，NHS(O)$_2R^3$，NR^3S(O)$_2R^3$，NHC(O)OR^3，NR^3C(O)OR^3，NHC(O)NH_2，

NHC(O)NHR^3，NHC(O)N(R^3)$_2$，NR^3C(O)NHR^3，NR^3C(O)N(R^3)$_2$，C(O)NH_2，C(O)NHR^3，

C(O)N(R^3)$_2$，C(O)NHOH，C(O)NHOR^3，C(O)NHSO_2R^3，C(O)NR^3SO_2R^3，SO_2NH_2，

SO_2NHR^3，SO_2N(R^3)$_2$，C(O)H，C(O)OH，C(N)NH_2，C(N)NHR^3，C(N)N(R^3)$_2$，CNOH，

C$NOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：

R^4，OR^4，SR^4，S(O)R^4，SO_2R^4，C(O)R^4，OC(O)OR^4，NH_2，NHR^4，

N(R^4)$_2$，NHC(O)R^4，NR^4C(O)R^4，NHS(O)$_2R^4$，NR^4S(O)$_2R^4$，NHC(O)OR^4，NR^4C(O)OR^4，

NHC(O)NH_2，NHC(O)NHR^4，NHC(O)N(R^4)$_2$，NR^4C(O)NHR^4，NR^4C(O)N(R^4)$_2$，C(O)NH_2，

$C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH, $C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$,

SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H, C(O)OH, C(N)NH_2, C(N)NHR^4, C(N)$N(R^4)_2$,

CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, 和 I。在式 (IVC) 和 (IVD) 的另一个实施方案中，R^2为芳基；其中 R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、F、Cl、和 I。在式 (IVC) 和 (IVD) 的另一个实施方案中，R^2为芳基；其中 R^2中的芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。在式 (IVC) 和 (IVD) 的另一个实施方案中，R^2为苯基；其中 R^2中的苯基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。在式 (IVC) 和 (IVD) 的另一个实施方案中，R^2为苯基；其中 R^2中的苯基各自被独立地选自以下的一个取代基取代：R^4、OR^4、和 SO_2R^4。

[0252] 在式 (IVC) 和 (IVD) 的另一个实施方案中，R^2为 5-6 元杂芳基；其中 R^2中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、F、Cl、和 I。在式 (IVC) 和 (IVD) 的另一个实施方案中，R^2为 5-6 元杂芳基；其中 R^2中的 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。在式 (IVC) 和 (IVD) 的另一个实施方案中，R^2为吡啶基、呋喃基、噻吩基、吡唑、或噻唑基；其中 R^2中的吡啶基、呋喃基、噻吩基、吡唑、和噻唑基各自任选被一个或多个独立地选自以下的取代基取代：R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。

[0253] 在式 (IVC) 和 (IVD) 的一个实施方案中，R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$,

$NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$,

$NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$,

$C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$,

SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, C(N)NH_2, C(N)NHR^7, C(N)$N(R^7)_2$,

CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, FCl, Br 和 I。在式 (IVC) 和 (IVD) 的另一个实施方案中，R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基。

[0254] 在式 (IVC) 和 (IVD) 的一个实施方案中，R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$, $OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$,

$NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$,

$NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$,

$C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$,

SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H, C(O)OH, C(N)NH_2, C(N)NHR^7, C(N)$N(R^7)_2$,

CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (IVC) 和 (IVD) 的另一个实施方案中，R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7、OR^7、$N(R^7)_2$、F、Cl、Br 和 I。

[0255] 在式 (IVC) 和 (IVD) 的一个实施方案中，R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。在式 (IVC) 和 (IVD) 的另一个实施方案中，R^7在每

次出现时独立地选自烷基、芳基、杂环基、和环烷基。

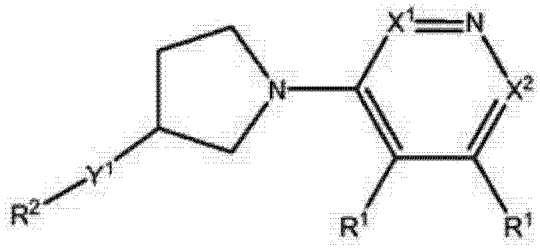
[0256] 在式 (IVC) 和 (IVD) 的一个实施方案中，R^4和 R^7中的环状基团各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}，OR^{10}，SR^{10}，$S(O)R^{10}$，SO_2R^{10}，$C(O)R^{10}$，$CO(O)R^{10}$，$OC(O)R^{10}$，$OC(O)OR^{10}$，NH_2，NHR^{10}，$N(R^{10})_2$，$NHC(O)R^{10}$，$NR^{10}C(O)R^{10}$，$NHS(O)_2R^{10}$，$NR^{10}S(O)_2R^{10}$，$NHC(O)OR^{10}$，$NR^{10}C(O)OR^{10}$，$NHC(O)NH_2$，$NHC(O)NHR^{10}$，$NHC(O)N(R^{10})_2$，$NR^{10}C(O)NHR^{10}$，$NR^{10}C(O)N(R^{10})_2$，$C(O)NH_2C(O)NHR^{10}$，$C(O)N(R^{10})_2$，$C(O)NHOH$，$C(O)NHOR^{10}$，$C(O)NHSO_2R^{10}C(O)NR^{10}SO_2R^{10}$，$SO_2NH_2$，$SO_2NHR^{10}$，$SO_2N(R^{10})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{10}$，$C(N)N(R^{10})_2$，$CNOH$，$CNOCH_2$，$OH$，$CN$，$N_3$，$NO_2$，F，Cl，Br 和 I；$R^{10}$在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}，OR^{11}，SR^{11}，$S(O)R^{11}$，SO_2R^{11}，$C(O)R^{11}$，$CO(O)R^{11}$，$OC(O)R^{11}$，$OC(O)OR^{11}$，NH_2，NHR^{11}，$N(R^{11})_2$，$NHC(O)R^{11}$，$NR^{11}C(O)R^{11}$，$NHS(O)_2R^{11}$，$NR^{11}S(O)_2R^{11}$，$NHC(O)OR^{11}$，$NR^{11}C(O)OR^{11}$，$NHC(O)NH_2$，$NHC(O)NHR^{11}$，$NHC(O)N(R^{11})_2$，$NR^{11}C(O)NHR^{11}$，$NR^{11}C(O)N(R^{11})_2$，$C(O)NH_2$，$C(O)NHR^{11}$，$C(O)N(R^{11})_2$，$C(O)NHOH$，$C(O)NHOR^{11}$，$C(O)NHSO_2R^{11}$，$C(O)NR^{11}SO_2R^{11}$，SO_2NH_2，SO_2NHR^{11}，$SO_2N(R^{11})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，$CNOH$，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：

R^{12}，OR^{12}，SR^{12}，$S(O)R^{12}$，SO_2R^{12}，$C(O)R^{12}$，$CO(O)R^{12}$，$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_2，NHR^{12}，$N(R^{12})_2$，$NHC(O)R^{12}$，$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，$NHC(O)NH_2$，$NHC(O)NHR^{12}$，$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，$CNOH$，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，Br 和 I；R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0257] 在式 (IVC) 和 (IVD) 的另一个实施方案中，R^4和 R^7中的环状基团各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)H$、OH、F、Cl、Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、NH_2、OH、CN、CF_3、OCF_3、F、和 Cl；R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、CF_3、F、和 Cl；R^{12}在每次出现时独立地选自烷基和芳

基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、和环烷基。

[0258] 本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式 (IVC)



式 (IVC)；

其中

X^1为 N 且 X^2为 CR^1；或

X^1为 CR^1且 X^2为 N；或

X^1为 CR^1且 X^2为 CR^1；

Y^1为 C(O)NH、或 NHC(O)；

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、Cl、和 F；

R^2为芳基或 5-6 元杂芳基，其中 R^2中的芳基和 5-6 元杂芳基各自任选被一个或多个独立地选自以下的取代基取代：R^4、SO_2R^4、OR^4、$C(O)NHR^4$、和 F；

R^4在每次出现时独立地选自烷基、烯基、芳基、杂环基、和环烷基；其中 R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7、OR^7、$N(R^7)_2$、和 F；

R^7在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；

其中由 R^4和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)R^{10}$、C(O)OH、OH 和 F；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代：R^{12}、OR^{12}、$C(O)R^{12}$、NH_2、OH、CN、CF_3、OCF_3、F、和 Cl；

R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl；

R^{12}在每次出现时独立地选自烷基、和芳基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、环烷基、和杂环基；

条件是

当 X^1为 CR^1且 X^2为 CR^1时；R^1为氢；Y^1为 NHC(O)；且 R^2为吡咯基；所述 R^2中的吡咯基未被两个烷基取代。

[0259] 仍另一个实施方案涉及具有式 (IV) 的化合物，其包括

叔丁基 4-[4-({[(3S)-1-(吡啶 -3- 基）吡咯烷 -3- 基］羰基｝氨基）苯氧基］哌啶 -1- 甲酸酯；

叔丁基 4-[4-({[(3R)-1-(吡啶 -3- 基）吡咯烷 -3- 基］羰基｝氨基）苯氧基］哌

啶 -1- 甲酸酯；

(3S)-1-(吡啶 -3- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 氧基 } 苯基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-[4-({1-[(2S)- 四氢呋喃 -2- 基羰基] 哌啶 -4- 基 } 氧基) 苯基] 吡咯烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-[4-({1-[(2R)- 四氢呋喃 -2- 基羰基] 哌啶 -4- 基 } 氧基) 苯基] 吡咯烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-(4-{[1-(四氢呋喃 -3- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(环丙基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 氧基 } 苯基) 吡咯烷 -3- 甲酰胺；

(3S)-N-[4-({1-[(2S)-2- 甲基丁酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

叔丁基 4-(4-{[(3S)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 氨基甲酰基 } 苯氧基) 哌啶 -1- 甲酸酯；

叔丁基 4-(4-{[(3R)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 氨基甲酰基 } 苯氧基) 哌啶 -1- 甲酸酯；

(3S)-N-{4-[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；及其药学上可接受的盐。

[0260] N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[(1- 苯甲酰基哌啶 -4- 基) 磺酰基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲

酰胺；

N-(4-{[1-(4-氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-(4-{[1-(环戊基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺；

N-[(3R)-1-(5,6-二氯哒嗪-4-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-2-甲酰胺；

N-[(3R)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-2-甲酰胺；

N-[(3S)-1-(5,6-二氯哒嗪-4-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-2-甲酰胺；

N-[(3S)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-2-甲酰胺；

N-[(3R)-1-(5,6-二氯哒嗪-4-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-3-甲酰胺；

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3R)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-3-甲酰胺；

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3R)-1-(哒嗪-4-基)吡咯烷-3-基]噻吩-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)哌啶-4-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)哌啶-4-甲酰胺；

N-{4-[1-(2-氟苯甲酰基)哌啶(piperidi)4-基]苯基}-1-(哒嗪-3-基)哌啶-4-甲酰胺；

1-(哒嗪-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}哌啶-4-甲酰胺；

N-[(3S)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(1,3-噻唑-5-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2S)-2-苯基丁酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2S)-2-甲氧基-2-苯基乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2R)-2-甲氧基-2-苯基乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(乙氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲

酰胺；

(3S)-N-(4-{1-[(4-甲基苯氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-3-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(萘-1-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2,6-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(萘-1-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-(4-{1-[4-(噻吩-2-基)丁酰基]哌啶-4-基}苯基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环丙基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(萘-2-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[3-(苯基磺酰基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-[4-(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(呋喃-2-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(N-苯甲酰基甘氨酰)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2,4-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(1-甲基环己基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(6-甲基吡啶-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(3-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环戊基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-氟-5-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-氟吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-氟-6-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

(3S)-N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,4-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-庚酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,4-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(4-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯

烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,3- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 己酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(3- 甲基噻吩 -2- 基）羰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,3- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 丁酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 甲基戊酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(3,5- 二甲基苯基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,5- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(4- 氯苯基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(呋喃 -3- 基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,4- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[2- 氯 -5-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 乙酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,5- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 乙氧基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,5- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,5- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯

烷 -3- 甲酰胺；

(3S)-N-{4-[1-(5- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基] 苯基 }-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（二苯基乙酰基）哌啶 -4- 基] 苯基 }-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-（哒嗪 -3- 基）-N-(4-{1-[4-（三氟甲基） 苯甲酰基] 哌啶 -4- 基 } 苯基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（戊 -4- 烯酰基）哌啶 -4- 基] 苯基 }-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-（哒嗪 -3- 基）-N-(4-{1-[3-（三氟甲氧基） 苯甲酰基] 哌啶 -4- 基 } 苯基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(1- 苯基环丙基） 羰基] 哌啶 -4- 基 } 苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[2- 氟 -5-（三氟甲基）苯甲酰基] 哌啶 -4- 基 } 苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（环己基乙酰基）哌啶 -4- 基] 苯基 }-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 甲氧基苯甲酰基）哌啶 -4- 基] 苯基 }-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 甲基丁酰基）哌啶 -4- 基] 苯基 }-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 乙基丁酰基）哌啶 -4- 基] 苯基 }-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 叔丁基苯甲酰基）哌啶 -4- 基] 苯基 }-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氯苯甲酰基）哌啶 -4- 基] 苯基 }-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2- 氟苯基） 乙酰基] 哌啶 -4- 基 } 苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-（哒嗪 -3- 基）-N-(4-{1-[3-（三氟甲基） 苯甲酰基] 哌啶 -4- 基 } 苯基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(1- 甲基环丙基） 羰基] 哌啶 -4- 基 } 苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（戊 -4- 炔酰基）哌啶 -4- 基] 苯基 }-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(3- 氟苯基） 乙酰基] 哌啶 -4- 基 } 苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[3-（甲基巯基） 丙酰基] 哌啶 -4- 基 } 苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(1-乙酰基哌啶-4-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(丁-3-烯酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,2-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3-氟-4-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(N-乙酰基-L-亮氨酰)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,3-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[4-(丙烷-2-基)苯甲酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环己基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(噻吩-2-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲

酰胺；

(3S)-N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(4-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-氟-4-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺；

2-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-1,3-噻唑-5-甲酰胺；

(3S)-N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-甲基吡啶-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(2-甲基吡啶-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

N-[(3S)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]呋喃-2-甲酰胺；

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]呋喃-2-甲酰胺；

N-(4-{1-[(4-甲基四氢-2H-吡喃-4-基)甲基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[(3S)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-4-[1-(2-甲基丙酰基)哌啶-4-基]苯甲酰胺；

N-(4-{1-[2-(哌嗪-1-基)乙基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

4-[1-(2-甲基丙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]苯甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

5-[1-(3-氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺；

5-[1-(4-氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

(3S)-N-(4-{1-[(4-甲基四氢-2H-吡喃-4-基)甲基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(2-羟基-2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(四氢-2H-吡喃-4-基羰基)哌啶-4-基]噻吩-2-甲酰胺;

(3S)-N-{4-[1-(2,2-二甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

5-[1-(2-甲基丙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(2,4-二氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-{1-[(2-甲基环丙基)羰基]哌啶-4-基}-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-[1-(2-氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

5-(1-苯甲酰基哌啶-4-基)-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(四氢呋喃-3-基羰基)哌啶-4-基]噻吩-2-甲酰胺;

N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-{1-[(2R)-四氢呋喃-2-基羰基]哌啶-4-基}噻吩-2-甲酰胺;

5-{1-[(1-甲基哌啶-4-基)乙酰基]哌啶-4-基}-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺;

N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(1,3-噻唑-4-基羰基)哌啶-4-基]噻吩-2-甲酰胺;

(3S)-N-{4-[1-(2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(丙烷-2-基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-{4-[1-(环丙基甲基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢-2H-吡喃-2-基甲基)-1H-吡唑-4-基]苯基}吡咯烷-3-甲酰胺;

(3S)-N-[4-(1-叔丁基-1H-吡唑-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[(3R)-1-苯甲酰基吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯

烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(2- 氟苯甲酰基）吡咯烷 -3- 基］氧基} 苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(3- 氟苯甲酰基）吡咯烷 -3- 基］氧基} 苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(4- 氟苯甲酰基）吡咯烷 -3- 基］氧基} 苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(3,5- 二氟苯甲酰基）吡咯烷 -3- 基］氧基} 苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(2- 甲基苯甲酰基）吡咯烷 -3- 基］氧基} 苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(2,2- 二甲基丙酰基）吡咯烷 -3- 基］氧基} 苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-({(3R)-1-[(4,4- 二氟环己基）羰基］吡咯烷 -3- 基} 氧基）苯基]-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-(4-{[(3R)-1-(4,4,4- 三氟丁酰基）吡咯烷 -3- 基］氧基} 苯基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基）吡咯烷 -3- 基］氧基} 苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

N-[4-(5- 丙基 -1,2,4- 氧杂二唑 -3- 基）苯基]-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 氟苯甲酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氟苯甲酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 氟苯甲酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 苯甲酰基氮杂环丁烷 -3- 基）苯基]-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,2- 二甲基丙酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,5- 二氟苯甲酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 甲基苯甲酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,4- 二氟苯甲酰基）氮杂环丁烷 -3- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3R)-N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3R)-N-{4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲

酰胺；

(3R)-N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(环己基羰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(3-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[(1-苯甲酰基哌啶-4-基)氧基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(4-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-({1-[(2-甲基环丙基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

N-{4-[5-(2,2-二甲基丙基)-1,3,4-氧杂二唑-2-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙基)-1H-咪唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[4-(3-环丙基-1-甲基-1H-吡唑-5-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[5-(2,2-二甲基丙基)-1,2,4-氧杂二唑-3-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[3-环丙基-1-(2-甲氧基乙基)-1H-吡唑-5-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

叔丁基4-(5-{[1-(哒嗪-3-基)氮杂环丁烷-3-基]氨基甲酰基}噻吩-2-基)哌啶-1-甲酸酯；

叔丁基4-氟-4-[4-({[1-(哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]哌啶-1-甲酸酯；

5-(1-苯甲酰基哌啶-4-基)-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

5-[1-(2-氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

5-[1-(2-甲基苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

5-[1-(2,4-二氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

5-[1-(3-氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺;

5-[1-(4-氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺;

5-[1-(3,5-二氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺;

N-{4-[3-环丙基-1-(2-羟基乙基)-1H-吡唑-5-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

1-(6-氟哒嗪-3-基)-N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2-乙基丁酰基)哌啶-4-基]苯基}-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(6-氟哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

(3S)-N-(4-{[(3S)-1-苯甲酰基吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[(3S)-1-(2-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[(3S)-1-(3,5-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

(3S)-N-(4-{[(3S)-1-(2,2-二甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺;

N-{2-氟-4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-[4-(1-苯甲酰基哌啶-4-基)-2-氟苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{2-氟-4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{2-氟-4-[1-(2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{2-氟-4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺;

N-{4-[1-(2,4-二氟苯甲酰基)哌啶-4-基]-2-氟苯基}-1-(哒嗪-3-基)氮杂环丁

烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二氟苯甲酰基）哌啶 -4- 基]-2- 氟苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基）哌啶 -4- 基]-2- 氟苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2- 氟苯甲酰基）哌啶 -4- 基] 氧基 } 苯基)-1-(6- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[(1- 苯甲酰基哌啶 -4- 基）氧基] 苯基 }-1-(6- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2,2- 二甲基丙酰基）哌啶 -4- 基] 氧基 } 苯基)-1-(6- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-（环己基羰基）哌啶 -4- 基] 氧基 } 苯基)-1-(6- 甲基哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

N-{4-[8-(2- 甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

1-（哒嗪 -3- 基)-N-{4-[8-(4,4,4- 三氟丁酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-[4-(8- 苯甲酰基 -8- 氮杂双环 [3.2.1] 辛 -3- 基）苯基]-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[8-(2- 氟苯甲酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[8-(2,2- 二甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-(4-{8-[(1- 甲基环丙基）羰基]-8- 氮杂双环 [3.2.1] 辛 -3- 基 } 苯基)-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 甲氧基乙基)-3-(2- 甲基丙基)-1H- 吡唑 -5- 基] 苯基 }-1-（哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

5-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基]-N-[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺；

5-{1-[(1- 甲基环丙基）羰基] 哌啶 -4- 基 }-N-[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺；

N-[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基]-5-[1-(3,3,3- 三氟丙酰基）哌啶 -4- 基] 噻吩 -2- 甲酰胺；

5-[1-(2,2- 二甲基丁酰基）哌啶 -4- 基]-N-[1-（哒嗪 -3- 基）氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基）哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基）哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺；

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基]-4- 氟哌啶 -1- 甲酸酯 ;

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基]-4- 羟基哌啶 -1- 甲酸酯 ;

N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基]-5-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(环丙基羰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺 ;

N-{4-[4- 氟 -1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环丙基羰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(2- 氟 -4-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(环丙基乙酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基 -4- 氟哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基)-4- 氟哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[3- 叔丁基 -1-(2- 甲氧基乙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 丁基 -3- 叔丁基 -1H- 吡唑 -5- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[3- 叔丁基 -1-(四氢 -2H- 吡喃 -4- 基甲基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基)-2- 氟苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{2- 氟 -4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环

丁烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

5-[1-(2- 氟苯甲酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 呋喃 -2- 甲酰胺 ;

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(4- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(4- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

5-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(2,2- 二甲基丁酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-{1-[(1- 甲基环丙基) 羰基] 哌啶 -4- 基 }-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

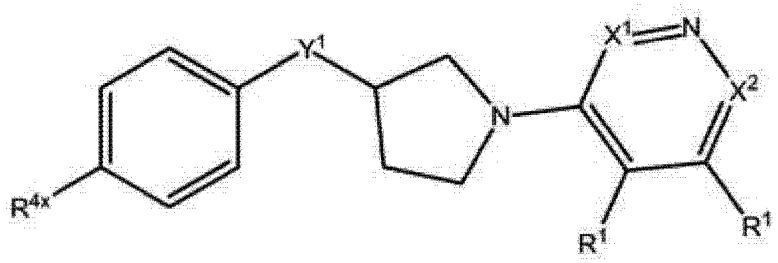
N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(环丙基乙酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(双环 [2.2.1] 庚 -2- 基乙酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺 ;及其药学上可接受的盐。

[0261] 式 (VC) 的实施方案

在另一方面,本发明提供式 (VC) 的化合物



(VC);

及其药学上可接受的盐 ;其中当式 (IC) 中 R^2 的为芳基时,X^1、X^2、R^1、和 Y^1 如本文式 (IC) 中所描述且 R^{4x} 如本文对 R^2 上的取代基所描述。

[0262] 本发明的一个实施方案涉及式 (VC) 的化合物或其药学上可接受的盐 ;

其中

X^1为 N 且 X^2为 CR^1;或

X^1为 CR^1且 X^2为 N;或

X^1为 CR^1且 X^2为 CR^1;

Y^1为 C(O)NH、或 NHC(O);

R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I;

R^{4X}独立地选自 R^4, OR^4, SR^4, $S(O)R^4$,

SO_2R^4, $C(O)R^4$, $OC(O)OR^4$, NH_2, NHR^4, $N(R^4)_2$, $NHC(O)R^4$, $NR^4C(O)R^4$, $NHS(O)_2R^4$,

$NR^4S(O)_2R^4$, $NHC(O)OR^4$, $NR^4C(O)OR^4$, $NHC(O)NH_2$, $NHC(O)NHR^4$, $NHC(O)N(R^4)_2$,

$NR^4C(O)NHR^4$, $NR^4C(O)N(R^4)_2$, $C(O)NH_2$, $C(O)NHR^4$, $C(O)N(R^4)_2$, C(O)NHOH,

$C(O)NHOR^4$, $C(O)NHSO_2R^4$, $C(O)NR^4SO_2R^4$, SO_2NH_2, SO_2NHR^4, $SO_2N(R^4)_2$, C(O)H,

C(O)OH, $C(N)NH_2$, $C(N)NHR^4$, $C(N)N(R^4)_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl,

和 I;

R^4在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基;其中 R^4中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代:

R^7, OR^7, SR^7, $S(O)R^7$, SO_2R^7, $C(O)R^7$, $CO(O)R^7$,

$OC(O)R^7$, $OC(O)OR^7$, NH_2, NHR^7, $N(R^7)_2$, $NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$,

$NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$,

$NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, C(O)NHOH,

$C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, C(O)H,

C(O)OH, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F,

Cl, Br 和 I;

R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基;

其中由 R^4、和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代:

R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$,

$C(O)C(O)R^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$,

$NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$,

$NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, C(O)NHOH,

$C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, C(O)H,

C(O)OH, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, CNOH, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl,

Br 和 I;

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基;其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代:

R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$,

$OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$,

$NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$,

$NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$,

$C(O)NHOH$，$C(O)NHOR^{11}$，$C(O)NHSO_2R^{11}$，$C(O)NR^{11}SO_2R^{11}$，SO_2NH_2，SO_2NHR^{11}，

$SO_2N(R^{11})_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^{11}$，$C(N)N(R^{11})_2$，CNOH，$CNOCH_3$，OH，

(O)，CN，N_3，NO_2，F，Cl，Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}，OR^{12}，SR^{12}，$S(O)R^{12}$，SO_2R^{12}，$C(O)R^{12}$，$CO(O)R^{12}$，

$OC(O)R^{12}$，$OC(O)OR^{12}$，NH_2，NHR^{12}，$N(R^{12})_2$，$NHC(O)R^{12}$，$NR^{12}C(O)R^{12}$，$NHS(O)_2R^{12}$，

$NR^{12}S(O)_2R^{12}$，$NHC(O)OR^{12}$，$NR^{12}C(O)OR^{12}$，$NHC(O)NH_2$，$NHC(O)NHR^{12}$，

$NHC(O)N(R^{12})_2$，$NR^{12}C(O)NHR^{12}$，$NR^{12}C(O)N(R^{12})_2$，$C(O)NH_2$，$C(O)NHR^{12}$，$C(O)N(R^{12})_2$，

$C(O)NHOH$，$C(O)NHOR^{12}$，$C(O)NHSO_2R^{12}$，$C(O)NR^{12}SO_2R^{12}$，SO_2NH_2，SO_2NHR^{12}，

$SO_2N(R^{12})_2$，$C(O)H$，$C(O)OH$、$C(N)NH_2$，$C(N)NHR^{12}$，$C(N)N(R^{12})_2$，CNOH、$CNOCH_3$，OH，

CN，N_3，NO_2，CF_3，OCF_3，F，Cl，Br 和 I；

R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；

R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和

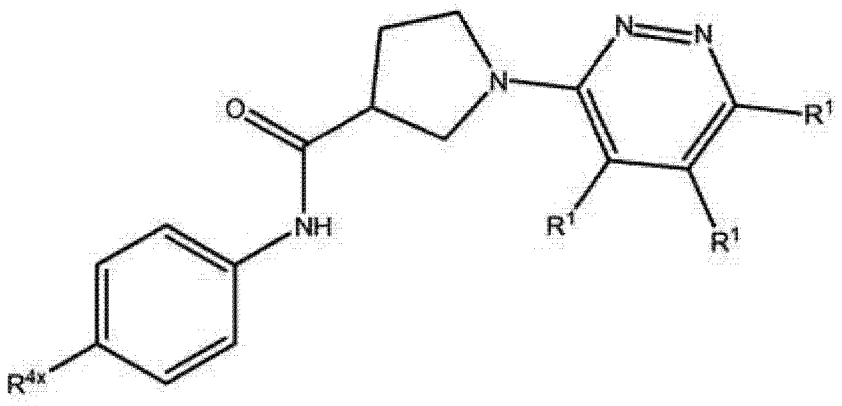
R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0263] 在式 (VC) 的一个实施方案中，X^1为 N 且 X^2为 CR^1；或 X^1为 CR^1且 X^2为 N；或 X^1为 CR^1且 X^2为 CR^1。在式 (VC) 的另一个实施方案中，X^1为 N 且 X^2为 CR^1。在式 (VC) 的另一个实施方案中，X^1为 CR^1且 X^2为 N。在式 (VC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1。

[0264] 在式 (VC) 的一个实施方案中，Y^1为 C(O)NH、或 NHC(O)。在式 (VC) 的另一个实施方案中，Y^1为 C(O)NH。在式 (VC) 的另一个实施方案中，Y^1为 NHC(O)。

[0265] 在式 (VC) 的一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (VC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (VC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (VC) 的另一个实施方案中，X^1为 CR^1且 X^2为 CR^1；且 R^1在每次出现时为氢。

[0266] 在另一方面，本发明提供式 (VD) 的化合物，



式 (VD)

及其药学上可接受的盐；其中当式 (IC) 中的 R^2 为芳基时，R^1 如本文对式 (IC) 所描述且 R^{4x} 如本文对 R^2 上的取代基所描述。

[0267] 在式 (VC) 和 (VD) 的一个实施方案中，R^1 在每次出现时独立地选自氢、烷基、烯基、炔基、卤代烷基、羟烷基、烷氧基、OH、NH_2、CN、NO_2、F、Cl、Br 和 I。在式 (VC) 和 (VD) 的另一个实施方案中，R^1 在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、Cl、Br 和 I。在式 (VC) 和 (VD) 的另一个实施方案中，R^1 在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、F、和 Cl。在式 (VC) 和 (VD) 的另一个实施方案中，R^1 在每次出现时为氢。

[0268] 在式 (VC) 和 (VD) 的一个实施方案中，R^{4X} 独立地选自

R^4，OR^4，SR^4，$S(O)R^4$，SO_2R^4，$C(O)R^4$，$OC(O)OR^4$，NH_2，NHR^4，

$N(R^4)_2$，$NHC(O)R^4$，$NR^4C(O)R^4$，$NHS(O)_2R^4$，$NR^4S(O)_2R^4$，$NHC(O)OR^4$，$NR^4C(O)OR^4$，

$NHC(O)NH_2$，$NHC(O)NHR^4$，$NHC(O)N(R^4)_2$，$NR^4C(O)NHR^4$，$NR^4C(O)N(R^4)_2$，$C(O)NH_2$，

$C(O)NHR^4$，$C(O)N(R^4)_2$，$C(O)NHOH$，$C(O)NHOR^4$，$C(O)NHSO_2R^4$，$C(O)NR^4SO_2R^4$，

SO_2NH_2，SO_2NHR^4，$SO_2N(R^4)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^4$，$C(N)N(R^4)_2$，

CNOH，$CNOCH_3$，OH，CN，N_3，NO_2，F，Cl，和 I。在式 (VC) 和 (VD) 的另一个实施方案中，R^{4X} 独立地选自 R^4、OR^4、SO_2R^4、$C(O)NHR^4$、F、Cl、和 I。在式 (VC) 和 (VD) 的另一个实施方案中，R^{4X} 独立地选自 R^4、OR^4、SO_2R^4、$C(O)NHR^4$、和 F。

[0269] 在式 (VC) 和 (VD) 的一个实施方案中，R^4 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^4 中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：

R^7OR^7，SR^7，$S(O)R^7$，SO_2R^7，$C(O)R^7$，$CO(O)R^7$，$OC(O)R^7$，$OC(O)OR^7$，NH_2，NHR^7，$N(R^7)_2$，

$NHC(O)R^7$，$NR^7C(O)R^7$，$NHS(O)_2R^7$，$NR^7S(O)_2R^7$，$NHC(O)OR^7$，$NR^7C(O)OR^7$，

$NHC(O)NH_2$，$NHC(O)NHR^7$，$NHC(O)N(R^7)_2$，$NR^7C(O)NHR^7$，$NR^7C(O)N(R^7)_2$，$C(O)NH_2$，

$C(O)NHR^7$，$C(O)N(R^7)_2$，$C(O)NHOH$，$C(O)NHOR^7$，$C(O)NHSO_2R^7$，$C(O)NR^7SO_2R^7$，

SO_2NH_2，SO_2NHR^7，$SO_2N(R^7)_2$，$C(O)H$，$C(O)OH$，$C(N)NH_2$，$C(N)NHR^7$，$C(N)N(R^7)_2$，

CNOH，$CNOCH_3$，OH，(O)，CN，N_3，NO_2，F，Cl，Br 和 I。在式 (VC) 和 (VD) 的另一个实施方案中，R^4 在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基。

[0270] 在式 (VC) 和 (VD) 的一个实施方案中，R^4 中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7，OR^7，

SR^7，$S(O)R^7$，SO_2R^7，$C(O)R^7$，$CO(O)R^7$，$OC(O)R^7$，$OC(O)OR^7$，NH_2，NHR^7，$N(R^7)_2$，

$NHC(O)R^7$, $NR^7C(O)R^7$, $NHS(O)_2R^7$, $NR^7S(O)_2R^7$, $NHC(O)OR^7$, $NR^7C(O)OR^7$, $NHC(O)NH_2$, $NHC(O)NHR^7$, $NHC(O)N(R^7)_2$, $NR^7C(O)NHR^7$, $NR^7C(O)N(R^7)_2$, $C(O)NH_2$, $C(O)NHR^7$, $C(O)N(R^7)_2$, $C(O)NHOH$, $C(O)NHOR^7$, $C(O)NHSO_2R^7$, $C(O)NR^7SO_2R^7$, SO_2NH_2, SO_2NHR^7, $SO_2N(R^7)_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^7$, $C(N)N(R^7)_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I。在式 (VC) 和 (VD) 的另一个实施方案中，R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7、OR^7、$N(R^7)_2$、F、Cl、Br 和 I。

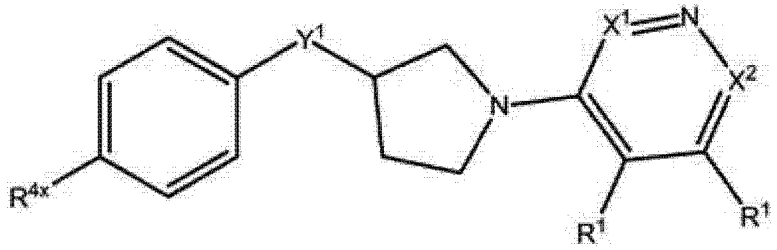
[0271] 在式 (VC) 和 (VD) 的一个实施方案中，R^7在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。在式 (VC) 和 (VD) 的另一个实施方案中，R^7在每次出现时独立地选自烷基、芳基、杂环基、和环烷基。

[0272] 在式 (VC) 和 (VD) 的一个实施方案中，R^4和 R^7中的环状基团各自独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}, OR^{10}, SR^{10}, $S(O)R^{10}$, SO_2R^{10}, $C(O)R^{10}$, $CO(O)R^{10}$, $OC(O)R^{10}$, $OC(O)OR^{10}$, NH_2, NHR^{10}, $N(R^{10})_2$, $NHC(O)R^{10}$, $NR^{10}C(O)R^{10}$, $NHS(O)_2R^{10}$, $NR^{10}S(O)_2R^{10}$, $NHC(O)OR^{10}$, $NR^{10}C(O)OR^{10}$, $NHC(O)NH_2$, $NHC(O)NHR^{10}$, $NHC(O)N(R^{10})_2$, $NR^{10}C(O)NHR^{10}$, $NR^{10}C(O)N(R^{10})_2$, $C(O)NH_2$, $C(O)NHR^{10}$, $C(O)N(R^{10})_2$, $C(O)NHOH$, $C(O)NHOR^{10}$, $C(O)NHSO_2R^{10}$, $C(O)NR^{10}SO_2R^{10}$, SO_2NH_2, SO_2NHR^{10}, $SO_2N(R^{10})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{10}$, $C(N)N(R^{10})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}, OR^{11}, SR^{11}, $S(O)R^{11}$, SO_2R^{11}, $C(O)R^{11}$, $CO(O)R^{11}$, $OC(O)R^{11}$, $OC(O)OR^{11}$, NH_2, NHR^{11}, $N(R^{11})_2$, $NHC(O)R^{11}$, $NR^{11}C(O)R^{11}$, $NHS(O)_2R^{11}$, $NR^{11}S(O)_2R^{11}$, $NHC(O)OR^{11}$, $NR^{11}C(O)OR^{11}$, $NHC(O)NH_2$, $NHC(O)NHR^{11}$, $NHC(O)N(R^{11})_2$, $NR^{11}C(O)NHR^{11}$, $NR^{11}C(O)N(R^{11})_2$, $C(O)NH_2$, $C(O)NHR^{11}$, $C(O)N(R^{11})_2$, $C(O)NHOH$, $C(O)NHOR^{11}$, $C(O)NHSO_2R^{11}$, $C(O)NR^{11}SO_2R^{11}$, SO_2NH_2, SO_2NHR^{11}, $SO_2N(R^{11})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{11}$, $C(N)N(R^{11})_2$, $CNOH$, $CNOCH_3$, OH, (O), CN, N_3, NO_2, F, Cl, Br 和 I；其中 R^{10}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}, OR^{12}, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, $C(O)R^{12}$, $CO(O)R^{12}$, $OC(O)R^{12}$, $OC(O)OR^{12}$, NH_2, NHR^{12}, $N(R^{12})_2$, $NHC(O)R^{12}$, $NR^{12}C(O)R^{12}$, $NHS(O)_2R^{12}$, $NR^{12}S(O)_2R^{12}$, $NHC(O)OR^{12}$, $NR^{12}C(O)OR^{12}$, $NHC(O)NH_2$, $NHC(O)NHR^{12}$, $NHC(O)N(R^{12})_2$, $NR^{12}C(O)NHR^{12}$, $NR^{12}C(O)N(R^{12})_2$, $C(O)NH_2$, $C(O)NHR^{12}$, $C(O)N(R^{12})_2C(O)NHOH$, $C(O)NHOR^{12}$, $C(O)NHSO_2R^{12}$, $C(O)NR^{12}SO_2R^{12}$, SO_2NH_2, SO_2NHR^{12}, $SO_2N(R^{12})_2$, $C(O)H$, $C(O)OH$, $C(N)NH_2$, $C(N)NHR^{12}$, $C(N)N(R^{12})_2$, $CNOH$, $CNOCH_3$, OH, CN, N_3, NO_2, F, Cl, Br 和 I；R^{11}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；其中 R^{11}中的烷基、烯基、和炔基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、杂环基、环烷基、和环烯基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、OR^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、Cl、Br 和 I；R^{12}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、烯基、炔基、芳基、杂环基、环烷基、和环烯基。

[0273] 在式 (VC) 和 (VD) 的另一个实施方案中，R^4和 R^7中的环状基团各自独立地任选被

一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$CO(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)H$、OH、F、Cl、Br 和 I；R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基、烯基、和炔基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{12}、OR^{12}、$C(O)R^{12}$、NH_2、OH、CN、CF_3、OCF_3、F、和 Cl；R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、CF_3、F、和 Cl；R^{12}在每次出现时独立地选自烷基和芳基；和 R^{13}在每次出现时独立地选自烷基、卤代烷基、和环烷基。

[0274] 本发明的一个实施方案涉及化合物或其药学上可接受的盐，其用作 NAMPT 的抑制剂，所述化合物具有式 (VC)



(VC);

其中

X^1为 N 且 X^2为 CR^1；或

X^1为 CR^1且 X^2为 N；或

X^1为 CR^1且 X^2为 CR^1；

Y^1为 $C(O)NH$、或 $NHC(O)$；

R^1在每次出现时独立地选自氢、烷基、卤代烷基、烷氧基、CN、Cl、和 F；

R^{4x}独立地选自 R^4、SO_2R^4、OR^4、和 F；

R^4在每次出现时独立地选自烷基、烯基、芳基、杂环基、和环烷基；其中 R^4中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^7、OR^7、$N(R^7)_2$、和 F；

R^7在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；

其中由 R^4和 R^7表示的环状基团独立地任选被一个或多个独立地选自以下的取代基取代：R^{10}、$C(O)R^{10}$、$C(O)C(O)R^{10}$、$CO(O)R^{10}$、$C(O)OH$、OH 和 F；

R^{10}在每次出现时独立地选自烷基、烯基、炔基、芳基、杂环基、和环烷基；其中 R^{10}中的烷基各自任选被一个或多个独立地选自以下的取代基取代：R^{11}、OR^{11}、SR^{11}、SO_2R^{11}、NH_2、$N(R^{11})_2$、$NHC(O)R^{11}$、$NHS(O)_2R^{11}$、OH、NO_2、和 F；其中 R^{10}中的芳基、杂环基和环烷基各自任选被以下的一个或多个取代：R^{12}、OR^{12}、$C(O)R^{12}$、NH_2、OH、CN、CF_3、OCF_3、F、和 Cl；

R^{11}在每次出现时独立地选自烷基、芳基、杂环基、和环烷基；其中 R^{11}中的烷基各自任选被烷氧基或芳基取代；其中 R^{11}中的芳基、和杂环基各自任选被一个或多个独立地选自以下的取代基取代：R^{13}、$C(O)OR^{13}$、OCF_3、CF_3、F、和 Cl；

R^{12}在每次出现时独立地选自烷基、和芳基；和

R^{13}在每次出现时独立地选自烷基、卤代烷基、环烷基、和杂环基。

[0275] 仍另一个实施方案涉及具有式 (VC) 的化合物，其包括

叔丁基 4-[4-({[(3S)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 羰基 } 氨基) 苯氧基] 哌啶 -1- 甲酸酯；

叔丁基 4-[4-({[(3R)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 羰基 } 氨基) 苯氧基] 哌啶 -1- 甲酸酯；

(3S)-1-(吡啶 -3- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 氧基 } 苯基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-[4-({1-[(2S)- 四氢呋喃 -2- 基羰基] 哌啶 -4- 基 } 氧基) 苯基] 吡咯烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-[4-({1-[(2R)- 四氢呋喃 -2- 基羰基] 哌啶 -4- 基 } 氧基) 苯基] 吡咯烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-(4-{[1-(四氢呋喃 -3- 基羰基) 哌啶 -4- 基] 氧基 } 苯基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(环丙基乙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(吡啶 -3- 基)-N-(4-{[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 氧基 } 苯基) 吡咯烷 -3- 甲酰胺；

(3S)-N-[4-({1-[(2S)-2- 甲基丁酰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

叔丁基 4-(4-{[(3S)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 氨基甲酰基 } 苯氧基) 哌啶 -1- 甲酸酯；

叔丁基 4-(4-{[(3R)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 氨基甲酰基 } 苯氧基) 哌啶 -1- 甲酸酯；

(3S)-N-{4-[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯

烷 -3- 甲酰胺 ;及其药学上可接受的盐。

[0276] N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[(1- 苯甲酰基哌啶 -4- 基) 磺酰基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-(4-{[1-(环戊基羰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 哌啶 -4- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 哌啶 -4- 甲酰胺 ;

N-{4-[1-(2- 氟苯甲酰基) 哌啶 (piperidi)4- 基] 苯基 }-1-(哒嗪 -3- 基) 哌啶 -4- 甲酰胺 ;

1-(哒嗪 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 哌啶 -4- 甲酰胺 ;

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(1,3- 噻唑 -5- 基羰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(4- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(2S)-2- 苯基丁酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(2S)-2- 甲氧基 -2- 苯基乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(2R)-2- 甲氧基 -2- 苯基乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(乙氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(4- 甲基苯氧基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(四氢呋喃 -3- 基羰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(萘 -1- 基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[(2,6- 二氯苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(萘 -1- 基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲

酰胺；

(3S)-1-(哒嗪-3-基)-N-(4-{1-[4-(噻吩-2-基)丁酰基]哌啶-4-基}苯基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环丙基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(萘-2-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[3-(苯基磺酰基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-[4-(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(呋喃-2-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(N-苯甲酰基甘氨酰)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(2,4-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(1-甲基环己基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(6-甲基吡啶-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{1-[(3-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环戊基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}吡咯

烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环丙基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 氟 -5- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(5- 氟吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(2- 氟 -6- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,4- 二甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 庚酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,4- 二氯苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(4- 氟苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,3- 二氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 己酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(3- 甲基噻吩 -2- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 丁酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 甲基戊酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(3,5- 二甲基苯基) 乙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基)

吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,5- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(4- 氯苯基）乙酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（呋喃 -3- 基羰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,4- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[2- 氯 -5-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 乙酰基哌啶 -4- 基）苯基］-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,4- 二氟苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,5- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 乙氧基丙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,5- 二氯苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,5- 二甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(5- 氟 -2- 甲基苯甲酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（二苯基乙酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-（哒嗪 -3- 基）-N-(4-{1-[4-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-（戊 -4- 烯酰基）哌啶 -4- 基］苯基}-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-（哒嗪 -3- 基）-N-(4-{1-[3-（三氟甲氧基）苯甲酰基］哌啶 -4- 基｝苯基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(1- 苯基环丙基）羰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[2- 氟 -5-（三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基)-1-（哒嗪 -3- 基）

吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(环己基乙酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 甲氧基苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 甲基丁酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 乙基丁酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(4- 叔丁基苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氯苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2- 氟苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-1-(哒嗪 -3- 基)-N-(4-{1-[3-(三氟甲基）苯甲酰基］哌啶 -4- 基｝苯基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(1- 甲基环丙基）羰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(戊 -4- 炔酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(3- 氟苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[3-(甲基巯基）丙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(1- 乙酰基哌啶 -4- 基）羰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(丁 -3- 烯酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,2- 二甲基丁酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 氟 -4- 甲基苯甲酰基）哌啶 -4- 基］苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3- 甲氧基苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2- 氯苯基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{1-[(2- 甲氧基乙氧基）乙酰基］哌啶 -4- 基｝苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(N- 乙酰基 -L- 亮氨酰) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(4- 氰基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2- 甲氧基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(2,3- 二甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{1-[4-(丙烷 -2- 基) 苯甲酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(环己基羰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(噻吩 -2- 基羰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(4- 羟基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3- 氰基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(3,3,3- 三氟丙酰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(甲氧基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[1-(3- 甲基丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(2- 氰基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(4- 氰基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 氟 -4- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(5- 氰基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(5- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(2- 甲基吡啶 -3- 基) 吡咯烷 -3- 甲

酰胺；

(3S)-N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(2-甲基吡啶-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺；

N-(4-{1-[(4-甲基四氢-2H-吡喃-4-基)甲基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-[(3S)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-4-[1-(2-甲基丙酰基)哌啶-4-基]苯甲酰胺；

N-(4-{1-[2-(哌嗪-1-基)乙基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

4-[1-(2-甲基丙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]苯甲酰胺；

N-{4-[1-(2-羟基-2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

(3S)-N-(4-{1-[(4-甲基四氢-2H-吡喃-4-基)甲基]-1H-吡唑-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-羟基-2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,2-二甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(丙烷-2-基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(环丙基甲基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢-2H-吡喃-2-基甲基)-1H-吡唑-4-基]苯基}吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-叔丁基-1H-吡唑-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-苯甲酰基吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-(2-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-(3-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-(4-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-(3,5-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-(2-甲基苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[(3R)-1-(2,2-二甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-({(3R)-1-[(4,4-二氟环己基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-1-(哒嗪-3-基)-N-(4-{[(3R)-1-(4,4,4-三氟丁酰基)吡咯烷-3-基]氧基}苯基)吡咯烷-3-甲酰胺；

(3S)-N-(4-[(3R)-1-(2,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

N-[4-(5-丙基-1,2,4-氧杂二唑-3-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

(3S)-N-{4-[1-(2-氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3-氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(4-氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-苯甲酰基氮杂环丁烷-3-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,2-二甲基丙酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(3,5-二氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2-甲基苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,4-二氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3R)-N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3R)-N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3R)-N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(环己基羰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-{4-[(1- 苯甲酰基哌啶 -4- 基) 氧基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-(4-{[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

(3S)-N-[4-({1-[(2- 甲基环丙基) 羰基] 哌啶 -4- 基 } 氧基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺 ;

N-{4-[5-(2,2- 二甲基丙基)-1,3,4- 氧杂二唑 -2- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[1-(2,2- 二甲基丙基)-1H- 咪唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-[4-(3- 环丙基 -1- 甲基 -1H- 吡唑 -5- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[5-(2,2- 二甲基丙基)-1,2,4- 氧杂二唑 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

N-{4-[3- 环丙基 -1-(2- 甲氧基乙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺 ;

叔丁基 4-(5-{[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 氨基甲酰基 } 噻吩 -2- 基) 哌啶 -1- 甲酸酯 ;

叔丁基 4- 氟 -4-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基] 哌啶 -1- 甲酸酯 ;

5-(1- 苯甲酰基哌啶 -4- 基)-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(2- 氟苯甲酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(2- 甲基苯甲酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(3- 氟苯甲酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(4- 氟苯甲酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺 ;

5-[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基]

噻吩 -2- 甲酰胺；

N-{4-[3- 环丙基 -1-(2- 羟基乙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

1-(6- 氟哒嗪 -3- 基)-N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2- 乙基丁酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

(3S)-N-(4-{[(3S)-1- 苯甲酰基吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3S)-1-(2- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3S)-1-(3,5- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

(3S)-N-(4-{[(3S)-1-(2,2- 二甲基丙酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基)-2- 氟苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(2- 甲基苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,4- 二氟苯甲酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,5- 二氟苯甲酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺；

(3S)-N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(6-甲基哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[(1-苯甲酰基哌啶-4-基)氧基]苯基}-1-(6-甲基哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(6-甲基哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-(4-{[1-(环己基羰基)哌啶-4-基]氧基}苯基)-1-(6-甲基哒嗪-3-基)吡咯烷-3-甲酰胺；

N-{4-[8-(2-甲基丙酰基)-8-氮杂双环[3.2.1]辛-3-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

1-(哒嗪-3-基)-N-{4-[8-(4,4,4-三氟丁酰基)-8-氮杂双环[3.2.1]辛-3-基]苯基}氮杂环丁烷-3-甲酰胺；

N-[4-(8-苯甲酰基-8-氮杂双环[3.2.1]辛-3-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[8-(2-氟苯甲酰基)-8-氮杂双环[3.2.1]辛-3-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[8-(2,2-二甲基丙酰基)-8-氮杂双环[3.2.1]辛-3-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-(4-{8-[(1-甲基环丙基)羰基]-8-氮杂双环[3.2.1]辛-3-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2-甲氧基乙基)-3-(2-甲基丙基)-1H-吡唑-5-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

5-[1-(2,2-二甲基丙酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

5-{1-[(1-甲基环丙基)羰基]哌啶-4-基}-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]-5-[1-(3,3,3-三氟丙酰基)哌啶-4-基]噻吩-2-甲酰胺；

5-[1-(2,2-二甲基丁酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺；

N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺；

苄基 4-[4-({[1-(6-氯哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]-4-氟哌啶-1-甲酸酯；

苄基 4-[4-({[1-(6-氯哒嗪-3-基)氮杂环丁烷-3-基]羰基}氨基)苯基]-4-羟基哌啶-1-甲酸酯；

N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]-5-[1-(4,4,4-三氟丁酰基)哌啶-4-基]

噻吩 -2- 甲酰胺；

5-[1-(环丙基羰基)哌啶 -4- 基]-N-[1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基]噻吩 -2- 甲酰胺；

N-{4-[4- 氟 -1-(2- 氟苯甲酰基)哌啶 -4- 基]苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(2- 甲基丙酰基)哌啶 -4- 基]苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基)哌啶 -4- 基]-2- 氟苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环丙基羰基)哌啶 -4- 基]-2- 氟苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺；

N-(2- 氟 -4-{1-[(1- 甲基环丙基)羰基]哌啶 -4- 基}苯基)-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(环丙基乙酰基)哌啶 -4- 基]-2- 氟苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基 -4- 氟哌啶 -4- 基)苯基]-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基)-4- 氟哌啶 -4- 基]苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺；

N-{4-[3- 叔丁基 -1-(2- 甲氧基乙基)-1H- 吡唑 -5- 基]苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 丁基 -3- 叔丁基 -1H- 吡唑 -5- 基)苯基]-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺；

N-{4-[3- 叔丁基 -1-(四氢 -2H- 吡喃 -4- 基甲基)-1H- 吡唑 -5- 基]苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(2- 氟苯甲酰基)哌啶 -4- 基]苯基}-1-(哒嗪 -4- 基)氮杂环丁烷 -3- 甲酰胺；

N-[4-(1- 苯甲酰基哌啶 -4- 基)-2- 氟苯基]-1-(哒嗪 -4- 基)氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(2,2- 二甲基丙酰基)哌啶 -4- 基]-2- 氟苯基}-1-(哒嗪 -4- 基)氮杂环丁烷 -3- 甲酰胺；

N-{4-[1-(3,3- 二甲基丁酰基)哌啶 -4- 基]-2- 氟苯基}-1-(哒嗪 -4- 基)氮杂环丁烷 -3- 甲酰胺；

N-{2- 氟 -4-[1-(4,4,4- 三氟丁酰基)哌啶 -4- 基]苯基}-1-(哒嗪 -4- 基)氮杂环丁烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2- 氟苯甲酰基)哌啶 -4- 基]苯基}-1-(6- 甲基哒嗪 -3- 基)吡咯烷 -3- 甲酰胺；

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基)苯基]-1-(6- 甲基哒嗪 -3- 基)吡咯烷 -3- 甲酰胺；

(3S)-N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(6-甲基哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(4-甲基哒嗪-3-基)吡咯烷-3-甲酰胺；

(3S)-N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(4-甲基哒嗪-3-基)吡咯烷-3-甲酰胺；及其药学上可接受的盐。

[0277] 药物组合物、组合疗法、治疗方法和施用

另一实施方案包含这样的药物组合物，其包含具有式(I)的化合物和赋形剂。

[0278] 又一实施方案包含在哺乳动物中治疗癌症的方法，其包括向其中施用治疗可接受量的具有式(I)的化合物。

[0279] 又一实施方案涉及用于治疗在所述疾病期间表达NAMPT的疾病的组合物，所述组合物包含赋形剂和治疗有效量的具有式(I)的化合物。

[0280] 又一实施方案涉及用于在患者中治疗在所述疾病期间表达NAMPT的疾病的方法，所述方法包括向所述患者施用治疗有效量的具有式(I)的化合物。

[0281] 又一实施方案涉及用于治疗炎性和组织修复病症；尤其是类风湿关节炎、炎性肠病、哮喘和COPD(慢性阻塞性肺病)、骨关节炎、骨质疏松和纤维化病；皮肤病，包括银屑病、特应性皮炎和紫外线引起的皮肤损伤；自身免疫性疾病包括全身性红斑狼疮、多发性硬化、银屑病关节炎、强直性脊柱炎、组织和器官排斥、阿尔茨海默氏病、中风、动脉粥样硬化(atherosclerosis)、再狭窄、糖尿病、肾小球肾炎、癌症，特别是其中所述癌症选自乳腺癌、前列腺癌、肺癌、结肠癌、宫颈癌、卵巢癌、皮肤癌、中枢神经系统癌、膀胱癌、胰腺癌、白血病、淋巴瘤或霍奇金氏病、恶病质、与感染和某些病毒感染相关的炎性，包括获得性免疫缺陷综合征(AIDS)、成人呼吸窘迫综合征和共济失调毛细血管扩张(telengiectasia)的组合物，所述组合物包含赋形剂和治疗有效量的具有式(I)的化合物。

[0282] 又一实施方案涉及在患者中治疗炎性和组织修复病症；尤其是类风湿关节炎、炎性肠病、哮喘和COPD(慢性阻塞性肺病)、骨关节炎、骨质疏松和纤维化病；皮肤病，包括银屑病、特应性皮炎和紫外线引起的皮肤损伤；自身免疫性疾病包括全身性红斑狼疮、多发性硬化、银屑病关节炎、强直性脊柱炎、组织和器官排斥、阿尔茨海默氏病、中风、动脉粥样硬化、再狭窄、糖尿病、肾小球肾炎、癌症，特别是其中所述癌症选自乳腺癌、前列腺癌、肺癌、结肠癌、宫颈癌、卵巢癌、皮肤癌、中枢神经系统癌、膀胱癌、胰腺癌、白血病、淋巴瘤或霍奇金氏病、恶病质、与感染和某些病毒感染相关的炎症，包括获得性免疫缺陷综合征(AIDS)、成人呼吸窘迫综合征和共济失调毛细血管扩张的方法，所述方法包括向所述患者施用治疗有效量的具有式(I)的化合物。

[0283] 又一实施方案涉及用于治疗在所述疾病期间表达NAMPT的疾病的组合物，所述组合物包含赋形剂和治疗有效量的具有式(I)的化合物以及治疗有效量的一种额外的治疗剂或多于一种额外的治疗剂。

[0284] 又一实施方案涉及在患者中治疗在所述疾病期间表达NAMPT的疾病的方法，所述方法包括向所述患者施用治疗有效量的具有式(I)的化合物和治疗有效量的一种额外的治疗剂或多于一种额外的治疗剂。

[0285] 又一实施方案涉及用于治疗炎性和组织修复病症；尤其是类风湿关节炎、炎性肠

病、哮喘和 COPD（慢性阻塞性肺病）、骨关节炎、骨质疏松和纤维化病；皮肤病，包括银屑病、特应性皮炎和紫外线引起的皮肤损伤；自身免疫性疾病包括全身性红斑狼疮、多发性硬化、银屑病关节炎、强直性脊柱炎、组织和器官排斥、阿尔茨海默氏病、中风、动脉粥样硬化、再狭窄、糖尿病、肾小球肾炎、癌症，特别是其中所述癌症选自乳腺癌、前列腺癌、肺癌、结肠癌、宫颈癌、卵巢癌、皮肤癌、中枢神经系统癌、膀胱癌、胰腺癌、白血病、淋巴瘤或霍奇金氏病、恶病质、与感染和某些病毒感染相关的炎症，包括获得性免疫缺陷综合征 (AIDS)、成人呼吸窘迫综合征和共济失调毛细血管扩张的组合物，所述组合物包含赋形剂和治疗有效量的具有式 (I) 的化合物以及治疗有效量的一种额外的治疗剂或多于一种额外的治疗剂。

[0286] 又一实施方案涉及在患者中治疗炎性和组织修复病症；尤其是类风湿关节炎、炎性肠病、哮喘和 COPD（慢性阻塞性肺病）、骨关节炎、骨质疏松和纤维化病；皮肤病，包括银屑病、特应性皮炎和紫外线引起的皮肤损伤；自身免疫性疾病包括全身性红斑狼疮、多发性硬化、银屑病关节炎、强直性脊柱炎、组织和器官排斥、阿尔茨海默氏病、中风、动脉粥样硬化、再狭窄、糖尿病、肾小球肾炎、癌症，特别是其中所述癌症选自乳腺癌、前列腺癌、肺癌、结肠癌、宫颈癌、卵巢癌、皮肤癌、中枢神经系统癌、膀胱癌、胰腺癌、白血病、淋巴瘤或霍奇金氏病、恶病质、与感染和某些病毒感染相关的炎症，包括获得性免疫缺陷综合征 (AIDS)、成人呼吸窘迫综合征和共济失调毛细血管扩张的方法，所述方法包括向所述患者施用治疗有效量的具有式 (I) 的化合物以及治疗有效量的一种额外的治疗剂或多于一种额外的治疗剂。

[0287] 通过体外或体内代谢方法产生的具有式 (I) 的化合物的代谢物也可以具有用于治疗与 NAMPT 相关的疾病的效用。

[0288] 可以在体外或体内代谢形成具有式 (I) 的化合物的某些前体化合物也可以具有用于治疗与 NAMPT 相关的疾病的效用。

[0289] 具有式 (I) 的化合物可以以酸加成盐、碱加成盐或兼性离子存在。在化合物的分离过程中或纯化之后制备化合物的盐。化合物的酸加成盐是衍生自化合物与酸的反应的那些。例如，化合物的乙酸盐、己二酸盐、藻酸盐、碳酸氢盐、柠檬酸盐、天冬氨酸盐、苯甲酸盐、苯磺酸盐、硫酸氢盐、丁酸盐、樟脑酸盐、樟脑磺酸盐 (camphorsufonate)、二葡糖酸盐、甲酸盐、富马酸盐、甘油磷酸盐、谷氨酸盐、半硫酸盐、庚酸盐、己酸盐、盐酸盐、氢溴酸盐、氢碘酸盐、乳糖醛酸盐、乳酸盐、马来酸盐、均三甲苯磺酸盐、甲磺酸盐、萘磺酸盐 (naphthylenesulfonate)、烟酸盐、草酸盐、扑酸盐、果胶酯酸盐 (pectinate)、过硫酸盐、磷酸盐、苦味酸盐、丙酸盐、琥珀酸盐、酒石酸酯、硫氰酸盐、三氯乙酸（盐）、三氟乙酸（盐）、对甲苯磺酸盐和十一烷酸盐被预期是被本发明包含的。化合物的碱加成盐是衍生自化合物与阳离子如锂、钠、钾、钙和镁的氢氧化物、碳酸盐或碳酸氢盐的反应的那些。

[0290] 具有式 (I) 的化合物可以例如含服 (bucally)、经眼、口服、渗透、胃肠外（肌内、腹膜内、胸骨内、静脉内、皮下）、直肠、局部、经皮或阴道施用。

[0291] 治疗有效量的具有式 (I) 的化合物取决于治疗的受体、被治疗的病症和其严重程度、含有该化合物的组合物、施用时间、施用途径、治疗的持续时间、化合物效力、其清除率和是否共同施用另外的药物。用于制备待以单次剂量或以分次剂量向患者每日施用的组合物的本发明具有式 (I) 的化合物的量是约 0.03- 约 200mg/kg 体重。单次剂量组合物含有这些量或其约数的组合。

[0292] 可以在有或者没有赋形剂的情况下施用具有式 (I) 的化合物。赋形剂包括，例如，封装材料或添加剂如吸收促进剂、抗氧化剂、粘合剂、缓冲剂、涂层剂、着色剂、稀释剂、崩解剂、乳化剂、填充剂、填料、调味剂、保湿剂、润滑剂、芳香剂、防腐剂、推进剂、释放剂、灭菌剂、甜味剂、增溶剂、湿润剂及其混合物。

[0293] 用于制备待以固体剂型口服施用的包含具有式 (I) 的化合物的组合物的赋形剂包括，例如，琼脂、海藻酸、氢氧化铝、苯甲醇、苯甲酸苄酯、1,3- 丁二醇、卡波姆、蓖麻油、纤维素、乙酸纤维素、可可脂、玉米淀粉、玉米油、棉子油、交联的聚乙烯吡咯烷酮、甘油二酯、乙醇、乙基纤维素、月桂酸乙酯 (ethyl laureate)、油酸乙酯、脂肪酸酯、明胶、胚芽油、葡萄糖、甘油、花生油 (groundnut oil)、羟丙基甲基纤维素、异丙醇、等渗盐水、乳糖、氢氧化镁、硬脂酸镁、麦芽、甘露醇、甘油单酯、橄榄油、花生油 (peanut oil)、磷酸钾盐、马铃薯淀粉、聚乙烯吡咯烷酮、丙二醇、林格溶液、红花油、芝麻油、羧甲基纤维素钠、磷酸钠盐、月桂基硫酸钠、山梨醇钠、大豆油、硬脂酸、富马酸十八烷基酯、蔗糖、表面活性剂、滑石、西黄蓍胶、四氢糠醇、甘油三酯、水及其混合物。用于制备待以液体剂型经眼或口服施用的包含具有式 (I) 的本发明的化合物的组合物的赋形剂包括，例如，1,3- 丁二醇、蓖麻油、玉米油、棉子油、乙醇、脱水山梨糖醇的脂肪酸酯、胚芽油、花生油 (groundnut oil)、甘油、异丙醇、橄榄油、聚乙二醇、丙二醇、芝麻油、水及其混合物。用于制备待渗透施用的包含具有式 (I) 的本发明的化合物的组合物的赋形剂包括，例如，氯氟烃、乙醇、水及其混合物。用于制备待肠胃外施用的包含具有式 (I) 的本发明的化合物的组合物的赋形剂包括，例如，1,3- 丁二醇、蓖麻油、玉米油、棉子油、葡萄糖、胚芽油、花生油 (groundnut oil)、脂质体、油酸、橄榄油、花生油 (peanut oil)、林格溶液、红花油、芝麻油、大豆油、U.S.P. 或等渗氯化钠溶液、水及其混合物。用于制备待直肠或阴道施用的包含具有式 (I) 的本发明的化合物的组合物的赋形剂包括，例如，可可脂、聚乙二醇、蜡及其混合物。

[0294] 具有式 (I) 的化合物，当与烷基化剂，血管生成抑制剂、抗体、抗代谢剂、抗有丝分裂剂、抗增殖剂、抗病毒剂、极光激酶抑制剂、细胞凋亡启动子 (例如，Bcl-xL、Bcl-w 和 Bfl-1) 抑制剂、死亡受体途径的活化剂、Bcr-Abl 激酶抑制剂、BiTE(双特异性 T 细胞接合器 (Bi-Specific T cell engager)) 抗体、抗体药物缀合物、生物响应改性剂、细胞周期蛋白依赖性激酶抑制剂、细胞周期抑制剂、环加氧酶 -2 抑制剂、DVDs、白血病病毒癌基因同系物 (ErbB2) 受体抑制剂、生长因子抑制剂、热休克蛋白 (HSP)-90 抑制剂、组蛋白去乙酰酶 (HDAC) 抑制剂、激素疗法、免疫制剂 (immunologicals)、细胞凋亡蛋白质的抑制剂的抑制剂 (IAPs)、嵌入抗生素、激酶抑制剂、驱动蛋白抑制剂、Jak2 抑制剂、雷帕霉素抑制剂的哺乳动物目标、microRNA′ s、促细胞分裂剂 - 活化的胞外信号调节激酶抑制剂、多价结合蛋白、非类固醇抗炎药物 (NSAIDs)、聚 ADP(腺苷二磷酸)- 核糖聚合酶 (PARP) 抑制剂、铂化疗药物、polo 样激酶 (Plk) 抑制剂、磷酸肌醇 -3 激酶 (PI3K) 抑制剂、蛋白酶体抑制剂、嘌呤类似物、嘧啶类似物、受体酪氨酸激酶抑制剂、类视黄醇 / 三角肌植物生物碱、小抑制性核糖核酸 (siRNAs)、拓扑异构酶抑制剂、泛素连接酶抑制剂等，以及与这些药剂中的一个或多个组合使用时，被预计是有用的。

[0295] BiTE 抗体是双特异性抗体，其通过同时结合两种细胞而指导 T 细胞来攻击癌细胞。T 细胞然后攻击目标癌细胞。BiTE 抗体的实例包括 adecatumumab(Micromet MT201)、blinatumomab(Micromet MT103) 等。在不受限于理论的情况下，T 细胞引起目标癌细胞的

细胞凋亡的机制之一是通过细胞溶解颗粒组分（其包括穿孔蛋白和粒酶 B）的胞吐作用。

[0296] siRNAs 是具有内源性 RNA 碱基或化学修饰的核苷酸的分子。修饰没有消除细胞活性，而是赋予提高的稳定性和 / 或提高的细胞效力。化学修饰的实例包括磷硫酰基团、2′ -脱氧核苷酸、含 2′ -OCH_3- 的核糖核苷酸、2′ -F- 核糖核苷酸、2′ -甲氧基乙基核糖核苷酸、其组合等。siRNA 可以具有不同长度（例如，10-200bps）和结构（例如，发夹、单 / 双链、凸出、切口 / 缺口、错配）并且在细胞中被加工而提供活性基因沉默。双链 siRNA(dsRNA) 可以在每条链（平端）或非对称末端（悬突）上具有相同数目的核苷酸。1-2 个核苷酸的悬突可以存在于有义链和 / 或反义链上，以及存在于给定链的 5′ -和 / 或 3′ -末端上。

[0297] 多价结合蛋白是包含两个或更多个抗原结合位点的结合蛋白。多价结合蛋白被改造以具有三个或更多个抗原结合位点并且一般地不是天然存在的抗体。术语“多特异性结合蛋白”是指能结合两个或更多个相关或不相关靶标的结合蛋白。双可变域 (DVD) 结合蛋白是四价或多价结合蛋白结合蛋白，其包含两个或更多个抗原结合位点。该 DVDs 可以是单特异性的（即，能结合一个抗原）或多特异性的（即，能结合两个或更多个抗原）。包含两个重链 DVD 多肽和两个轻链 DVD 多肽的 DVD 结合蛋白被称为 DVD Ig′ s。DVD Ig 的每一半包含重链 DVD 多肽、轻链 DVD 多肽和两个抗原结合位点。每个结合位点包含重链可变域和轻链可变域，具有总共 6 个抗原结合中涉及的 CDRs/ 抗原结合位点。

[0298] 烷基化剂包括六甲密胺、AMD-473、AP-5280、apaziquone、苯达莫司汀、brostallicin、白消安、卡波醌、卡莫司汀 (BCNU)、苯丁酸氮芥、CLORETAZINE®、(laromustine、VNP 40101M)、环磷酰胺、氨烯咪胺、雌莫司汀、福莫司汀、葡磷酰胺、异磷酰胺、KW-2170、洛莫司汀 (CCNU)、马磷酰胺、美法仑、二溴甘露醇、二溴卫矛醇、尼莫司汀、氮芥 N- 氧化物、雷莫司汀、替莫唑胺、塞替派、TREANDA®（苯达莫司汀）、苏消安、氯乙环磷酰胺等。

[0299] 血管生成抑制剂包括内皮 - 特异性受体酪氨酸激酶 (Tie-2) 抑制剂、表皮生长因子受体 (EGFR) 抑制剂、胰岛素生长因子 -2 受体 (IGFR-2) 抑制剂、基质金属蛋白酶 -2(MMP-2) 抑制剂、基质金属蛋白酶 -9(MMP-9) 抑制剂、血小板衍生生长因子受体 (PDGFR) 抑制剂、血小板反应蛋白类似物、血管内皮细胞生长因子受体酪氨酸激酶 (VEGFR) 抑制剂等。

[0300] 抗代谢剂包括 ALIMTA®（培美曲塞二钠、LY231514、MTA）、5- 阿扎胞苷、XELODA®（卡培他滨）、卡莫氟、LEUSTAT®（克拉屈滨）、clofarabine、阿糖胞苷、阿糖胞苷 ocfosfate、阿糖胞苷、地西他滨、去铁胺、去氧氟尿苷、依氟鸟氨酸、EICAR(5- 乙炔基 -1-β -D- 呋喃核糖基咪唑 (ribofuranosylimidazole)-4- 氨甲酰）、依诺他滨、ethnylcytidine、氟达拉滨、单独或与亚叶酸结合的 5- 氟尿嘧啶、GEMZAR®（吉西他滨）、羟基脲、ALKERAN®（美法仑）、巯嘌呤、6- 巯基嘌呤核糖核苷、氨甲蝶呤、霉酚酸、奈拉滨、诺拉曲塞、ocfosfate、pelitrexol、喷司他丁、雷替曲塞、利巴韦林、triapine、曲美沙特、S-1、噻唑呋林 (tiazofurin)、替加氟、TS-1、阿糖腺苷、UFT 等。

[0301] 抗病毒剂包括利托那韦、羟氯喹等。

[0302] 极光激酶抑制剂包括 ABT-348、AZD-1152、MLN-8054、VX-680、极光 A- 特异性激酶

抑制剂、极光 B- 特异性激酶抑制剂和泛极光激酶抑制剂等。

[0303] Bcl-2 蛋白抑制剂包括 AT-101((-) 棉酚)、GENASENSE® (G3139 或 oblimersen(Bcl-2- 靶向反义寡核苷酸))、IPI-194、IPI-565、N-(4-(4-((4′ - 氯 (1,1′ - 联苯)-2- 基) 甲基) 哌嗪 -1- 基) 苯甲酰基)-4-(((1R)-3-(二甲基氨基)-1-((苯基硫基) 甲基) 丙基) 氨基)-3- 硝基苯磺酰胺)(ABT-737)、N-(4-(4-((2-(4- 氯苯基)-5,5- 二甲基 -1- 环己 -1- 烯 -1- 基) 甲基) 哌嗪 -1- 基) 苯甲酰基)-4-(((1R)-3-(吗啉 -4- 基)-1-((苯基硫基) 甲基) 丙基) 氨基)-3-((三氟甲基) 磺酰基) 苯磺酰胺 (ABT-263)、GX-070(obatoclax) 等。

[0304] Bcr-Abl 激酶抑制剂包括 DASATINIB® (BMS-354825)、GLEEVEC® (伊马替尼 (imatinib)) 等。

[0305] CDK 抑制剂包括 AZD-5438、BMI-1040、BMS-032、BMS-387、CVT-2584、flavopyridol、GPC-286199、MCS-5A、PD0332991、PHA-690509、seliciclib(CYC-202, R-roscovitine)、ZK-304709 等。

[0306] COX-2 抑制剂包括 ABT-963、ARCOXIA® (艾托考昔)、BEXTRA® (伐地考昔)、BMS347070、CELEBREX® (塞来考昔)、COX-189(lumiracoxib)、CT-3、DERAMAXX® (地拉考昔)、JTE-522、4- 甲基 -2-(3,4- 二甲基苯基)-1-(4- 氨磺酰苯基 -1H- 吡咯)、MK-663(艾托考昔)、NS-398、帕瑞考昔、RS-57067、SC-58125、SD-8381、SVT-2016、S-2474、T-614、VIOXX® (罗非考昔) 等。

[0307] EGFR 抑制剂包括 ABX-EGF、抗 EGFR 免疫脂质体、EGF- 疫苗、EMD-7200、ERBITUX® (西妥昔单抗)、HR3、IgA 抗体、IRESSA® (吉非替尼 (gefitinib))、TARCEVA® (埃洛替尼 (erlotinib) 或 OSI-774)、TP-38、EGFR 融合蛋白、TYKERB® (拉帕替尼 (lapatinib)) 等。

[0308] ErbB2 受体抑制剂包括 CP-724-714、CI-1033(canertinib)、HERCEPTIN® (曲妥单抗)、(拉帕替尼 (lapatinib))、OMNITARG® (2C4、petuzumab)、TAK-165、GW-572016(ionafamib)、GW-282974、EKB-569、PI-166、dHER2(HER2 疫苗)、APC-8024(HER-2 疫苗)、抗 HER/2neu 双特异性抗体、B7.her2IgG3、AS HER2 三功能双特异性抗体、mAB AR-209、mAB 2B-1 等。

[0309] 组蛋白去乙酰酶抑制剂包括缩酚酸肽、LAQ-824、MS-275、trapoxin、辛二酰苯胺异羟肟酸 (suberoylanilide hydroxamic acid)(SAHA)、TSA、丙戊酸等。

[0310] HSP-90 抑制剂包括 17-AAG-nab、17-AAG、CNF-101、CNF-1010、CNF-2024、17-DMAG、格尔德霉素、IPI-504、KOS-953、MYCOGRAB® (HSP-90 的人重组体抗体)、NCS-683664、PU24FC1、PU-3、根赤壳菌素、SNX-2112、STA-9090VER49009 等。

[0311] 细胞凋亡蛋白质的抑制剂的抑制剂包括 HGS1029、GDC-0145、GDC-0152、LCL-161、LBW-242 等。

[0312] 抗体药物缀合物包括抗 CD22-MC-MMAF、抗 CD22-MC-MMAE、抗 CD22-MCC-DM1、

CR-011-vcMMAE、PSMA-ADC、MEDI-547、SGN-19Am SGN-35、SGN-75 等。

[0313] 死亡受体途径的活化剂包括 TRAIL、靶向 TRAIL 或死亡受体（例如 DR4 和 DR5）的抗体或其它药剂如 pomab、conatumumab、ETR2-ST01、GDC0145(lexatumumab)、HGS-1029、LBY-135、PRO-1762 和曲妥单抗。

[0314] 驱动蛋白抑制剂包括 Eg5 抑制剂如 AZD4877、ARRY-520 ;CENPE 抑制剂如 GSK923295A 等。

[0315] JAK-2 抑制剂包括 CEP-701(lesaurtinib)、XL019 和 INCB018424 等。

[0316] MEK 抑制剂包括 ARRY-142886、ARRY-438162PD-325901、PD-98059 等。

[0317] mTOR 抑制剂包括 AP-23573、CCI-779、依维莫司、RAD-001、雷帕霉素、temsirolimus、ATP- 竞争性 TORC1/TORC2 抑制剂、包括 PI-103、PP242、PP30、Torin 1 等。

[0318] 非类固醇抗炎药物包括 AMIGESIC®（双水杨酯）、DOLOBID®（二氟尼柳）、MOTRIN®（布洛芬）、ORUDIS®（酮洛芬 (ketoprofen)）、RELAFEN®（萘丁美酮）、FELDENE®（吡罗昔康）、布洛芬乳膏、ALEVE®（萘普生）和 NAPROSYN®（萘普生）、VOLTAREN®（双氯芬酸）、INDOCIN®（吲哚美辛）、CLINORIL®（舒林酸）、TOLECTIN®（托美丁）、LODINE®（依托度酸）、TORADOL®（酮咯酸）、DAYPRO®（奥沙普秦）等。

[0319] PDGFR 抑制剂包括 C-451、CP-673、CP-868596 等。

[0320] 铂化疗药物包括顺铂、ELOXATIN®（奥沙利铂）依他铂、洛铂、奈达铂、PARAPLATIN®（卡铂）、沙铂、picoplatin 等。

[0321] Polo 样激酶抑制剂包括 BI-2536 等。

[0322] 磷酸肌醇 -3 激酶 (PI3K) 抑制剂包括渥曼青霉素、LY294002、X1-147、CAL-120、ONC-21、AEZS-127、ETP-45658、PX-866、GDC-0941、BGT226、BEZ235、XL765 等。

[0323] 凝血栓蛋白类似物包括 ABT-510、ABT-567、ABT-898、TSP-1 等。

[0324] VEGFR 抑制剂包括 AVASTIN®（贝伐单抗）、ABT-869、AEE-788、ANGIOZYME™（抑制血管生成的核糖酶 (Ribozyme Pharmaceuticals(Boulder,CO.) 和 Chiron(Emeryville, CA))、axitinib(AG-13736)、AZD-2171、CP-547,632、IM-862、MACUGEN(pegaptamib)、NEXAVAR®（索拉非尼 (sorafenib)、BAY43-9006)、pazopanib(GW-786034)、瓦他拉尼 (vatalanib)(PTK-787、ZK-222584)、SUTENT®（舒尼替尼 (Sunitinib)、SU-11248)、VEGF 阱、ZACTIMA™(vandetanib、ZD-6474) 等。

[0325] 抗生素包括插入抗生素阿柔比星、放线菌素 D、氨柔比星、annamycin、多柔比星、BLENOXANE®（争光霉素）、柔红霉素、CAELYX®或 MYOCET®（多柔比星脂质体）、依沙芦星、epirbucin、glarbuicin、ZAVEDOS®（伊达比星）、丝裂霉素 C、奈莫柔比星、新制癌菌素、培洛霉素、吡柔比星、rebeccamycin、stimalamer、链佐星、VALSTAR®（戊柔比星）、净司他丁等。

[0326] 拓扑异构酶抑制剂包括阿柔比星、9- 氨基喜树碱、amonafide、amsacrine、becatecarin、belotecan、BN-80915、CAMPTOSAR®（伊立替康盐酸盐）、喜树

碱、CARDIOXANE®（右旋丙亚胺）、diflomotecan、edotecarin、ELLENCE® 或 PHARMORUBICIN®（表柔比星）、依托泊苷、依沙替康、10-羟喜树碱、gimatecan、勒托替康、米托蒽醌、orathecin、pirarbucin、pixantrone、卢比替康、索布佐生、SN-38、tafluposide、托泊替康等。

[0327] 抗体包括 AVASTIN®（贝伐单抗）、CD40-特异性抗体、chTNT-1/B、denosumab、ERBITUX®（西妥昔单抗 (cetuximab)）、HUMAX-CD4® (zanolimumab)、IGF1R-特异性抗体、林妥珠单抗、PANOREX®（依决洛单抗）、RENCAREX® (WX G250)、RITUXAN®（利妥昔单抗）、ticilimumab、trastuzimab、I 和 II 型 CD20 抗体等。

[0328] 激素疗法包括 ARIMIDEX®（阿纳托（司）唑）、AROMASIN®（依西美坦）、阿佐昔芬、CASODEX®（比卡鲁胺）、CETROTIDE®（西曲瑞克）、degarelix、地洛瑞林、DESOPAN®（曲洛司坦）、地塞米松 (dexamethasone)、DROGENIL®（氟他胺）、EVISTA®（雷洛昔芬）、AFEMA™（法倔唑）、FARESTON®（托瑞米芬）、FASLODEX®（氟维司群）、FEMARA®（来曲唑）、福美坦、糖皮质激素、HECTOROL®（度骨化醇）、RENAGEL®（司维拉姆碳酸盐）、拉索昔芬、亮丙瑞林 (leuprolide) 乙酸盐、MEGACE® (megesterol)、MIFEPREX®（米非司酮）、NILANDRON™（尼鲁米特）、NOLVADEX®（枸橼酸它莫西芬）、PLENAXIS™（阿巴瑞克）、泼尼松、PROPECIA®（非那雄胺）、rilostane、SUPREFACT®（布舍瑞林）、TRELSTAR®（促黄体素释放激素 (LHRH)）、VANTAS® (Histrelin 移植物）、VETORYL®（曲洛司坦或 modrastane）、ZOLADEX® (fosrelin、戈舍瑞林）等。

[0329] Deltoids 和类视黄醇包括西奥骨化醇 (EB1089、CB1093)、lexacalcitrol (KH1060)、芬维 A 胺、PANRETIN® (aliretinoin)、ATRAGEN®（脂质体维 A 酸）、TARGRETIN®（贝沙罗汀）、LGD-1550 等。

[0330] PARP 抑制剂包括 ABT-888 (veliparib)、olaparib、KU-59436、AZD-2281、AG-014699、BSI-201、BGP-15、INO-1001、ONO-2231 等。

[0331] 植物生物碱包括但不限于长春新碱、长春碱、长春地辛、长春瑞滨等。

[0332] 蛋白酶体 (Proteasome) 抑制剂包括 VELCADE® (bortezomib)、MG132、NPI-0052、PR-171 等。

[0333] 免疫制剂的例子包括干扰素和其它提高免疫性的试剂。干扰素包括干扰素 α、干扰素 α-2a、干扰素 α-2b、干扰素 β、干扰素 γ-1a、ACTIMMUNE®（干扰素 γ-1b）或干扰素 γ-n1、其组合等。其他的药剂包括 ALFAFERONE®、(IFN-α)、BAM-002（氧化谷胱甘肽）、BEROMUN®（他索纳明）、BEXXAR®（托西莫单抗）、CAMPATH®（阿仑单抗 (alemtuzumab)）、CTLA4（细胞毒素淋巴细胞抗原 4）、氨烯咪胺、地尼白介素、依帕珠单抗、GRANOCYTE®（来格司亭）、蘑菇多糖、白血球 α 干扰素、咪喹莫

特、MDX-010(抗-CTLA-4)、黑色素瘤疫苗、米妥莫单抗、莫拉司亭、MYLOTARG™(吉姆单抗奥佐米星)、NEUPOGEN®(非格司亭)、OncoVAC-CL、OVAREX®(oregovomab)、pemtumomab(Y-muHMFG1)、PROVENGE®(sipuleucel-T)、sargaramostim、sizofilan、替西白介素、THERACYS®(卡介苗)、乌苯美司、VIRULIZIN®(immunotherapeutic、Lorus Pharmaceuticals)、Z-100(Maruyama 的特异性物质(SSM))、WF-10(Tetrachlorodecaoxide(TCDO))、PROLEUKIN®(阿地白介素)、ZADAXIN®(胸腺法新)、ZENAPAX®(西利珠单抗)、ZEVALIN®(90Y-替伊莫单抗)等。

[0334] 生物响应改性剂是这样的药剂,其改变活的生物的防卫机制或生物响应,如组织细胞的存活,生长或分化以便引导它们来具有抗肿瘤活性并且包括云芝糖肽、蘑菇多糖、西佐喃、溶链菌 PF-3512676(CpG-8954)、乌苯美司等。

[0335] 嘧啶类似物包括阿糖胞苷(ara C 或阿糖胞苷 C)、阿糖胞苷、去氧氟尿苷、FLUDARA®(氟达拉滨)、5-FU(5-氟尿嘧啶)、氮尿苷、GEMZAR®(吉西他滨)、TOMUDEX®(ratitrexed)、TROXATYL™(三乙酰尿核甙曲沙他滨)等。

[0336] 嘌呤类似物包括 LANVIS®(硫鸟嘌呤)和 PURI-NETHOL®(巯嘌呤)。

[0337] 抗有丝分裂剂包括 batabulin、epothilone D(KOS-862)、N-(2-((4-羟苯基)氨基)吡啶-3-基)-4-甲氧基苯磺酰胺、ixabepilone(BMS 247550)、紫杉醇、TAXOTERE®(多西他赛)、PNU100940(109881)、patupilone、XRP-9881(larotaxel)、长春氟宁、ZK-EPO(合成 epothilone)等。

[0338] 泛素连接酶抑制剂包括 MDM2 抑制剂,如 nutlins,NEDD8 抑制剂如 MLN4924 等。

[0339] 本发明的化合物还可用作提高放射疗法效力的放射致敏剂。放射疗法的例子包括外束放射疗法、远距疗法、近距疗法和密封、非密封源放射疗法等。

[0340] 此外,具有式(I)的化合物可以与其它化疗剂相结合,如 ABRAXANE™(ABI-007)、ABT-100(法尼基转移酶抑制剂)、ADVEXIN®(Ad5CMV-p53 疫苗)、ALTOCOR®或 MEVACOR®(洛伐他汀)、AMPLIGEN®(聚 I:聚 C12U、一种合成 RNA)、APTOSYN®(依昔舒林)、AREDIA®(帕米膦酸)、arglabin、L-天冬酰胺酶、阿他美坦(1-甲基-3,17-二酮-雄(甾)烷-1,4-二烯)、AVAGE®(他扎罗汀)、AVE-8062(combreastatin 衍生物)BEC2(米妥莫单抗)、恶液质因子或 cachexin(肿瘤坏死因子)、canvaxin(疫苗)、CEAVAC®(癌疫苗)、CELEUK®(西莫白介素)、CEPLENE®(二盐酸组胺)、CERVARIX®(人乳头瘤病毒疫苗)、CHOP®(C:CYTOXAN®(环磷酰胺);H:ADRIAMYCIN®(hydroxydoxorubicin);O:长春新碱(ONCOVIN®);P:泼尼松)、CYPAT™(醋酸环丙氯地孕酮)、combrestatin A4P、DAB(389)EGF(通过至人表皮生长因子的 His-Ala 接头融合的白喉毒素的催化和易位域)或 TransMID-107R™(白喉毒素)、达卡巴嗪、放线菌素 D、5,6-二甲基氧杂蒽酮-4-乙酸(DMXAA)、恩尿嘧啶、EVIZON™(角鲨胺

乳酸盐）、DIMERICINE®（T4N5 脂质体洗剂）、discodermolide、DX-8951f（依沙替康甲磺酸盐）、enzastaurin、EP0906(epithilone B)、GARDASIL®（四价人乳头瘤病毒(6、11、16、18 型）重组疫苗）、GASTRIMMUNE®、GENASENSE®、GMK（神经节糖苷缀合物疫苗）、GVAX®（前列腺癌疫苗）、常山酮(halofuginone)、histerelin、羟基脲、伊班膦酸、IGN-101、IL-13-PE38、IL-13-PE38QQR(cintredekin besudotox)、IL-13-假单胞菌外毒素、干扰素-α、干扰素-γ、JUNOVAN™或 MEPACT ™(mifamurtide)、lonafarnib、5,10-亚甲基四氢叶酸酯(methylenetetrahydrofolate)、米替福新（十六烷基磷酸胆碱）、NEOVASTAT®(AE-941)、NEUTREXIN®（三甲曲沙葡糖醛酸盐）、NIPENT®(pentostatin)、ONCONASE®（一种核糖核酸酶）、ONCOPHAGE®（黑色素瘤疫苗治疗）、ONCOVAX®(IL-2 疫苗)、ORATHECIN™(卢比替康)、OSIDEM®（抗体型细胞药物）、OVAREX® MAb（鼠科单克隆抗体）、紫杉醇、PANDIMEX™(来自人参的糖苷配基皂草,其含 20(S) 原人参萜二醇(aPPD) 和 20(S) 原人参萜三醇(aPPT))、panitumumab、PANVAC®-VF（试验癌疫苗）、培门冬酶、PEG 干扰素 A、phenoxodiol、丙卡巴肼、rebimastat、REMOVAB®(catumaxomab)、REVLIMID®(lenalidomide)、RSR13(efaproxiral)、SOMATULINE® LA（兰瑞肽）、SORIATANE®（阿维 A)、十字孢碱（链霉菌属星状孢子）、talabostat(PT100)、TARGRETIN®（贝沙罗汀）、TAXOPREXIN®(DHA-paclitaxel)、TELCYTA®(canfosfamide、TLK286)、temilifene、TEMODAR®（替莫唑胺）、替米利芬、沙利度胺、THERATOPE®(STn-KLH)、thymitaq(2-氨基-3,4-二氢-6-甲基-4-氧代-5-(4-吡啶基硫基）喹唑啉二盐酸盐）、TNFERADE™(adenovector：含肿瘤坏死因子-α的基因的 DNA 载体）、TRACLEER®或 ZAVESCA®（波生坦）、维 A 酸(Retin-A)、粉防己碱、TRISENOX®（三氧化二砷）、VIRULIZIN®、ukrain（来自白屈菜植物的生物碱的衍生物）、vitaxin（抗-alphavbeta3 抗体）、XCYTRIN®（莫特沙芬钆）、XINLAY™（阿曲生坦）、XYOTAX™（紫杉醇 poliglumex)、YONDELIS®(trabectedin)、ZD-6126、ZINECARD®(dexrazoxane)、ZOMETA®（唑来膦酸）、佐柔比星等。

[0341] 数据

使用时间分辨荧光共振能量转移(TR-FRET) 结合测定法进行具有式(I) 的化合物作为 NAMPT 的结合剂和抑制剂的功效确定。

[0342] NAMPT 的时间分辨荧光共振能量转移(TR-FRET) 结合测定法

在利用测定缓冲液(50mM HEPES(NaOH),pH 7.5,100mM NaCl,10mM $MgCl_2$,1mM DTT,1% 甘油）稀释至 3X 和 6% DMSO 之前,将测试化合物在纯 DMSO 中连续稀释（通常是 11 半对数稀释）至 50X 终浓度。将 6μL 转移至 384-孔低容积板(Owens Corning#3673) 中。向其中加入 12μL 含有酶、探针和抗体的 1.5X 溶液。18μL 反应中的终浓度是 1X 测定缓冲液,2% DMSO、6.8nM NAMPT（人,重组的,C 末端 His-标签）、200nM 探针（缀合 Oregon Green 488

的有效烟酰胺竞争性抑制剂）和 1nM Tb- 抗 -His 抗体 (Invitrogen#PV5895)。在 Envision 多标记平板读数器 (Perkin Elmer ;Ex = 337nm、Em = 520 和 495nm) 上读数之前，将反应在室温下平衡 3 小时。将时间分辨 FRET 比值 (Em_{s20}/Em_{495}) 针对对照进行归一化，绘制成化合物浓度的函数并利用四参数逻辑方程进行拟合以确定 IC50s。

[0343] 含有 PRPP 的 NAMPT 的时间分辨荧光共振能量转移 (TR-FRET) 结合测定法

化合物处理和数据加工与缺少底物的测定法（上文）相同。终浓度是 1X 测定缓冲液、2％ DMSO、2nM NAMPT、2nM 探针、1nM Tb- 抗 -His 抗体 (Invitrogen#PV5895)、200μM PRPP 和 2.5mM ATP。在测定之前将反应平衡 16 小时以允许测试化合物可能的酶修饰。

[0344] 表 1 显示了具有式 I 的化合物在功能上抑制 NAMPT 的效用。

表 1

实施例	TR-FRET 结合 - IC50 (μM)	TR-FRET 结合 - IC50 (含有 PRPP) (μM)	实施例	TR-FRET 结合 - IC50 (μM)	TR-FRET 结合 - IC50 (含有 PRPP) (μM)
1	0.120000	0.000386	194	0.122000	0.062600
2	0.022300	0.020000	195	0.305000	0.094100
3	0.357000	0.019200	196	0.083800	0.098500
4	0.424000	0.024000	197	0.126000	0.079800
5	0.107000	0.010200	198	0.084500	0.103000
6	0.544000	0.002340	199	0.033700	0.028000
7	0.104000	0.084700	200	0.033100	0.034400
8	3.360000	0.005300	201	0.012100	0.018200
9	8.620000	0.017200	202	0.117000	0.089500
10	0.034500	0.000518	203	0.034200	0.021100
11	2.370000	0.001930	204	0.380000	0.002760
12	1.410000	0.002050	205	0.025100	0.034000
13	0.858000	0.002880	206	0.023800	0.024100
14	3.840000	0.003080	207	0.141000	0.086700
15	1.660000	0.002490	208	0.117000	0.049600
16	2.480000	0.004130	209	0.061700	0.028900
17	3.510000	0.002360	210	0.031700	0.038300
18	2.740000	0.005320	211	0.031900	0.000801
19	1.170000	0.000554	212	0.070400	0.000787
20	0.006740	0.000296	213	0.104000	0.000678
21	7.380000	0.000507	214	0.165000	0.000841
22	0.011700	0.000169	215	0.068200	0.001140
23	1.950000	0.000610	216	0.228000	0.001410
24	5.880000	0.000861	217	0.043900	0.001510
25	0.028100	0.000598	218	0.265000	0.001640
26	0.005050	0.000761	219	0.105000	0.000480
27	nd	0.011200	220	0.267000	0.001010
28	nd	0.002510	221	0.164000	0.000576
29	0.079800	0.016700	222	0.215000	0.001030
30	0.015000	0.000267	223	0.150000	0.000959
31	0.135000	0.000693	224	0.151000	0.001390
32	0.010200	0.000284	225	0.158000	0.001070

33	0.109000	0.000342	226	0.242000	0.000896
34	0.071400	0.000886	227	0.065900	0.000696
35	0.091600	0.000866	228	0.054600	0.000911
36	0.040100	0.000882	229	0.048000	0.000584
37	0.068900	0.000983	230	0.158000	0.000843
38	0.046500	0.000900	231	0.174000	0.000831
39	0.104000	0.001050	232	0.141000	0.000563
40	0.042800	0.000490	233	0.113000	0.000614
41	0.069200	0.000780	234	0.185000	0.000730
42	0.226000	0.002390	235	0.283000	0.001410
43	0.086500	0.000803	236	0.130000	0.001110
44	0.138000	0.001010	237	0.240000	0.001270
45	0.087300	0.001080	238	0.207000	0.000554
46	0.093400	0.001020	239	0.112000	0.000833
47	0.080500	0.001780	240	0.192000	0.000925
48	0.112000	0.000861	241	0.131000	0.000811
49	0.066100	0.001020	242	0.278000	0.001170
50	0.063500	0.001100	243	0.269000	0.000970
51	0.109000	0.001170	244	0.449000	0.000916
52	0.051000	0.000696	245	0.101000	0.000707
53	0.025600	0.000689	246	0.178000	0.000676
54	0.072100	0.000806	247	0.086000	0.001020
55	0.168000	0.002220	248	0.082600	0.000817
56	0.360000	0.000812	249	0.059900	0.000600
57	0.180000	0.001070	250	0.107000	0.000641
58	0.059500	0.000683	251	0.230000	0.000880
59	0.027900	0.000606	252	0.238000	0.001100
60	0.150000	0.001010	253	0.134000	0.000639
61	0.033700	0.000675	254	0.033900	0.011200
62	0.041600	0.000666	255	0.047300	0.037800
63	0.052700	0.000514	256	0.091100	0.038400
64	0.055200	0.000927	257	0.064700	0.041900
65	0.121000	0.000704	258	0.108000	0.034800
66	0.056600	0.000535	259	0.032500	0.017700
67	0.452000	0.000497	260	0.075400	0.019000
68	0.080600	0.000569	261	0.062900	0.023700
69	0.068600	0.000918	262	0.130000	0.034300
70	0.035700	0.000742	263	0.031300	0.020200
71	0.041200	0.014600	264	0.052800	0.013400
72	0.006540	0.007340	265	0.029500	0.021800
73	0.224000	0.071100	266	0.120000	0.053200
74	0.911000	0.000666	267	0.274000	0.056500
75	1.340000	0.000719	268	0.119000	0.042100
76	1.920000	0.000440	269	0.037700	0.022300
77	3.010000	0.000832	270	0.074800	0.035700

78	0.265000	0.000632	271	0.078000	0.025200
79	2.690000	0.000824	272	0.165000	0.052400
80	1.600000	0.000686	273	0.128000	0.042100
81	3.720000	0.001130	274	0.152000	0.064500
82	0.955000	0.000526	275	0.231000	0.045100
83	1.210000	0.000503	276	0.134000	0.034900
84	6.070000	0.001810	277	0.062400	0.026700
85	0.032200	0.017000	278	0.075800	0.033400
86	1.260000	0.000833	279	0.020200	0.015500
87	1.390000	0.001270	280	0.123000	0.051900
88	0.574000	0.000640	281	0.020500	0.014900
89	2.000000	0.000647	282	0.383000	0.090000
90	1.410000	0.000902	283	0.072300	0.032200
91	0.992000	0.000868	284	0.062400	0.038200
92	0.784000	0.000548	285	0.149000	0.086200
93	1.220000	0.001250	286	0.127000	0.066400
94	2.270000	0.001030	287	0.125000	0.063200
95	1.360000	0.001020	288	0.044900	0.019500
96	0.115000	0.282000	289	0.041600	0.032100
97	0.036600	0.131000	290	0.099300	0.045700
98	0.013000	0.000209	291	0.045600	0.018200
99	0.013500	0.000169	292	0.099000	0.064700
100	0.030600	0.000497	293	0.078200	0.025300
101	0.016500	0.000486	294	0.112000	0.055100
102	0.008840	0.000210	295	0.077600	0.051000
103	0.056200	0.000493	296	0.149000	0.057100
104	0.001200	0.000193	297	0.104000	0.047000
105	0.296000	0.000244	298	0.192000	0.061100
106	0.160000	0.000221	299	0.154000	0.086900
107	0.163000	0.000169	300	0.064200	0.039100
108	0.003330	0.000176	301	0.143000	0.048300
109	0.005030	0.000398	302	0.150000	0.048300
110	0.006630	0.000169	303	0.030900	0.015500
111	0.002840	0.000199	304	0.055400	0.024200
112	0.040200	0.000362	305	0.109000	0.035000
113	0.060600	0.000254	306	0.112000	0.046300
114	0.083900	0.000247	307	0.037700	0.015900
115	0.048200	0.000178	308	0.036900	0.018400
116	0.026500	0.000204	309	4.150000	0.000293
117	0.006270	0.000355	310	0.456000	0.005370
118	0.014100	0.000169	311	0.030200	0.003960
119	0.006120	0.000169	312	1.130000	0.008940
120	0.011600	0.000294	313	0.217000	0.004130
121	0.009940	0.000169	314	3.860000	0.000572
122	0.007940	0.000169	315	0.469000	0.000641

123	0.065600	0.000282	316	0.104000	0.000924
124	0.123000	0.000278	317	0.043900	0.000991
125	0.015400	0.000518	318	0.037700	0.000716
126	0.014900	0.000359	319	0.024900	0.000747
127	0.003640	0.000391	320	0.026400	0.000611
128	0.008360	0.000610	321	0.038700	0.000864
129	0.004490	0.000367	322	0.028600	0.000843
130	0.288000	0.000535	323	0.025300	0.000885
131	0.069900	0.000474	324	0.047300	0.001040
132	0.008460	0.000441	325	0.014000	0.001080
133	0.012000	0.000626	326	0.018300	0.000626
134	0.016900	0.000361	327	0.012600	0.000655
135	0.033900	0.000293	328	0.012200	0.000614
136	0.020400	0.000635	329	0.024200	0.000616
137	0.017600	0.000459	330	0.031700	0.000887
138	0.021800	0.000445	331	0.024900	0.000830
139	0.012000	0.000473	332	0.021900	0.000699
140	0.011000	0.008870	333	0.050900	0.000631
141	1.240000	0.075200	334	0.018200	0.000578
142	1.560000	0.032800	335	0.210000	0.001020
143	0.017000	0.031100	336	0.077300	0.000494
144	0.014600	0.034400	337	0.050000	0.000522
145	0.040600	0.058100	338	0.027600	0.000520
146	0.065900	0.109000	339	0.017900	0.000663
147	0.034600	0.001470	340	0.017600	0.000722
148	0.042900	0.020100	341	0.035100	0.000727
149	0.020700	0.054300	342	0.013100	0.000698
150	0.006530	0.043800	343	0.006180	0.000728
151	0.017400	0.043600	344	0.037800	0.000569
152	0.087600	0.101000	345	0.009540	0.000392
153	0.266000	0.122000	346	0.030800	0.000457
154	0.524000	0.016100	347	0.066200	0.000940
155	0.294000	0.044000	348	0.015300	0.000628
156	0.396000	0.084300	349	0.059500	0.000738
157	1.070000	0.192000	350	0.004620	0.000642
158	2.900000	0.224000	351	0.037100	0.000765
159	0.137000	0.061200	352	0.095800	0.000615
160	0.074500	0.070800	353	0.088200	0.000472
161	0.128000	0.059700	354	0.082800	0.000837
162	0.144000	0.071000	355	0.115000	0.000986
163	0.166000	0.083100	356	0.067700	0.000878
164	0.987000	0.124000	357	0.017700	0.001140
165	0.035200	0.068300	358	0.015900	0.000815
166	2.270000	0.206000	359	0.021300	0.000869
167	3.740000	0.204000	360	0.022000	0.000782

168	2.940000	0.171000	361	0.037400	0.000988
169	0.033700	0.067900	362	0.015200	0.000832
170	0.091500	0.089800	363	0.010400	0.000798
171	0.019700	0.037900	364	0.036900	0.000334
172	0.286000	0.170000	365	0.050100	0.001050
173	0.524000	0.154000	366	0.035100	0.000681
174	2.100000	0.158000	367	0.033700	0.000735
175	0.664000	0.161000	368	0.064000	0.000635
176	0.165000	0.111000	369	0.018300	0.000479
177	0.060400	0.091300	370	0.030535	0.000555
178	0.247000	0.065200	371	0.056700	0.000438
179	0.099200	0.070700	372	0.016600	0.000633
180	0.304000	0.123000	373	0.022400	0.000576
181	0.284000	0.128000	374	0.023900	0.000973
182	0.140000	0.104000	375	0.006720	0.000679
183	1.040000	0.185000	376	0.003220	0.000468
184	0.625000	0.078900	377	0.016200	0.000632
185	0.081300	0.044100	378	0.077100	0.000632
186	0.098900	0.118000	379	0.015900	0.000432
187	0.010200	0.027300	380	0.109000	0.000883
188	0.020500	0.049900	381	0.015100	0.001130
189	0.006910	0.026900	382	0.065800	0.000657
190	1.910000	0.103000	383	0.103000	0.000859
191	0.743000	0.184000	384	0.028800	0.000497
192	0.047300	0.072300	385	0.055100	0.001240
193	0.040200	0.054000	528	0.026200	0.017300

nd =无数据

[0345] NAMPT 细胞增殖测定

将 PC3 细胞以 500 个细胞 / 孔接种在 96 孔黑色板 (Corning#3904) 中的含有 10％热灭活 FBS 的 90μl RPMI 培养基中并在 37℃和 5％ CO_2下温育过夜以允许细胞粘附到孔上。第二天，在利用 RPMI 培养基稀释至 10X 和 1％ DMSO 之前将测试化合物在纯 DMSO 中连续稀释至 1000X 终浓度。然后将 10μL 的 10X 化合物转移到含有细胞的孔中以产生从 10μM 至 $1x10^{-5}$μM 的 10 倍稀释的剂量响应。将细胞在 37℃和 5％ CO_2下温育 5 天，然后使用 Cell Titer Glo 试剂 (Promega#G7571) 测定细胞活力。计算百分比抑制值并使用 Assay Explorer 软件拟合到 S 形剂量响应曲线上来确定 IC50s。为了评估细胞活力的抑制是否是由于 NAMPT 抑制，还在存在 0.3mM 烟酰胺单核苷酸的情况下进行增殖测定。

[0346] 表 2 显示了细胞增殖测定的结果。

表 2

实施例	细胞滴度-Glo - IC50 (μM)	实施例	细胞滴度-Glo - IC50 (μM)	实施例	细胞滴度-Glo - IC50 (μM)	实施例	细胞滴度-Glo - IC50 (μM)
1	0.00656	258	0.309	515	0.00085	772	0.0636
2	>10	259	0.0726	516	0.00226	773	0.0857
3	7.33	260	0.0746	517	0.00921	774	0.00252
4	0.112	261	0.0715	518	0.00087	775	0.00215
5	0.00675	262	0.119	519	0.00321	776	0.00764
6	0.0677	263	0.0595	520	0.00047	777	0.0192
7	0.876	264	0.1	521	0.00472	778	0.0197
8	0.0708	265	0.0701	522	0.00078	779	0.00148
9	0.739	266	0.083	523	0.00099	780	0.00407
10	0.00184	267	0.622	524	0.00573	781	0.01
11	0.0227	268	0.0829	525	0.00093	782	0.0669
12	0.0844	269	0.0604	526	0.00094	783	0.00646
13	0.0791	270	0.0627	527	0.00778	784	0.016
14	0.0548	271	0.0515	528	0.01923	785	0.00117
15	0.0347	272	0.0795	529	0.00933	786	0.012
16	0.0926	273	0.634	530	0.00202	787	0.0639
17	0.0937	274	0.107	531	0.0176	788	0.00759
18	0.148	275	0.683	532	0.00724	789	0.0284
19	0.0564	276	0.13	533	0.0246	790	0.0746
20	0.00028	277	0.0731	534	0.00546	791	0.00748
21	0.15	278	0.0791	535	0.00939	792	0.0088
22	0.00125	279	0.00972	536	0.00614	793	0.329
23	0.0725	280	0.0719	537	0.0033	794	0.196
24	0.169	281	0.0169	538	0.0137	795	0.773
25	0.00141	282	0.629	539	0.00257	796	0.0117
26	0.000682	283	0.0725	540	0.00391	797	0.0126
27	>10	284	0.0666	541	0.0042	798	0.0664
28	>10	285	0.0692	542	0.0676	799	0.0255
29	0.135	286	0.074	543	0.0077	800	0.06
30	0.00197	287	0.121	544	0.00717	801	0.024555
31	0.0069	288	0.0248	545	0.0152	802	0.0263
32	0.00654	289	0.0532	546	0.00141	803	0.00161
33	0.00366	290	0.0807	547	0.00302	804	0.00792
34	0.0068	291	0.0736	548	0.0649	805	0.065
35	0.00692	292	0.0934	549	0.00067	806	0.00313
36	0.00966	293	0.0723	550	0.00821	807	0.00415
37	0.00648	294	0.0832	551	0.00048	808	0.0411
38	0.00639	295	0.0715	552	0.00332	809	0.0024
39	0.00738	296	0.0689	553	0.0441	810	0.0611
40	0.00217	297	0.0932	554	0.00263	811	0.011
41	0.00376	298	0.0979	555	0.0239	812	0.0102

42	0.0646	299	0.0846	556	0.00598	813	0.0786
43	0.00688	300	0.0259	557	0.0102	814	0.0819
44	0.00547	301	0.0905	558	0.00066	815	0.185
45	0.00677	302	0.0824	559	0.00133	816	0.188
46	0.00301	303	0.0586	560	0.00585	817	0.0641
47	0.00335	304	0.0332	561	0.0622	818	0.0294
48	0.00288	305	0.102	562	0.00945	819	0.00856
49	0.00696	306	0.0347	563	0.0242	820	0.0754
50	0.00895	307	0.0208	564	0.0792	821	0.165
51	0.00362	308	0.0614	565	0.0741	822	0.0605
52	0.00628	309	8.2	566	0.0822	823	0.247
53	0.00367	310	0.0161	567	0.0765	824	0.0706
54	0.00331	311	0.0029	568	0.0482	825	0.0623
55	0.0211	312	0.0217	569	0.207	826	0.0983
56	0.00927	313	0.00603	570	0.631	827	0.0737
57	0.00875	314	0.621	571	0.118	828	0.000826
58	0.00648	315	0.0868	572	0.0598	829	0.00295
59	0.00614	316	0.00312	573	0.0819	830	0.00796
60	0.00507	317	0.00183	574	0.0553	831	0.00725
61	0.00352	318	0.00272	575	0.269	832	0.0167
62	0.0142	319	0.00124	576	0.0848	833	0.00667
63	0.00635	320	0.00237	577	0.093	834	0.0144
64	0.00632	321	0.00321	578	0.0887	835	0.00235
65	0.00638	322	0.00214	579	0.267	836	0.658
66	0.00581	323	0.00281	580	0.078	837	0.769
67	0.386	324	0.00708	581	0.0807	838	1.77
68	0.00354	325	0.00128	582	0.627	839	2
69	0.00422	326	0.00577	583	0.0874	840	0.0028
70	0.00397	327	0.00123	584	0.0872	841	0.00355
71	0.0729	328	0.00159	585	0.283	842	0.000665
72	0.00569	329	0.00283	586	0.107	843	0.00061
73	1.98	330	0.00138	587	0.0814	844	0.00252
74	0.0114	331	0.00209	588	0.113	845	0.00209
75	nd	332	0.00099	589	0.0979	846	0.00724
76	0.0191	333	0.00568	590	0.0822	847	0.115
77	nd	334	0.00097	591	0.0936	848	0.609
78	0.0212	335	0.00607	592	0.62	849	0.685
79	nd	336	0.00826	593	0.0634	850	0.0705
80	0.0255	337	0.00694	594	0.0478	851	0.00275
81	nd	338	0.00111	595	0.0806	852	0.0124
82	0.00955	339	0.00183	596	0.0846	853	>10
83	nd	340	0.00242	597	0.117	854	>10
84	0.0389	341	0.00198	598	0.208	855	0.747
85	0.0205	342	0.0023	599	0.0797	856	0.729
86	0.0697	343	0.00653	600	0.219	857	0.00252

87	0.0317	344	0.0089	601	0.0968	858	0.00436
88	0.0663	345	0.00199	602	0.002	859	0.0027
89	0.0646	346	0.0038	603	0.576	860	0.01
90	0.0601	347	0.00806	604	8.26127	861	0.00758
91	0.0599	348	0.002	605	1.4	862	0.00849
92	0.024	349	0.00728	606	0.0867	863	0.00567
93	0.0584	350	0.00075	607	7.65	864	0.00529
94	0.0657	351	0.00236	608	0.712	865	0.00406
95	0.0739	352	0.00888	609	0.00205	866	0.00792
96	7.61	353	0.00715	610	0.0079	867	0.00784
97	0.922	354	0.00751	611	0.09	868	0.00229
98	0.00605	355	0.00979	612	0.0536	869	0.00198
99	0.00572	356	0.00909	613	0.70691	870	0.0032
100	0.00613	357	0.00147	614	7.66	871	0.00361
101	0.00031	358	0.00186	615	6.15	872	0.0236
102	0.00059	359	0.00177	616	7.29	873	0.675
103	0.00144	360	0.00235	617	1.87	874	0.0711
104	0.00018	361	0.00277	618	>10	875	>10
105	0.00617	362	0.00261	619	>10	876	0.0292
106	0.0618	363	0.0056	620	2.83	877	0.02960
107	0.00688	364	0.00863	621	>10	878	0.0706
108	0.00013	365	0.00784	622	>10	879	0.00583
109	0.00066	366	0.00657	623	6.17	880	0.01540
110	0.00026	367	0.00638	624	>10	881	0.00818
111	0.00064	368	0.0077	625	1.9	882	0.00643
112	0.00076	369	0.00214	626	5.22	883	0.0309
113	0.00634	370	0.00879	627	0.853	884	0.00275
114	0.0181	371	0.00894	628	>10	885	0.00163
115	0.0004	372	0.00706	629	5.01	886	0.00766
116	0.00064	373	0.00595	630	0.00812	887	0.00847
117	0.00063	374	0.00632	631	0.00958	888	0.00976
118	0.00022	375	0.00087	632	0.00881	889	0.00285
119	0.00019	376	0.00062	633	0.00895	890	0.00409
120	0.00023	377	0.00213	634	0.00922	891	0.0656
121	0.00062	378	0.00709	635	0.0416	892	0.146
122	0.00061	379	0.00107	636	0.0828	893	0.681
123	0.00103	380	0.00757	637	0.00124	894	0.752
124	0.00144	381	0.00187	638	0.0299	895	0.00215
125	0.00024	382	0.00899	639	0.00816	896	0.00109
126	0.00026	383	0.0627	640	0.00292	897	0.00156
127	0.00014	384	0.00827	641	0.0726	898	.000851
128	0.00016	385	0.0232	642	0.00726	899	.000401
129	0.00016	386	0.00318	643	0.00846	900	0.00224
130	0.00181	387	0.0022	644	0.00823	901	0.00207
131	0.0003	388	0.00088	645	0.0033	902	0.00645

132	0.00023	389	0.00717	646	0.0587	903	.000618
133	0.00062	390	0.0015	647	0.00573	904	0.00195
134	0.00064	391	0.00599	648	0.0268	905	0.0133
135	0.0003	392	0.00354	649	0.00111	906	.000879
136	0.00023	393	0.00372	650	0.0869	907	6.75
137	0.00031	394	0.00199	651	0.0276	908	0.0925
138	0.00023	395	0.00214	652	0.00614	909	0.067
139	0.00018	396	0.06848	653	0.00972	910	0.00651
140	0.00354	397	0.00335	654	0.00276	911	>10
141	0.834	398	0.00819	655	0.000475	912	0.0642
142	0.7406	399	0.00635	656	0.061	913	0.0663
143	0.00496	400	0.0068	657	0.00844	914	0.0027
144	0.0184	401	0.00854	658	0.0144	915	0.139
145	0.0709	402	0.00168	659	0.0112	916	0.646
146	0.0707	403	0.0041	660	0.00523	917	0.101
147	0.00095	404	0.0027	661	0.0216	918	0.717
148	0.0761	405	0.00675	662	0.0159	919	0.0519
149	0.058	406	0.00742	663	0.0316	920	0.00543
150	0.0589	407	0.00101	664	1.15	921	0.0029
151	0.0609	408	0.0299	665	7.62	922	0.00338
152	0.116	409	0.00672	666	0.008059	923	0.0694
153	0.699	410	0.00868	667	0.01248	924	0.00117
154	0.803	411	0.00715	668	>10	925	0.0101
155	0.701	412	0.00137	669	0.00188	926	0.602
156	0.712	413	0.01	670	0.00853	927	0.0039
157	0.948	414	0.0074	671	0.00853	928	0.00256
158	1.3	415	0.00228	672	0.00405	929	0.0271
159	0.182	416	0.00112	673	0.0116	930	0.0027
160	0.173	417	0.00645	674	0.00572	931	0.00317
161	0.213	418	0.00826	675	0.0693	932	0.00582
162	0.225	419	0.00217	676	0.00202	933	0.00239
163	0.12	420	0.00235	677	0.0093	934	0.00245
164	0.202	421	0.00372	678	0.00609	935	0.002
165	0.0682	422	0.00112	679	0.0006	936	0.00218
166	1.07	423	0.00038	680	0.00355	937	0.00262
167	6.25	424	0.0015	681	0.00902	938	0.00875
168	1.01	425	0.00091	682	0.00273	939	0.00296
169	0.0654	426	0.00207	683	0.00902	940	0.00197
170	0.0655	427	0.00203	684	0.0766	941	0.0021
171	0.0681	428	0.00019	685	0.00828	942	0.00276
172	0.329	429	0.0008	686	0.0649	943	0.0076
173	0.627	430	0.00142	687	0.00611	944	0.00714
174	1.13	431	0.00167	688	0.0094	945	0.00451
175	0.683	432	0.008	689	0.00968	946	0.00289
176	0.218	433	0.00577	690	0.00314	947	0.00256

177	0.107	434	0.00635	691	0.03	948	0.00226
178	0.3	435	0.0003	692	0.00423	949	0.00595
179	0.192	436	0.00067	693	0.0136	950	0.00606
180	0.164	437	0.00098	694	0.0716	951	0.00277
181	0.238	438	0.00196	695	0.00616	952	0.00217
182	0.0879	439	0.00336	696	0.00467	953	0.00334
183	0.346	440	0.0018	697	0.00596	954	0.00638
184	0.604	441	0.00683	698	0.0679	955	0.00597
185	0.0742	442	0.00625	699	0.065	956	0.00640
186	0.627	443	0.00565	700	0.00876	957	0.00193
187	0.0206	444	0.078	701	0.0752	958	0.00263
188	0.0224	445	0.0191	702	0.00207	959	0.00233
189	0.0146	446	0.108	703	0.00843	960	0.00286
190	0.694	447	0.903	704	0.0053	961	0.00557
191	0.677	448	0.00932	705	0.0202	962	0.0024
192	0.0693	449	0.678	706	0.0077	963	0.00214
193	0.071	450	0.0509	707	0.00693	964	0.00184
194	0.124	451	0.0868	708	0.0142	965	0.00260
195	0.701	452	0.0632	709	0.0145	966	0.00323
196	0.111	453	0.105	710	0.0103	967	0.00305
197	0.103	454	0.106	711	0.0595	968	0.0037
198	0.0716	455	0.458	712	0.00679	969	.000347
199	0.0974	456	0.0395	713	0.00999	970	0.0285
200	0.0719	457	0.142	714	0.0176	971	0.0708
201	0.0609	458	0.0644	715	0.0118	972	0.667
202	0.168	459	0.0369	716	0.0692	973	0.00553
203	0.606	460	0.223	717	0.0121	974	0.00784
204	0.0245	461	0.646	718	0.00627	975	0.098
205	0.0387	462	0.214	719	0.00963	976	0.0612
206	0.0674	463	0.0709	720	0.00857	977	0.0124
207	0.671	464	0.0659	721	0.00839	978	1.07
208	0.593	465	0.616	722	0.0848	979	0.072
209	0.0816	466	0.00807	723	0.003507	980	0.0822
210	0.0627	467	0.0156	724	0.0809	981	1.06
211	0.00594	468	0.73	725	0.00401	982	0.0835
212	0.00579	469	0.00861	726	0.0327	983	0.604
213	0.00688	470	0.715	727	0.0046	984	0.696
214	0.00909	471	0.072	728	0.00697	985	0.635
215	0.00695	472	0.00656	729	0.0135	986	7.47
216	0.00599	473	0.0093	730	0.00681	987	0.609
217	0.00255	474	0.0685	731	0.00050	988	1.24
218	0.00886	475	0.594	732	0.0299	989	0.602
219	0.00886	476	0.0174	733	0.0375	990	6.81
220	0.0132	477	0.235	734	0.00833	991	0.76
221	0.00899	478	0.0143	735	0.0689	992	1.51

222	0.0155	479	0.0689	736	0.00809	993	0.809
223	0.0055	480	0.00424	737	1.86	994	0.059
224	0.00752	481	0.0121	738	0.853926	995	0.245
225	0.00876	482	0.0326	739	7.31	996	0.104
226	0.00889	483	0.00214	740	0.914369	997	0.0935
227	0.00453	484	0.00056	741	0.181262	998	1.28
228	0.00597	485	0.00635	742	0.734	999	0.25
229	0.00646	486	0.00624	743	6.62	1000	0.077
230	0.00905	487	0.072	744	2.72	1001	0.0532
231	0.00875	488	0.0642	745	>10	1002	0.911
232	0.00874	489	0.00207	746	>10	1003	1.07
233	0.00873	490	0.00068	747	5.92	1004	7.92
234	0.0105	491	0.00845	748	0.00258	1005	0.592
235	0.0124	492	0.00373	749	>10	1006	0.00536
236	0.00925	493	0.00673	750	0.226	1007	0.0567
237	0.0103	494	0.00105	751	0.00271	1008	0.299
238	0.0157	495	0.00706	752	2.45	1009	0.0818
239	0.0067	496	0.0063	753	0.00892	1010	0.0709
240	0.0103	497	0.0234	754	0.0948	1011	0.113
241	0.00773	498	0.00664	755	0.19	1012	0.782
242	0.00906	499	0.0121	756	0.00908	1013	0.213
243	0.00928	500	0.00102	757	0.0677	1014	0.219
244	0.0104	501	0.00607	758	0.857	1015	0.0901
245	0.00706	502	0.00474	759	0.0062	1016	0.212
246	0.00965	503	0.0582	760	0.253	1017	0.752
247	0.00798	504	0.00775	761	0.0923	1018	0.716
248	0.00658	505	0.00684	762	0.709	1019	2.46
249	0.00235	506	0.00128	763	0.00841	1020	7.27
250	0.00911	507	0.00834	764	0.022126	1021	0.0477
251	0.00787	508	0.00079	765	1.02	1022	8.16
252	0.00951	509	0.00119	766	0.787	1023	0.508
253	0.00809	510	0.0664	767	1.28	1024	nd
254	0.012	511	0.00082	768	0.111	1025	nd
255	0.0241	512	0.0155	769	0.0186		
256	0.145	513	0.0035	770	0.138		
257	0.0761	514	0.00032	771	0.0699		

nd =无数据

[0347] 抑制NAMPT的化合物用于治疗其中牵涉NF-KB激活的疾病。此类方法用于治疗多种疾病，包括炎性和组织修复病症；尤其是类风湿关节炎、炎性肠病、哮喘和COPD（慢性阻塞性肺病）、骨关节炎、骨质疏松和纤维化病；皮肤病，包括银屑病、特应性皮炎和紫外线引起的皮肤损伤；自身免疫性疾病包括全身性红斑狼疮、多发性硬化、银屑病关节炎、强直性脊柱炎、组织和器官排斥、阿尔茨海默氏病、中风、动脉粥样硬化、再狭窄、糖尿病、肾小球肾炎、癌症，特别是其中所述癌症选自乳腺癌、前列腺癌、肺癌、结肠癌、宫颈癌、卵巢癌、皮肤癌、中枢神经系统癌、膀胱癌、胰腺癌、白血病、淋巴瘤或霍奇金氏病、恶病质、与感染和某些病毒感染相关的炎症，包括获得性免疫缺陷综合征（AIDS）、成人呼吸窘迫综合征和共济失调毛细血管扩张。

[0348] 在WO 97/48696中描述了NAMPT参与治疗癌症。在WO 97/48397中描述了

NAMPT 参与免疫抑制。在 WO 2003/80054 中描述了 NAMPT 参与治疗涉及血管发生的疾病。在 WO 2008/025857 中描述了 NAMPT 参与治疗类风湿性关节炎和败血症性休克。在 WO 2009/109610 中描述了 NAMPT 参与预防和治疗局部缺血 (ischaemia)。

[0349] 癌症包括但不限于血液和实体肿瘤类型，如听神经瘤、急性白血病、急性成淋巴细胞性白血病、急性骨髓性白血病（单核细胞白血病、成髓细胞白血病、腺癌、血管肉瘤、星形细胞瘤、髓性单核细胞白血病和前髓细胞性白血病）、急性 t 细胞白血病、基底细胞癌、胆管癌、膀胱癌、脑癌、乳腺癌（包括雌激素 - 受体阳性乳腺癌）、支气管癌、伯基特氏肿瘤、宫颈癌、软骨肉瘤、脊索瘤、绒毛膜癌、慢性白血病、慢性淋巴细胞性白血病、慢性髓细胞性（粒细胞性）白血病、慢性髓细胞性白血病、结肠癌、结肠直肠癌、颅咽管瘤、囊腺癌、异常增生性变化（发育异常和组织变形）、胚胎性癌、子宫内膜癌、内皮肉瘤、室管膜瘤、上皮癌、红白血病、食道癌、雌激素 - 受体阳性乳腺癌、特发性血小板增多症、尤因瘤、纤维肉瘤、胃癌、生殖细胞睾丸癌、妊娠性滋养层细胞病、恶性胶质瘤、头和颈部癌、重链病、成血管细胞瘤、肝瘤、肝细胞癌、激素非敏感性前列腺癌、平滑肌肉瘤、脂肉瘤、肺癌（包括小细胞肺癌和非小细胞肺癌）、淋巴管内皮 - 肉瘤、淋巴管肉瘤、成淋巴细胞性白血病、淋巴瘤（淋巴瘤，包括弥漫性大 B 细胞淋巴瘤、滤泡性淋巴瘤、霍杰金淋巴瘤和非霍杰金淋巴瘤）、膀胱、乳房、结肠、肺、卵巢、胰腺、前列腺、皮肤和子宫的恶性肿瘤和超增生性病症、T 细胞或 B 细胞源的淋巴恶性肿瘤、白血病、髓样癌、成神经管细胞瘤、黑色素瘤、脑膜瘤、间皮瘤、多发性骨髓瘤、髓细胞性白血病、骨髓瘤、粘液肉瘤、成神经细胞瘤、寡枝神经胶质细胞瘤、口腔癌、骨肉瘤、卵巢癌、胰腺癌、乳头状腺癌、乳头状癌、外围 T 细胞淋巴瘤、松果体瘤、真性红细胞增多症、前列腺癌（包括激素非敏感性（难治疗的）前列腺癌）、直肠癌、肾细胞癌、成视网膜细胞瘤、横纹肌肉瘤、肉瘤、皮脂腺癌、精原细胞瘤、皮肤癌、小细胞肺癌、实体瘤（癌和肉瘤）、胃癌、鳞状细胞癌、滑膜瘤、汗腺癌、睾丸癌（包括生殖细胞睾丸癌）、甲状腺癌、瓦尔登斯特伦巨球蛋白血症、睾丸瘤、子宫癌、维尔姆斯瘤等。

[0350] 方案和实验

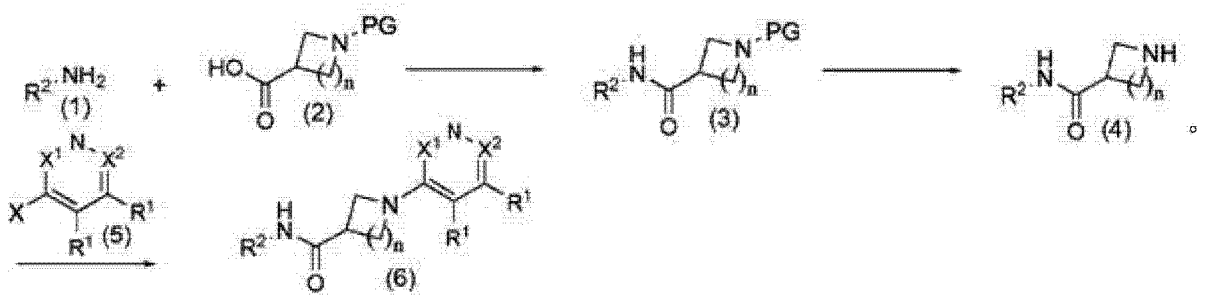
以下缩写具有所指出的含义。ADDP 是指 1,1′ -（偶氮二羰基）二哌啶 ;AD- 混合 (mix)-β 是指 $(DHQD)_2PHAL$、$K_3Fe(CN)_6$、K_2CO_3和 K_2SO_4的混合物 ;9-BBN 是指 9- 硼杂二环 (3.3.1) 壬烷 ;Boc 是指叔丁氧羰基 ;$(DHQD)_2PHAL$ 是指氢化奎尼定 1,4- 酞嗪二基乙醚 ;DBU 是指 1,8- 二氮杂双环 [5.4.0] 十一碳 -7- 烯 ;DIBAL 是指氢化二异丁基铝 ;DIEA 是指二异丙基乙胺 ;DMAP 是指 N,N- 二甲基氨基吡啶 ;DMF 是指 N,N- 二甲基甲酰胺 ;dmpe 是指 1,2- 双（二甲基膦基）乙烷 ;DMSO 是指二甲亚砜 ;dppb 是指 1,4- 双（二苯基膦基）- 丁烷 ;dppe 是指 1,2- 双（二苯基膦基）乙烷 ;dppf 是指 1,1′ - 双（二苯基膦基）二茂铁 ;dppm 是指 1,1- 双（二苯基膦基）甲烷 ;EDAC•HCl 是指 1-(3- 二甲基氨基丙基)-3- 乙基碳二亚胺盐酸盐 ;Fmoc 是指芴基甲氧基羰基 ;HATU 是指 O-(7- 氮杂苯并三唑 -1- 基)-N,N′ N′ N′ - 四甲基脲鎓六氟磷酸盐 ;HMPA 是指六甲基磷酰胺 ;IPA 是指异丙醇 ;MP-BH_3是指大孔的三乙铵甲基聚苯乙烯氰基硼氢化物 ;TEA 是指三乙胺 ;TFA 是指三氟乙酸 ;THF 是指四氢呋喃 ;NCS 是指 N- 氯琥珀酰亚胺 ;NMM 是指 N- 甲基吗啉 ;NMP 是指 N- 甲基吡咯烷 ;PPh_3是指三苯膦。

[0351] 呈现以下方案以提供据信是本发明的程序和概念方面的最有用的且易于理解的描述的内容。本发明的化合物可以通过合成化学方法来制备，其实例显示在本文中。应该理解的是方法中的步骤的顺序可以改变，试剂、溶剂和反应条件可以替换特别提及的那些，

并且根据需要可以保护和去保护不稳定部分。

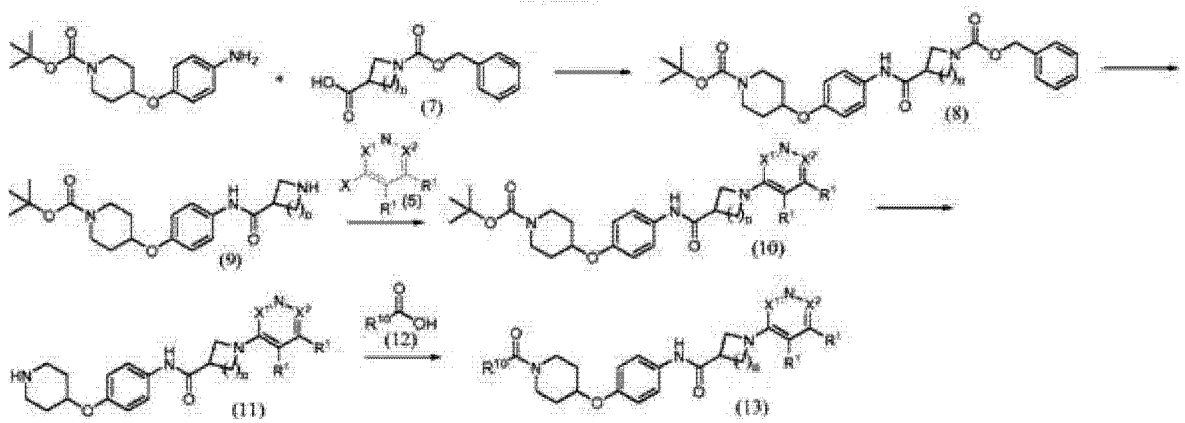
[0352] 方案

方案1



[0353] 如方案 1 中所示，式 (1) 的化合物（其中 R^2如本文所述）可以与式 (2) 的酸（其中 PG 是合适的保护基团并且 n 是 1、2 或 3）在存在碱，如但不限于二异丙基乙胺的情况下反应，以提供式 (3) 的化合物。反应可以涉及使用羧基活化剂，如但不限于 N-(3- 二甲基氨基丙基)-N' - 乙基碳二亚胺盐酸盐，和酯活化剂，如但不限于 1- 羟基苯并三唑水合物。通常在溶剂，如但不限于 N,N- 二甲基甲酰胺、N,N- 二甲基乙酰胺或其混合物中于室温下进行反应。可以在使用本领域技术人员已知的并且可以在文献中容易得到的标准反应条件去除合适的保护基团后从式 (3) 的化合物制备式 (4) 的化合物。式 (5) 的化合物（其中 X^1、X^2和 R^1如本文所述并且 X 是适当的卤化物）可以与式 (4) 的化合物反应以提供式 (6) 的化合物，其代表式 (I) 的化合物。该 C-N 交叉偶联反应通常使用碱，如但不限于碳酸铯，钯催化剂，如但不限于双（二亚苄基丙酮）钯 (0)，和配体，如但不限于 (9,9- 二甲基 -9H- 氧杂蒽 -4,5- 二基）双（二苯基磷）。通常在溶剂，如但不限于二噁烷中于升高的温度下进行反应。

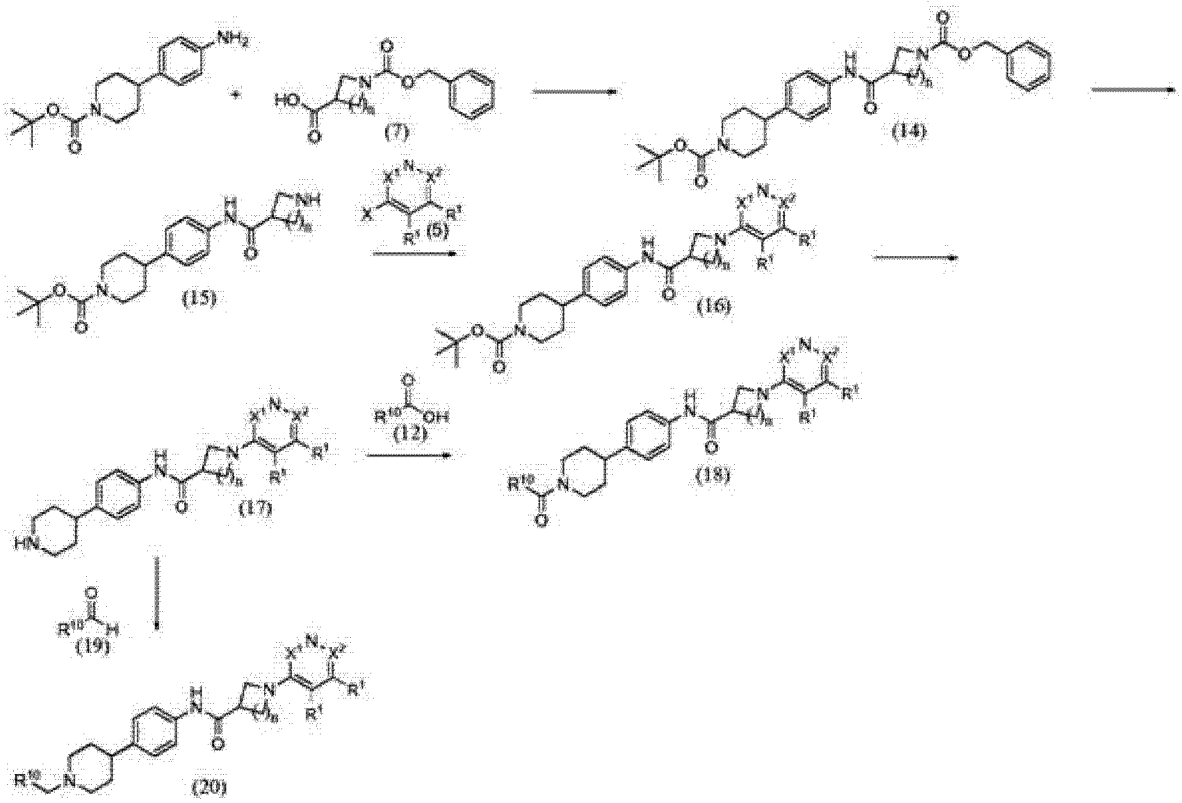
方案2



[0354] 叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯可以与式 (7) 的酸（其中 n 是 1、2 或 3）在存在碱，如但不限于二异丙基乙胺的情况下反应以提供式 (8) 的化合物。反应可以涉及使用羧基活化剂，如但不限于 N-(3- 二甲氨基丙基)-N' - 乙基碳二亚胺盐酸盐，和酯活化剂，如但不限于 1- 羟基苯并三唑水合物。通常在溶剂，如但不限于 N, N- 二甲基甲酰胺、N, N- 二甲基乙酰胺或其混合物中于室温下进行反应。可以在存在氢氧化钯的情况下通过使式 (8) 的化合物与氢反应从中来制备式 (9) 的化合物。通常在溶剂，如但不限于四氢呋喃中于室温下进行反应。式 (5) 的化合物（其中 X^1、X^2和 R^1如本文所述并且 X 是适当的卤化物）可以与式 (9) 的化合物反应以提供式 (10) 的化合物。该 C-N 交叉偶联反应通常使

用碱，如但不限于碳酸铯，钯催化剂，如但不限于双（二亚苄基丙酮）钯 (0)，和配体，如但不限于 (9,9- 二甲基 -9H- 氧杂蒽 -4,5- 二基）双（二苯基磷）。通常在溶剂，如但不限于二噁烷中于升高的温度下进行反应。可以通过在溶剂，如但不限于二氯甲烷中，利用酸，如但不限于三氟乙酸处理式 (10) 的化合物来制备式 (11) 的化合物。可以在存在碱，如但不限于二异丙基乙胺的情况下，通过使式 (11) 的化合物与式 (12) 的化合物（其中 R^{10} 如本文所述）反应来制备式 (13) 的化合物，其代表式 (I) 的化合物。反应可以涉及使用羧基活化剂，如但不限于 N-(3- 二甲基氨基丙基)-N'- 乙基碳二亚胺盐酸盐，和酯活化剂，如但不限于 1- 羟基苯并三唑水合物。通常在溶剂，如但不限于 N,N- 二甲基甲酰胺、N,N- 二甲基乙酰胺或其混合物中于室温下进行反应。

方案3



[0355] 如方案 3 中所示，叔丁基 4-(4- 氨基苯基）哌啶 -1- 甲酸酯可以与式 (7) 的酸（其中 n 是 1、2 或 3）在存在碱，如但不限于二异丙基乙胺的情况下反应以提供式 (14) 的化合物。反应可以涉及使用羧基活化剂，如但不限于 N-(3- 二甲基氨基丙基)-N'- 乙基碳二亚胺盐酸盐，和酯活化剂，如但不限于 1- 羟基苯并三唑水合物。通常在溶剂，如但不限于 N,N- 二甲基甲酰胺、N,N- 二甲基乙酰胺或其混合物中于室温下进行反应。可以在存在氢氧化钯的情况下通过使式 (14) 的化合物与氢反应从中来制备式 (15) 的化合物。通常在溶剂，如但不限于四氢呋喃中于室温下进行反应。式 (5) 的化合物（其中 X^1、X^2 和 R^1 如本文所述并且 X 是适当的卤化物）可以与式 (15) 的化合物反应以提供式 (16) 的化合物。该 C-N 交叉偶联反应通常使用碱，如但不限于碳酸铯，钯催化剂，如但不限于双（二亚苄基丙酮）钯 (0)，和配体，如但不限于 (9,9- 二甲基 -9H- 氧杂蒽 -4,5- 二基）双（二苯基磷）。通常在溶剂，如但不限于二噁烷中于升高的温度下进行反应。可以通过在溶剂，如但不限于二氯甲烷中，利用酸，如但不限于三氟乙酸处理式 (16) 的化合物来制备式 (17) 的化合物。可以在

存在碱，如但不限于二异丙基乙胺的情况下，通过使式 (17) 的化合物与式 (12) 的化合物（其中 R^{10} 如本文所述）反应来制备式 (18) 的化合物，其代表式 (I) 的化合物。反应可以涉及使用羧基活化剂，如但不限于 N-(3- 二甲基氨基丙基)-N'- 乙基碳二亚胺盐酸盐，和酯活化剂，如但不限于 1- 羟基苯并三唑水合物。通常在溶剂，如但不限于 N,N- 二甲基甲酰胺、N,N- 二甲基乙酰胺或其混合物中于室温下进行反应。或者，式 (17) 的化合物可以与式 (19) 的化合物（其中 R^{10} 如本文所述）反应以提供式 (20) 的化合物，其代表式 (I) 的化合物。通常在存在还原剂，如但不限于三乙酰氧基硼氢化钠和乙酸的情况下，在溶剂，如但不限于甲醇中进行反应并且可以在升高的温度下进行反应。

实施例

[0356] 呈现以下实施例以提供据信是本发明的程序和概念方面的最有用的且易于理解的描述的内容。使用 ACD/ChemSketch 版本 12.5(2011 年 4 月 20 日）或 (2012 年 9 月 3 日)，Advanced Chemistry Development Inc.，Toronto，Ontario)，或 ChemDraw® 版本 9.0.7(CambridgeSoft，Cambridge，MA) 来命名每个示例性的化合物和中间体。

[0357] 实验

实施例 1

1-（吡啶 -3- 基）-N-(4-{[1-（四氢 -2H- 吡喃 -4- 基乙酰基）哌啶 -4- 基］氧基｝苯基）氮杂环丁烷 -3- 甲酰胺

实施例 1A

叔丁基 4-(4-(1-（苄基氧基羰基）氮杂环丁烷 -3- 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯

将 1-（苄基氧基羰基）氮杂环丁烷 -3- 甲酸 (5.10g，21.67mmol)、1- 羟基苯并三唑水合物 (4.15g，27.1mmol) 和叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯 (5.28g，18.06mmol) 悬浮于二甲基甲酰胺 (25ml) 中，随后添加二异丙基乙胺 (9.64ml，54.2mmol) 和 N-(3- 二甲基氨基丙基)-N'- 乙基碳二亚胺盐酸化物 (5.19g，27.1mmol)。混合物在室温下搅拌过夜，并将溶液用水稀释。所获的混浊混合物用乙酸乙酯和随后乙酸乙酯 / 四氢呋喃萃取。将有机物合并并用硫酸镁干燥，过滤并浓缩以产生固体，所述固体与醚研磨并过滤以产生标题化合物。

[0358] 实施例 1B

叔丁基 4-(4-（氮杂环丁烷 -3- 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯

将叔丁基 4-(4-(1-（苄基氧基羰基）氮杂环丁烷 -3- 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯 (50mg，0.098mmol) 和四氢呋喃 (5ml) 加入在 50ml 耐压瓶中在碳 (10mg，0.071mmol) 上的 20％湿润的氢氧化钯中，并将混合物在 30psi 和室温下搅拌 16 小时。混合物经尼龙膜过滤并将滤液浓缩以产生标题化合物。

[0359] 实施例 1C

叔丁基 4-(4-(1-（吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯

将叔丁基 4-(4-（氮杂环丁烷 -3- 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯 (4.97g，13.24mmol)、碳酸铯 (10.78g，33.1mmol)、3- 溴吡啶 (1.307ml，13.24mmol)、(9，9- 二甲基 -9H- 氧杂蒽 -4，5- 二基）双（二苯膦）(0.764g，1.32mmol) 和双（二亚苄基丙酮）钯 (0) (0.606g，0.662mmol) 悬浮于二噁烷 (50ml)，用氮气发泡 30 分钟并在 100℃下加热过夜。

将混合物经具有二氯甲烷洗涤物的次乙酰塑料垫 (celite pad) 过滤并将滤液浓缩。正相色谱提供标题化合物。

[0360] 实施例 1D

N-(4-(哌啶 -4- 基氧基) 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺

将叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯 (3.82g,8.44mmol) 溶于 60ml 二氯甲烷中,冷却至 0℃并用三氟乙酸 (10ml) 处理。允许混合物加温至室温并搅拌 2 小时。真空下去除溶剂提供标题化合物。

[0361] 实施例 1E

1-(吡啶 -3- 基)-N-(4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 氧基 } 苯基) 氮杂环丁烷 -3- 甲酰胺如实施例 1A 中所述制备标题化合物,用 N-(4-(哌啶 -4- 基氧基) 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2-(四氢 -2H- 吡喃 -4- 基) 乙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 9.95(bs,1H),7.93(d, J = 4.2Hz,1H),7.88-7.83(m,1H),7.55-7.47(m,2H),7.26-7.08(m,1H),7.01-6.78(m,3H),4.14-4.04(m,2H),4.02-3.62(m,6H),2.37-1.73(m,6H),1.66-1.00(m,8H) ;MS(ESI(+))m/e 479$(M+H)^+$。

[0362] 表 1.

以下实施例基本上如实施例 1 中所述制备,代替实施例 1C 中的合适的溴吡啶和实施例 1E 中合适的羧酸。一些产物通过快速色谱纯化而其他通过反向 HPLC 纯化。因此,一些实施例分离为三氟乙酸盐。

实施例		名称	^{1}H NMR	MS
3		N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-[2-(三氟甲基)吡啶-3-基]氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.96 (s, 1H), 8.02 (dd, J = 4.3, 1.2 Hz, 1H), 7.55 – 7.45 (m, 3H), 7.15 (d, J = 8.5 Hz, 1H), 6.97 – 6.90 (m, 2H), 4.59 – 4.47 (m, 1H), 4.28 – 4.05 (m, 4H), 3.93 – 3.53 (m, 6H), 2.27 (d, J = 1.3 Hz, 2H), 2.00 – 1.78 (m, 4H), 1.64 – 1.38 (m, 5H), 1.39 – 1.04 (m, 3H)	(ESI(+)) m/e 547 $(M+H)^+$
4		1-(2-甲基吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.92 (s, 1H), 7.88 (dd, J = 4.7, 1.4 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.07 (dd, J = 8.0, 4.7 Hz, 1H), 6.97 – 6.92 (m, 1H), 6.94 – 6.81 (m, 2H), 4.58 – 4.47 (m, 1H), 4.10 (t, J = 7.7 Hz, 2H), 3.98 (t, J = 6.8 Hz, 2H), 3.93 – 3.50 (m, 6H), 3.29 – 3.14 (m, 2H), 2.35 (s, 3H), 2.26 (d, J = 6.9 Hz, 2H), 2.05 – 1.79 (m, 3H), 1.66 – 1.32 (m, 5H), 1.31 – 1.06 (m, 2H)	(ESI(+)) m/e 493 $(M+H)^+$
5		1-(4-甲基吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.93 (s, 1H), 7.90 (d, J = 4.7 Hz, 1H), 7.76 (s, 1H), 7.55 – 7.48 (m, 2H), 7.03 – 6.89 (m, 3H), 4.58 – 4.47 (m, 1H), 4.20 – 3.95 (m, 4H), 3.95 – 3.53 (m, 5H), 3.26 – 3.15 (m, 4H), 2.26 (d, J = 6.9 Hz, 2H), 2.18 (s, 3H), 2.05 – 1.78 (m, 3H), 1.66 – 1.35 (m, 4H), 1.32 – 1.08 (m, 2H)	(ESI(+)) m/e 493 $(M+H)^+$
6		1-(4-氟吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.93 (bs, 1H), 7.95 (t, J = 11.6 Hz, 2H), 7.55 – 7.47 (m, 2H), 7.16 (dd, J = 12.7, 5.2 Hz, 1H), 6.97 – 6.90 (m, 2H), 4.59 – 4.48 (m, 1H), 4.29 – 4.00 (m, 5H), 3.93 – 3.41 (m, 5H), 2.30 – 2.23 (m, 2H), 1.99 – 1.78 (m, 4H), 1.66 – 1.39 (m, 5H), 1.40 – 1.00 (m, 3H)	(ESI(+)) m/e 497 $(M+H)^+$
7		N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.93 (bs, 1H), 7.95 (t, J = 11.6 Hz, 2H), 7.55 – 7.47 (m, 2H), 7.16 (dd, J = 12.7, 5.2 Hz, 1H), 6.97 – 6.90 (m, 2H), 4.59 – 4.48 (m, 1H), 4.29 – 4.00 (m, 5H), 3.93 – 3.41 (m, 5H), 2.30 – 2.23 (m, 2H), 1.99 – 1.78 (m, 4H), 1.66 – 1.39 (m, 5H), 1.40 – 1.00 (m,	(ESI(+)) m/e 547 $(M+H)^+$

		[4-(三氟甲基)吡啶-3-基]氮杂环丁烷-3-甲酰胺	3H)	
31		N-(4-{[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.94 (s, 1H), 7.97 – 7.70 (m, 2H), 7.55 – 7.47 (m, 2H), 7.18 (dd, J = 8.2, 4.6 Hz, 1H), 7.00 – 6.78 (m, 3H), 5.39 (s, 1H), 4.58 – 4.41 (m, 1H), 4.09 (t, J = 7.8 Hz, 2H), 3.95 (t, J = 6.7 Hz, 2H), 3.78 – 3.47 (m, 2H), 1.99 – 1.82 (m, 2H), 1.62 – 1.34 (m, 2H), 1.35 – 1.02 (m, 8H)	(ESI(+)) m/e 439 $(M+H)^+$
32		N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.94 (s, 1H), 7.94 (d, J = 4.7 Hz, 1H), 7.86 (d, J = 2.8 Hz, 1H), 7.55 – 7.47 (m, 2H), 7.24 – 7.04 (m, 1H), 7.02 – 6.80 (m, 3H), 4.59 – 4.48 (m, 1H), 4.09 (t, J = 7.8 Hz, 2H), 4.03 – 3.62 (m, 5H), 3.38 (dd, J = 13.6, 6.6 Hz, 1H), 2.80 – 2.64 (m, 1H), 2.01 – 1.78 (m, 2H), 1.64 – 1.36 (m, 3H), 1.38 – 1.15 (m, 1H), 1.15 – 0.86 (m, 4H), 0.81 (t, J = 7.3 Hz, 3H)	(ESI(+)) m/e 437 $(M+H)^+$
33		1-(吡啶-3-基)-N-[4-({1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.94 (s, 1H), 7.98 – 7.82 (m, 2H), 7.55 – 7.48 (m, 2H), 7.20 (dd, J = 8.3, 4.6 Hz, 1H), 7.00 – 6.80 (m, 3H), 4.67 (t, J = 6.5 Hz, 1H), 4.53 (s, 1H), 4.10 (t, J = 7.8 Hz, 2H), 3.96 (t, J = 6.6 Hz, 2H), 3.89 – 3.58 (m, 4H), 3.46 – 3.08 (m, 4H), 2.12 – 1.68 (m, 5H), 1.66 – 1.38 (m, 2H)	(ESI(+)) m/e 451 $(M+H)^+$
34		N-{4-[(1-戊酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.39, 2.29 Hz, 1 H) 7.51 (d, J=9.16 Hz, 2 H) 6.96 (d, J=8.85 Hz, 2 H) 4.51 - 4.59 (m, 1 H) 4.25 (t, J=8.24 Hz, 2 H) 4.14 (dd, J=7.93, 5.80 Hz, 2 H) 3.80 - 3.90 (m, 1 H) 3.73 - 3.79 (m, 2 H) 3.31 - 3.41 (m, 1 H) 3.19 - 3.27 (m, 1 H) 2.29 - 2.36 (m, 2 H) 1.83 - 2.00 (m, 2 H) 1.53 - 1.62 (m, 1 H) 1.42 - 1.51 (m, 3 H) 1.24 - 1.35 (m, 2 H) 0.87 (t, 3 H)	(ESI(+)) m/e 437 $(M+H)^+$
35		N-[4-({1-[(2-甲基环丙基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.59 (dd, J=8.70, 1.98 Hz, 1 H) 7.52 (d, J=8.85 Hz, 2 H) 6.97 (d, J=8.85 Hz, 2 H) 4.51 - 4.62 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 5.80 Hz, 2 H) 3.79 - 4.01 (m, 2 H) 3.73 - 3.78 (m, 1 H) 3.46 - 3.54 (m, 1 H) 3.16 - 3.28 (m, 1 H) 1.89 (d, J=1.53 Hz, 2 H) 1.70 - 1.76 (m, 1 H) 1.53 (d, J=55.85 Hz, 2 H) 1.03 - 1.17 (m, 4 H) 0.89 - 0.97 (m, 1 H) 0.49 - 0.59 (m, 1 H)	(ESI(+)) m/e 435 $(M+H)^+$
36		N-[4-({1-	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12	(ESI(+))

		[(1S,4R)-双环[2.2.1]庚-2-基乙酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	(d, J=5.19 Hz, 1 H) 8.04 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.54, 2.14 Hz, 1 H) 7.47 - 7.54 (m, 2 H) 6.93 - 6.99 (m, 2 H) 4.49 - 4.58 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.10 - 4.16 (m, J=8.09, 5.95 Hz, 2 H) 3.81 - 3.89 (m, 1 H) 3.73 - 3.79 (m, 2 H) 3.18 - 3.39 (m, 2 H) 2.27 - 2.36 (m, 1 H) 2.11 - 2.21 (m, 2 H) 1.73 - 1.99 (m, 4 H) 1.38 - 1.60 (m, 5 H) 1.34 (d, J=9.77 Hz, 1 H) 0.97 - 1.19 (m, 4 H)	m/e 489 $(M+H)^+$
37		**N-(4-{[1-(4-甲基戊酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺**	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.19 Hz, 1 H) 8.04 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.70, 5.34 Hz, 1 H) 7.59 (dd, J=8.70, 1.98 Hz, 1 H) 7.47 - 7.54 (m, 2 H) 6.93 - 6.99 (m, 2 H) 4.51 - 4.57 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.10 - 4.16 (m, J=8.09, 5.95 Hz, 2 H) 3.80 - 3.87 (m, J=17.70 Hz, 1 H) 3.74 - 3.79 (m, 2 H) 3.17 - 3.38 (m, 2 H) 2.27 - 2.36 (m, J=8.85, 6.71 Hz, 2 H) 1.83 - 1.99 (m, J=22.89 Hz, 2 H) 1.32 - 1.62 (m, 5 H) 0.87 (d, J=6.41 Hz, 6 H)	(ESI(+)) m/e 451 $(M+H)^+$
38		**N-(4-{[1-(3-甲基戊酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺**	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.19 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.54, 2.14 Hz, 1 H) 7.49 - 7.53 (m, 2 H) 6.93 - 6.97 (m, 2 H) 4.51 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.83 - 3.91 (m, 1 H) 3.73 - 3.79 (m, 2 H) 3.19 - 3.39 (m, 2 H) 2.27 - 2.34 (m, 1 H) 2.10 - 2.18 (m, 1 H) 1.84 - 1.98 (m, 2 H) 1.73 - 1.81 (m, 1 H) 1.42 - 1.59 (m, 2 H) 1.29 - 1.39 (m, 1 H) 1.11 - 1.21 (m, 1 H) 0.82 - 0.89 (m, 6 H)	(ESI(+)) m/e 451 $(M+H)^+$
39		**N-(4-{[1-(3-乙氧基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺**	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.85, 1.83 Hz, 1 H) 7.51 (d, J=9.16 Hz, 2 H) 6.92 - 6.98 (m, 2 H) 4.49 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 5.80 Hz, 2 H) 3.80 - 3.89 (m, 1 H) 3.74 - 3.79 (m, 2 H) 3.59 (t, J=6.56 Hz, 2 H) 3.42 (q, J=7.02 Hz, 2 H) 3.20 - 3.38 (m, 2 H) 2.55 - 2.63 (m, 2 H) 1.83 - 1.99 (m, 2 H) 1.41 - 1.63 (m, 2 H) 1.09 (t, J=7.02 Hz, 3 H)	(ESI(+)) m/e 453 $(M+H)^+$
40		**N-(4-{[1-(2,2-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺**	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.81 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.85, 1.83 Hz, 1 H) 7.49 - 7.53 (m, 2 H) 6.96 (d, J=9.16 Hz, 2 H) 4.53 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.12 - 4.18 (m, J=7.93, 6.10 Hz, 2 H) 3.87 - 3.93 (m, 1 H) 3.75 - 3.80 (m, 2 H) 3.28 - 3.38 (m, 2 H) 1.89 - 1.97 (m, 2 H) 1.60 (q, J=7.53 Hz, 2 H) 1.46 - 1.54 (m, 2 H) 1.16 (s, 6 H) 0.80 (t, J=7.48 Hz, 3 H)	(ESI(+)) m/e 451 $(M+H)^+$
41		**N-(4-{[1-(3,3-二甲基丁酰基)哌啶-4-基]**	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.49 - 7.52 (m, 2 H) 6.92 - 6.99 (m, 2 H)	(ESI(+)) m/e 451 $(M+H)^+$

		氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	4.47 - 4.58 (m, 1 H) 4.22 - 4.29 (m, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.85 - 3.92 (m, 1 H) 3.74 - 3.80 (m, 2 H) 3.34 - 3.43 (m, 1 H) 3.20 - 3.27 (m, 1 H) 2.26 (s, 2 H) 1.82 - 2.01 (m, 2 H) 1.38 - 1.60 (m, 2 H) 0.99 (s, 9 H)	
42		N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.59 - 7.61 (m, 1 H) 7.49 - 7.54 (m, 2 H) 6.93 - 6.98 (m, 2 H) 4.51 - 4.61 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.85 - 3.92 (m, 2 H) 3.73 - 3.79 (m, 1 H) 3.29 - 3.38 (m, 2 H) 1.89 - 1.99 (m, 2 H) 1.45 - 1.56 (m, 2 H) 1.20 (s, 9 H)	(ESI(+)) m/e 437 $(M+H)^+$
43		N-{4-[(1-丁酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.85, 1.83 Hz, 1 H) 7.49 - 7.53 (m, 2 H) 6.93 - 6.98 (m, 2 H) 4.49 - 4.60 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.82 - 3.90 (m, 1 H) 3.73 - 3.79 (m, 2 H) 3.20 - 3.37 (m, 2 H) 2.31 (t, J=7.17 Hz, 2 H) 1.82 - 1.98 (m, 2 H) 1.41 - 1.63 (m, 4 H) 0.89 (t, J=7.32 Hz, 3 H)	(ESI(+)) m/e 423 $(M+H)^+$
44		N-(4-{[1-(乙氧基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.54, 1.83 Hz, 1 H) 7.51 (d, J=9.16 Hz, 2 H) 6.96 (d, J=9.16 Hz, 2 H) 4.50 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.10 - 4.16 (m, 4 H) 3.80 - 3.87 (m, 1 H) 3.73 - 3.78 (m, 2 H) 3.47 (q, J=7.02 Hz, 2 H) 3.20 - 3.35 (m, 2 H) 1.86 - 1.98 (m, J=21.67 Hz, 2 H) 1.45 - 1.64 (m, 2 H) 1.13 (t, J=7.02 Hz, 3 H)	(ESI(+)) m/e 439 $(M+H)^+$
45		N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.47 - 7.55 (m, 2 H) 6.93 - 6.98 (m, 2 H) 4.51 - 4.57 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.83 - 3.90 (m, 1 H) 3.74 - 3.79 (m, 2 H) 3.19 - 3.37 (m, 2 H) 2.19 - 2.24 (m, 2 H) 1.82 - 2.03 (m, 3 H) 1.41 - 1.60 (m, 2 H) 0.90 (d, J=6.71 Hz, 6 H)	(ESI(+)) m/e 437 $(M+H)^+$
46		N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.49 - 7.54 (m, 2 H) 6.93 - 6.99 (m, 2 H) 4.52 - 4.60 (m, 1 H) 4.25 (t, J=8.24 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.84 (s, 1 H) 3.75 - 3.79 (m, 2 H) 3.18 - 3.42 (m, 2 H) 2.86 - 2.93 (m, 1 H) 1.84 - 1.99 (m, 2 H) 1.42 - 1.63 (m, 2 H) 1.00 (d, J=6.71 Hz, 6 H)	(ESI(+)) m/e 423 $(M+H)^+$
47		N-(4-{[1-(N-乙酰基-L-亮氨酰)哌啶-4-基]氧基}苯	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.81 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.85, 1.83 Hz, 1 H) 7.52 (d, J=8.85 Hz, 2 H) 6.95 - 6.99 (m, 2 H) 4.77 (dd, J=9.00, 3.81 Hz, 1 H) 4.53 - 4.62	(ESI(+)) m/e 508 $(M+H)^+$

		基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	(m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.12 - 4.17 (m, 2 H) 3.92 (d, J=13.12 Hz, 1 H) 3.74 - 3.79 (m, 2 H) 3.31 - 3.47 (m, 2 H) 3.14 - 3.21 (m, 1 H) 1.92 - 2.01 (m, 1 H) 1.85 (s, 3 H) 1.28 - 1.63 (m, 5 H) 0.85 - 0.91 (m, 6 H)	
48		N-[4-({1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.19 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.54, 2.14 Hz, 1 H) 7.51 (d, J=9.16 Hz, 2 H) 6.93 - 6.99 (m, J=9.61, 9.61 Hz, 2 H) 4.51 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.09 - 4.18 (m, 4 H) 3.80 - 3.86 (m, 1 H) 3.74 - 3.77 (m, 1 H) 3.54 - 3.57 (m, 2 H) 3.47 (dd, J=5.65, 3.51 Hz, 2 H) 3.20 - 3.33 (m, 6 H) 1.87 - 1.96 (m, 2 H) 1.45 - 1.66 (m, 2 H)	(ESI(+)) m/e 469 $(M+H)^+$
49		N-(4-{[1-(环己基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.51 (d, J=8.85 Hz, 2 H) 6.94 - 6.97 (m, 2 H) 4.49 - 4.58 (m, 1 H) 4.25 (t, J=8.24 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.84 (dd, 1 H) 3.73 - 3.78 (m, 2 H) 3.33 - 3.40 (m, J=9.77 Hz, 1 H) 3.17 - 3.27 (m, 1 H) 2.58 - 2.63 (m, 1 H) 1.82 - 1.99 (m, 2 H) 1.09 - 1.73 (m, 12 H)	(ESI(+)) m/e 463 $(M+H)^+$
50		N-(4-{[1-(环己基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.81 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.85, 1.83 Hz, 1 H) 7.48 - 7.53 (m, 2 H) 6.91 - 7.00 (m, 2 H) 4.51 - 4.57 (m, 1 H) 4.25 (t, J=8.24 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.84 (d, J=4.27 Hz, 1 H) 3.74 - 3.79 (m, 2 H) 3.31 - 3.38 (m, 1 H) 3.16 - 3.27 (m, 1 H) 2.18 - 2.23 (m, J=6.56, 2.90 Hz, 2 H) 1.83 - 1.97 (m, 2 H) 1.41 - 1.71 (m, 8 H) 1.06 - 1.27 (m, 3 H) 0.88 - 0.98 (m, 2 H)	(ESI(+)) m/e 477 $(M+H)^+$
51		1-(吡啶-3-基)-N-(4-{[1-(4,4,4-三氟丁酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.59 (dd, J=8.70, 1.98 Hz, 1 H) 7.49 - 7.54 (m, 2 H) 6.93 - 6.99 (m, 2 H) 4.52 - 4.60 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.81 - 3.89 (m, 1 H) 3.74 - 3.78 (m, 2 H) 3.25 - 3.39 (m, 2 H) 2.61 - 2.68 (m, 2 H) 2.43 - 2.51 (m, 2 H) 1.84 - 2.00 (m, 2 H) 1.44 - 1.65 (m, 2 H)	(ESI(+)) m/e 477 $(M+H)^+$
52		N-(4-{[1-(环戊基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.51 (d, J=8.85 Hz, 2 H) 6.96 (d, J=8.85 Hz, 2 H) 4.51 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.09 - 4.18 (m, 2 H) 3.81 - 3.90 (m, 1 H) 3.75 - 3.79 (m, 2 H) 3.33 - 3.42 (m, 1 H) 3.20 - 3.29 (m, 1 H) 2.96 - 3.02 (m, 1 H) 1.46 - 1.98 (m, 12 H)	(ESI(+)) m/e 449 $(M+H)^+$
53		N-[4-({1-[(1-甲基环己基)羰基]哌啶-4-	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.19 Hz, 1 H) 8.04 (d, J=2.44 Hz, 1 H) 7.79 (dd, J=8.54, 5.49 Hz, 1 H) 7.59 (dd, J=8.70, 1.98 Hz, 1 H) 7.49 - 7.53 (m, 2 H) 6.96 (d, J=8.85 Hz,	(ESI(+)) m/e 477 $(M+H)^+$

		基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	2 H) 4.50 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.90 (dd, J=9.00, 5.95 Hz, 2 H) 3.74 - 3.78 (m, 1 H) 3.27 - 3.36 (m, 2 H) 1.85 - 1.99 (m, 4 H) 1.24 - 1.55 (m, 10 H) 1.18 (s, 3 H)	
54		N-(4-{[1-(呋喃-3-基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.44 Hz, 1 H) 8.02 (s, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.71 - 7.73 (m, 1 H) 7.59 (dd, J=8.70, 2.29 Hz, 1 H) 7.52 (d, J=8.85 Hz, 2 H) 6.97 (d, J=8.85 Hz, 2 H) 6.67 (s, 1 H) 4.56 - 4.62 (m, 1 H) 4.25 (t, J=8.24 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.82 - 3.92 (m, 2 H) 3.73 - 3.77 (m, 1 H) 3.39 - 3.49 (m, 2 H) 1.91 - 2.00 (m, 2 H) 1.55 - 1.65 (m, 2 H)	(ESI(+)) m/e 447 $(M+H)^+$
55		1-(吡啶-3-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.09 (d, J=4.58 Hz, 1 H) 8.02 (s, 1 H) 7.73 (dd, J=8.54, 5.49 Hz, 1 H) 7.48 - 7.54 (m, J=9.16 Hz, 3 H) 6.96 (d, J=8.85 Hz, 2 H) 4.57 (s, 1 H) 4.23 (t, J=8.24 Hz, 2 H) 4.09 - 4.14 (m, 2 H) 3.80 - 3.87 (m, 1 H) 3.72 - 3.78 (m, 2 H) 3.59 - 3.63 (m, 2 H) 3.26 - 3.39 (m, 2 H) 1.93 (s, 2 H) 1.51 (s, 2 H)	(ESI(+)) m/e 463 $(M+H)^+$
56		N-{4-[(1-乙酰基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.19 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.81 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.49 - 7.53 (m, 2 H) 6.92 - 6.98 (m, 2 H) 4.50 - 4.58 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.79 - 3.85 (m, 1 H) 3.75 - 3.79 (m, 2 H) 3.19 - 3.40 (m, 2 H) 2.02 (s, 3 H) 1.83 - 1.99 (m, 2 H) 1.41 - 1.68 (m, 2 H)	(ESI(+)) m/e 395 $(M+H)^+$
57		N-(4-{[1-(甲氧基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.60 (dd, J=8.54, 2.44 Hz, 1 H) 7.51 (d, J=9.16 Hz, 2 H) 6.96 (d, J=9.16 Hz, 2 H) 4.51 - 4.59 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 4.10 (d, J=3.05 Hz, 2 H) 3.80 - 3.86 (m, 1 H) 3.74 - 3.77 (m, 1 H) 3.57 - 3.64 (m, 1 H) 3.18 - 3.34 (m, 5 H) 1.85 - 1.99 (m, 2 H) 1.44 - 1.64 (m, 2 H)	(ESI(+)) m/e 425 $(M+H)^+$
58		1-(吡啶-3-基)-N-(4-{[1-(噻吩-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.11 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.75 Hz, 1 H) 7.76 - 7.78 (m, 1 H) 7.59 - 7.61 (m, 2 H) 7.52 (d, J=8.85 Hz, 2 H) 7.44 (d, J=4.88 Hz, 1 H) 7.22 (d, J=5.19 Hz, 1 H) 6.97 (d, J=9.16 Hz, 2 H) 4.56 - 4.62 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.12 - 4.16 (m, 2 H) 3.87 - 3.96 (m, 1 H) 3.72 - 3.79 (m, 2 H) 3.33 - 3.46 (m, 2 H) 1.90 - 2.01 (m, J=1.83 Hz, 2 H) 1.54 - 1.70 (m, 2 H)	(ESI(+)) m/e 463 $(M+H)^+$
59		N-[4-({1-[(3-甲基噻吩-2-基)羰基]哌啶-4-基}氧基)	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.48 - 7.62 (m, 4 H) 6.93 - 6.99 (m, 3 H) 4.54 - 4.66 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H)	(ESI(+)) m/e 477 $(M+H)^+$

		苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	3.72 - 3.85 (m, 3 H) 3.34 - 3.45 (m, 2 H) 2.20 (s, 3 H) 1.91 - 2.00 (m, J=9.77 Hz, 2 H) 1.53 - 1.64 (m, 2 H)	
60		N-(4-{[1-(吗啉-4-基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.13 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.54, 2.14 Hz, 1 H) 7.53 (d, J=8.85 Hz, 2 H) 6.97 (d, J=9.16 Hz, 2 H) 4.54 - 4.64 (m, 1 H) 4.35 (s, 2 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.76 - 4.04 (m, 6 H) 3.52 - 3.60 (m, 1 H) 3.25 - 3.49 (m, 4 H) 3.08 - 3.22 (m, 2 H) 1.89 - 2.08 (m, 2 H) 1.50 - 1.77 (m, 2 H)	(ESI(+)) m/e 480 $(M+H)^+$
61		1-(吡啶-3-基)-N-(4-{[1-(噻吩-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=1.83 Hz, 1 H) 7.79 (dd, J=8.85, 5.49 Hz, 1 H) 7.58 (dd, J=8.54, 2.14 Hz, 1 H) 7.52 (d, J=9.16 Hz, 2 H) 7.42 (d, J=3.66 Hz, 1 H) 7.18 - 7.22 (m, 1 H) 7.14 (dd, J=4.88, 3.66 Hz, 1 H) 6.99 (d, 2 H) 4.58 - 4.66 (m, 1 H) 4.25 (t, J=8.24 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.89 - 3.96 (m, 2 H) 3.74 - 3.80 (m, 1 H) 3.52 (m, 2 H) 1.95 - 2.04 (m, 2 H) 1.59 - 1.70 (m, 2 H)	(ESI(+)) m/e 463 $(M+H)^+$
62		N-[4-({1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.04 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.54, 5.49 Hz, 1 H) 7.59 (dd, J=8.24, 2.14 Hz, 1 H) 7.52 (d, J=9.16 Hz, 2 H) 7.23 (d, J=3.36 Hz, 1 H) 6.98 (d, J=9.16 Hz, 2 H) 6.80 - 6.86 (m, 1 H) 4.56 - 4.65 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.12 - 4.17 (m, 2 H) 3.90 - 3.95 (m, 2 H) 3.74 - 3.79 (m, 1 H) 3.45 - 3.55 (m, 2 H) 2.47 (s, 3 H) 1.94 - 2.05 (m, 2 H) 1.58 - 1.67 (m, 2 H)	(ESI(+)) m/e 477 $(M+H)^+$
63		N-(4-{[1-(呋喃-2-基羰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.78 - 7.83 (m, 2 H) 7.60 (dd, J=8.39, 2.29 Hz, 1 H) 7.52 (d, J=9.16 Hz, 2 H) 6.96 - 7.02 (m, 3 H) 6.63 (dd, J=3.36, 1.83 Hz, 1 H) 4.58 - 4.67 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 5.80 Hz, 2 H) 3.92 - 3.99 (m, 2 H) 3.75 - 3.80 (m, 1 H) 3.41 - 3.59 (m, 2 H) 1.95 - 2.04 (m, 2 H) 1.58 - 1.67 (m, 2 H)	(ESI(+)) m/e 447 $(M+H)^+$
64		N-[4-({1-[(1-甲基-1H-吡咯-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.11 (s, 1 H) 8.04 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.70, 5.34 Hz, 1 H) 7.59 (dd, J=8.85, 1.83 Hz, 1 H) 7.52 (d, J=9.16 Hz, 2 H) 6.97 (d, J=9.16 Hz, 2 H) 6.88 (s, 1 H) 6.33 (dd, J=3.81, 1.68 Hz, 1 H) 6.01 - 6.05 (m, 1 H) 4.52 - 4.63 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.11 - 4.17 (m, 2 H) 3.90 - 3.96 (m, 2 H) 3.74 - 3.79 (m, 1 H) 3.66 (s, 3 H) 3.41 - 3.50 (m, 2 H) 1.91 - 2.04 (m, 2 H) 1.52 - 1.67 (m, 2 H)	(ESI(+)) m/e 460 $(M+H)^+$
65		N-{4-[(1-丙酰基哌啶-4-基)氧基]苯基}-1-	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.39, 2.29 Hz, 1 H) 7.51 (d, J=8.85 Hz, 2 H) 6.96 (d, 2 H)	(ESI(+)) m/e 409 $(M+H)^+$

		(吡啶-3-基)氮杂环丁烷-3-甲酰胺	4.48 - 4.60 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 6.10 Hz, 2 H) 3.81 - 3.90 (m, 1 H) 3.72 - 3.80 (m, 2 H) 3.17 - 3.41 (m, 2 H) 2.34 (q, J=7.53 Hz, 2 H) 1.82 - 2.01 (m, 2 H) 1.35 - 1.63 (m, 2 H) 1.00 (t, J=7.48 Hz, 3 H)	
66		N-[4-({1-[(1-甲基环丙基)羰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.55, 1.83 Hz, 1 H) 7.52 (d, J=8.85 Hz, 2 H) 6.96 (d, J=8.85 Hz, 2 H) 4.51 - 4.60 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 5.80 Hz, 2 H) 3.82 - 3.92 (m, 2 H) 3.74 - 3.78 (m, 1 H) 3.31 - 3.46 (m, 2 H) 1.85 - 1.96 (m, 2 H) 1.47 - 1.58 (m, J=7.32 Hz, 2 H) 1.23 (s, 3 H) 0.76 - 0.81 (m, 2 H) 0.52 - 0.56 (m, 2 H)	(ESI(+)) m/e 435 $(M+H)^+$
67		N-(4-{[1-(N,N-二甲基-β-丙氨酰)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.19 Hz, 1 H) 8.05 (d, J=2.75 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.39, 2.29 Hz, 1 H) 7.53 (d, J=9.16 Hz, 2 H) 6.99 (d, J=8.85 Hz, 2 H) 4.56 - 4.64 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=7.93, 5.80 Hz, 2 H) 3.72 - 3.82 (m, 3 H) 3.67 - 3.70 (m, 2 H) 3.19 - 3.54 (m, J=87.28 Hz, 4 H) 2.92 (d, J=10.68 Hz, 6 H) 1.97 - 2.16 (m, 2 H) 1.66 - 1.85 (m, 2 H)	N/A
68		1-(吡啶-3-基)-N-(4-{[1-(1,3-噻唑-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.98 - 8.02 (m, 2 H) 7.81 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.39, 2.29 Hz, 1 H) 7.53 (d, 2 H) 6.99 (d, 2 H) 4.55 - 4.69 (m, 2 H) 4.25 (t, J=8.39 Hz, 2 H) 4.15 (dd, J=7.93, 5.80 Hz, 2 H) 3.94 - 4.08 (m, J=41.20, 9.46 Hz, 2 H) 3.74 - 3.79 (m, 1 H) 3.49 - 3.58 (m, 1 H) 1.98 - 2.08 (m, 2 H) 1.67 (s, 2 H)	(ESI(+)) m/e 464 $(M+H)^+$
69		N-(4-{[1-(环戊基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.77 - 7.82 (m, 1 H) 7.60 (dd, J=8.70, 1.98 Hz, 1 H) 7.51 (d, J=8.85 Hz, 2 H) 6.96 (d, J=8.85 Hz, 2 H) 4.50 - 4.58 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.11 - 4.15 (m, 2 H) 3.81 - 3.90 (m, 1 H) 3.73 - 3.79 (m, 2 H) 3.18 - 3.40 (m, 2 H) 2.35 (dd, J=7.17, 2.59 Hz, 2 H) 2.05 - 2.16 (m, 1 H) 1.83 - 1.98 (m, 2 H) 1.68 - 1.77 (m, 2 H) 1.42 - 1.63 (m, 6 H) 1.05 - 1.19 (m, 2 H)	(ESI(+)) m/e 463 $(M+H)^+$
70		N-(4-{[1-(2,3-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, DMSO-d_6/D_2O) δ ppm 8.12 (d, J=5.49 Hz, 1 H) 8.05 (d, J=2.44 Hz, 1 H) 7.80 (dd, J=8.85, 5.49 Hz, 1 H) 7.60 (dd, J=8.70, 2.29 Hz, 1 H) 7.50 - 7.53 (m, 2 H) 6.96 (d, J=9.16 Hz, 2 H) 4.50 - 4.61 (m, 1 H) 4.25 (t, J=8.39 Hz, 2 H) 4.14 (dd, J=8.09, 5.95 Hz, 2 H) 3.92 - 3.97 (m, 1 H) 3.74 - 3.87 (m, 3 H) 3.20 - 3.43 (m, 2 H) 2.55 - 2.61 (m, 1 H) 1.38 - 2.03 (m, 5 H) 0.95 (d, J=6.71 Hz, 2 H) 0.81 - 0.88 (m, 6 H)	(ESI(+)) m/e 451 $(M+H)^+$

[0363] 实施例 8

叔丁基 4-[4-({[(3S)-1-(吡啶 -3- 基)吡咯烷 -3- 基]羰基)氨基)苯氧基]哌啶 -1- 甲酸酯

如实施例 1A-C 中所述制备标题化合物，用 (S)-1-(苄基氧基羰基)吡咯烷 -3- 甲酸代替实施例 1A 中的 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 9.96(s,1H),7.95(d, J = 2.9Hz,1H),7.85(dd, J = 4.6,1.3Hz,1H),7.54-7.48(m,2H),7.15(dd, J = 8.4,4.6Hz,1H),6.98-6.86(m,3H),4.53-4.41(m,1H),3.73-3.46(m,3H),3.45-3.30(m,2H),3.24(dd, J = 17.5,10.0Hz,2H),3.12(dd, J = 24.9,15.2Hz,2H),2.35-2.10(m,2H),2.01-1.78(m,2H),1.68-1.42(m,2H),1.40(s,9H) ;MS(ESI(+))m/e 467(M+H)$^+$.

[0364] 实施例 9

叔丁基 4-[4-({[(3R)-1-(吡啶 -3- 基)吡咯烷 -3- 基]羰基}氨基)苯氧基]哌啶 -1- 甲酸酯

如实施例 1A-C 中所述制备标题化合物,用 (R)-1-(苄基氧基羰基)吡咯烷 -3- 甲酸代替实施例 1A 中的 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 9.97(s,1H),7.95(d, J = 2.9Hz,1H),7.85(dd, J = 4.6,1.3Hz,1H),7.54-7.48(m,2H),7.16(dd, J = 8.4,4.6Hz,1H),6.98-6.86(m,3H),4.53-4.41(m,1H),3.75-3.45(m,3H),3.45-3.34(m,3H),3.25(dd, J = 8.8,6.2Hz,1H),3.23-3.09(m,2H),2.34-2.07(m,2H),1.95-1.75(m,2H),1.59-1.41(m,2H),1.40(s,9H) ;MS(ESI(+))m/e 467(M+H)$^+$.

[0365] 实施例 10

1-(吡啶 -3- 基)-N-(4-{1-[(2S)- 四氢呋喃 -2- 基羰基]哌啶 -4- 基}苯基)氮杂环丁烷 -3- 甲酰胺

实施例 10A

叔丁基 4-(4-(1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酰胺基)苯基)哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用叔丁基 4-(4- 氨基苯基)哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基)哌啶 -1- 甲酸酯。

[0366] 实施例 10B

叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基)苯基)哌啶 -1- 甲酸酯

如实施例 1B 中所述制备标题化合物,用叔丁基 4-(4-(1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酰胺基)苯基)哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酰胺基)苯氧基)哌啶 -1- 甲酸酯。

[0367] 实施例 10C

叔丁基 4-(4-(1-(吡啶 -3- 基)氮杂环丁烷 -3- 甲酰胺基)苯基)哌啶 -1- 甲酸酯

如实施例 1C 中所述制备标题化合物,用叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基)苯基)哌啶 -1- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基)苯氧基)哌啶 -1- 甲酸酯。

[0368] 实施例 10D

N-(4-(哌啶 -4- 基)苯基)-1-(吡啶 -3- 基)氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用叔丁基 4-(4-(1-(吡啶 -3- 基)氮杂环丁烷 -3- 甲酰胺基)苯基)哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基)氮杂环丁烷 -3- 甲酰胺基)苯氧基)哌啶 -1- 甲酸酯。

[0369] 实施例 10E

1-(吡啶 -3- 基)-N-(4-{1-[(2S)- 四氢呋喃 -2- 基羰基]哌啶 -4- 基}苯基)氮杂环

丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(4-(哌啶 -4- 基) 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 (S)- 四氢呋喃 -2- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300)MHz, DMSO-d_6) δ ppm10.01(s,1H),7.93(dd, J = 4.6,1.3Hz,1H),7.85(d, J = 2.8Hz,1H),7.57-7.49(m,2H),7.22-7.14(m,3H),6.86(ddd, J = 8.2,2.9,1.4Hz,1H), 4.68(dd, J = 7.5,5.7Hz,1H),4.53-4.43(m,1H),4.10(d, J = 8.0Hz,2H),3.95(d, J = 13.3Hz,2H),3.89-3.64(m,3H),3.15-3.00(m,1H),2.82-2.59(m,2H),2.19-1.68(m,6H), 1.61-1.29(m,3H) ;MS(ESI(+))m/e 435(M+H)$^+$.

[0370] 表 2.

以下实施例基本上如实施例 10 中所述制备，代替实施例 10C 中的合适的溴吡啶和实施例 10E 中合适的羧酸。一些产物通过快速色谱纯化而其他通过反向 HPLC 纯化。因此，一些实施例分离为三氟乙酸盐。

实施例	名称	^{1}H NMR	MS
2	1-(2-氯基吡啶-3-基)-N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.04 (s, 1H), 8.12 – 7.94 (m, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.48 – 7.37 (m, 1H), 7.21 – 7.16 (m, 2H), 7.14 (dt, J = 7.7, 1.9 Hz, 1H), 5.36 (s, 1H), 4.97 – 4.53 (m, 2H), 4.43 – 4.31 (m, 2H), 4.30 – 4.13 (m, 2H), 3.78 – 3.56 (m, 1H), 2.85 – 2.65 (m, 2H), 1.81 – 1.63 (m, 2H), 1.59 – 1.42 (m, 2H), 1.33 (s, 6H)	(ESI(+)) m/e 448 (M+H)$^+$
20	N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.01 (s, 1H), 7.93 (dd, J = 4.6, 1.3 Hz, 1H), 7.85 (d, J = 2.8 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.26 – 7.09 (m, 3H), 6.86 (ddd, J = 8.2, 2.9, 1.4 Hz, 1H), 5.37 (s, 1H), 4.77 (bs, 1H), 4.09 (t, J = 7.8 Hz, 2H), 3.95 (t, J = 6.6 Hz, 2H), 3.77 – 3.55 (m, 1H), 3.18 –	(ESI(+)) m/e 423 (M+H)$^+$

		烷-3-甲酰胺	2.62 (m, 2H), 1.81 – 1.71 (m, 2H), 1.67 – 1.35 (m, 2H), 1.33 (s, 6H), 1.30 – 1.00 (m, 1H)	
22		N-(4-{1-[(2S)-2-甲基丁酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.01 (s, 1H), 7.93 (dd, J = 4.6, 1.4 Hz, 1H), 7.86 (d, J = 2.8 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.25 – 7.09 (m, 3H), 6.90 – 6.82 (m, 1H), 4.63 – 4.52 (m, 1H), 4.18 – 3.87 (m, 5H), 3.78 – 3.63 (m, 1H), 3.16 – 2.99 (m, 1H), 2.81 – 2.67 (m, 2H), 2.59 (d, J = 12.4 Hz, 1H), 1.88 – 1.67 (m, 2H), 1.68 – 1.07 (m, 4H), 1.05 – 0.94 (m, 3H), 0.91 – 0.72 (m, 3H)	(ESI(+)) m/e 421 $(M+H)^+$
25		1-(吡啶-3-基)-N-{4-[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.01 (s, 1H), 7.93 (dd, J = 4.6, 1.3 Hz, 1H), 7.85 (d, J = 2.8 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.22 – 7.14 (m, 3H), 6.86 (ddd, J = 8.2, 2.8, 1.4 Hz, 1H), 4.60 – 4.49 (m, 1H), 4.09 (t, J = 7.8 Hz, 2H), 3.97 (dd, J = 16.6, 10.2 Hz, 2H), 3.88 – 3.62 (m, 3H), 3.14 – 3.00 (m, 1H), 2.77 – 2.65 (m, 1H), 2.57 (t, J = 11.1 Hz, 1H), 2.27 (d, J = 6.8 Hz, 2H), 1.91 (dd, J = 9.4, 5.6 Hz, 1H), 1.74 (d, J = 11.3 Hz, 3H), 1.59 (d, J = 12.9 Hz, 2H), 1.43 (dd, J = 31.3, 12.2 Hz, 3H), 1.20 (dd, J = 24.5, 12.0 Hz, 3H)	(ESI(+)) m/e 463 $(M+H)^+$
26		N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.01 (s, 1H), 7.93 (dd, J = 4.7, 1.3 Hz, 1H), 7.86 (d, J = 2.7 Hz, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.48 – 7.36 (m, 5H), 7.27 – 7.11 (m, 3H), 6.86 (ddd, J = 8.3, 2.8, 1.3 Hz, 1H), 4.62 (s, 1H), 4.13 – 4.01 (m, 2H), 3.97 (dd, J = 12.1, 5.8 Hz, 2H), 3.71 (ddd, J = 14.3, 8.1, 6.1 Hz, 2H), 3.13 (s, 1H), 2.76 (t, J = 11.7 Hz, 2H), 1.85 (d, J = 32.6 Hz, 2H), 1.66 – 1.40 (m, 2H)	(ESI(+)) m/e 441 $(M+H)^+$
29		N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.00 (s, 1H), 7.88 (dd, J = 4.7, 1.4 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.22 – 7.14 (m, 2H), 7.07 (dd, J = 8.0, 4.7 Hz, 1H), 6.85 (dd, J = 8.1, 1.4 Hz, 1H), 4.60 – 4.49 (m, 1H), 4.15 – 3.85 (m, 4H), 3.68 – 3.53 (m, 1H), 3.21 – 3.02 (m, 1H), 2.97 – 2.61 (m, 2H), 2.35 (s, 3H), 2.32 – 1.66 (m, 3H), 1.60 – 1.14 (m, 3H), 1.12 – 0.92 (m, 6H)	(ESI(+)) m/e 421 $(M+H)^+$
30		N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.01 (s, 1H), 8.11 – 7.82 (m, 2H), 7.80 – 7.31 (m, 2H), 7.33 – 7.07 (m, 2H), 6.86 (ddd, J = 8.3, 2.9, 1.4 Hz, 1H), 4.61 – 4.49 (m, 1H), 4.16 – 3.87 (m, 4H), 3.77 – 3.64 (m, 1H), 3.20 – 2.99 (m, 1H), 2.89 (p, J = 6.7 Hz, 1H), 2.80 – 2.61 (m, 1H), 2.64 – 2.47 (m, 1H), 1.89 – 1.60 (m, 2H), 1.61 – 1.30 (m, 2H), 1.08 (d, J = 6.8 Hz, 2H), 1.05 – 0.97 (m, 6H)	(ESI(+)) m/e 407 $(M+H)^+$
71		N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.00 (s, 1H), 7.88 (dd, J = 4.7, 1.4 Hz, 1H), 7.57 – 7.50 (m, 2H), 7.21 – 7.14 (m, 2H), 7.07 (dd, J = 8.0, 4.6 Hz, 1H), 6.85 (dd, J = 8.1, 1.4 Hz, 1H), 5.37 (s, 1H), 4.65 (bs, 1H), 4.10 (t, J = 7.7 Hz, 2H), 3.97 (t, J = 6.8 Hz, 2H), 3.70 – 3.56 (m, 1H),	(ESI(+)) m/e 437 $(M+H)^+$

		基)氮杂环丁烷-3-甲酰胺	3.05 – 2.63 (m, 2H), 2.35 (s, 3H), 1.81 – 1.71 (m, 2H), 1.66 – 1.36 (m, 3H), 1.33 (s, 6H), 1.28 – 1.13 (m, 1H)	
72		N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(4-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.99 (s, 1H), 7.90 (d, J = 4.7 Hz, 1H), 7.76 (s, 1H), 7.57 – 7.50 (m, 2H), 7.21 – 7.14 (m, 2H), 7.00 (d, J = 4.7 Hz, 1H), 5.35 (s, 1H), 4.71 (bs, 2H), 4.15 (t, J = 7.7 Hz, 2H), 4.05 (t, J = 6.8 Hz, 2H), 3.72 – 3.58 (m, 1H), 3.22 – 2.63 (m, 1H), 2.18 (s, 3H), 1.82 – 1.72 (m, 2H), 1.62 – 1.36 (m, 2H), 1.33 (s, 6H), 1.20 (d, J = 18.3 Hz, 1H), 0.89 – 0.72 (m, 1H)	(ESI(+)) m/e 437 $(M+H)^+$
73		N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(2-甲氧基吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.94 (s, 1H), 7.56 – 7.49 (m, 3H), 7.21 – 7.13 (m, 2H), 6.84 (dd, J = 7.5, 4.9 Hz, 1H), 6.72 (dd, J = 7.5, 1.6 Hz, 1H), 5.35 (s, 1H), 4.72 (bs, 2H), 4.07 (t, J = 7.9 Hz, 2H), 3.95 (d, J = 6.9 Hz, 2H), 3.83 (s, 3H), 3.66 – 3.52 (m, 1H), 2.73 (t, J = 11.9 Hz, 2H), 1.82 – 1.71 (m, 2H), 1.59 – 1.36 (m, 2H), 1.33 (s, 6H)	(ESI(+)) m/e 453 $(M+H)^+$
96		N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}-1-(4-甲氧基吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.94 (s, 1H), 7.93 (d, J = 5.3 Hz, 1H), 7.63 (s, 1H), 7.56 – 7.49 (m, 2H), 7.21 – 7.13 (m, 2H), 6.88 (d, J = 5.4 Hz, 1H), 5.35 (s, 1H), 4.71 (bs, 1H), 4.09 (t, J = 7.9 Hz, 2H), 3.96 (dd, J = 12.1, 4.8 Hz, 2H), 3.79 (s, 3H), 3.71 – 3.54 (m, 2H), 2.73 (t, J = 11.8 Hz, 1H), 1.76 (d, J = 11.4 Hz, 3H), 1.51 (s, 3H), 1.33 (s, 6H)	(ESI(+)) m/e 453 $(M+H)^+$
97		1-(4-氰基吡啶-3-基)-N-{4-[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.04 (s, 1H), 8.09 (s, 1H), 7.96 (d, J = 5.0 Hz, 1H), 7.54 (d, J = 8.6 Hz, 2H), 7.46 (dd, J = 5.1, 0.5 Hz, 1H), 7.18 (d, J = 8.6 Hz, 2H), 5.36 (s, 1H), 4.74 (s, 1H), 4.43 (t, J = 8.3 Hz, 2H), 4.31 (dd, J = 8.0, 5.8 Hz, 2H), 3.79 – 3.66 (m, 1H), 2.74 (dd, J = 13.8, 10.3 Hz, 2H), 1.81 – 1.72 (m, 3H), 1.65 – 1.45 (m, 3H), 1.33 (s, 6H)	(ESI(+)) m/e 448 $(M+H)^+$
98		N-[4-(1-戊酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 421 $(M+H)^+$
99		N-{4-[1-(3-甲基戊酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 435 $(M+H)^+$
100		N-(4-{1-[(1S,4R)-双环[2.2.1]庚-2-基乙		(ESI(+)) m/e 473 $(M+H)^+$

		酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		
101		N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 447 $(M+H)^+$
102		N-(4-{1-[(2-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 419 $(M+H)^+$
103		N-{4-[1-(吗啉-4-基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 464 $(M+H)^+$
104		N-{4-[1-(呋喃-3-基羰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 431 $(M+H)^+$
105		1-(吡啶-3-基)-N-{4-[1-(吡咯烷-1-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 474 $(M+H)^+$
106		N-{4-[1-(5-氧代-D-脯氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 448 $(M+H)^+$
107		N-{4-[1-(N,N-二甲基-β-丙氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-		(ESI(+)) m/e 436 $(M+H)^+$

	3-甲酰胺		
108	1-(吡啶-3-基)-N-{4-[1-(1,3-噻唑-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 448 $(M+H)^+$
109	1-(吡啶-3-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 447 $(M+H)^+$
110	N-(4-{1-[(1-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 419 $(M+H)^+$
111	N-(4-{1-[(3-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 461 $(M+H)^+$
112	1-(吡啶-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 461 $(M+H)^+$
113	N-(4-{1-[(4-甲基哌嗪-1-基)乙酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 477 $(M+H)^+$
114	N-{4-[1-(5-氧代-L-脯氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环		(ESI(+)) m/e 448 $(M+H)^+$

		丁烷-3-甲酰胺		
115		N-{4-[1-(3-乙氧基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 437 $(M+H)^+$
116		N-{4-[1-(4-甲基戊酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 435 $(M+H)^+$
117		N-(4-{1-[(1-甲基环己基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 461 $(M+H)^+$
118		N-[4-(1-乙酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 379 $(M+H)^+$
119		N-{4-[1-(环己基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 461 $(M+H)^+$
120		N-{4-[1-(N-乙酰基-L-亮氨酰)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 492 $(M+H)^+$
121		N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 393 $(M+H)^+$
122		1-(吡啶-3-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}氮杂环		(ESI(+)) m/e 447 $(M+H)^+$

		丁烷-3-甲酰胺		
123		N-(4-{1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 453 $(M+H)^+$
124		N-(4-{1-[3-(吗啉-4-基)丙酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 478 $(M+H)^+$
125		N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 421 $(M+H)^+$
126		N-(4-{1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 461 $(M+H)^+$
127		1-(吡啶-3-基)-N-{4-[1-(噻吩-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 447 $(M+H)^+$
128		N-(4-{1-[(1-甲基-1H-吡咯-2-基)羰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 444 $(M+H)^+$
129		N-{4-[1-(呋喃-2-基羰基)哌啶-4-基]苯基}-1-(吡		(ESI(+)) m/e 431 $(M+H)^+$

		啶-3-基)氮杂环丁烷-3-甲酰胺		
130		N-(4-{1-[3-(哌啶-1-基)丙酰基]哌啶-4-基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 476 $(M+H)^+$
131		N-{4-[1-(乙氧基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 423 $(M+H)^+$
132		N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 435 $(M+H)^+$
133		N-{4-[1-(2,2-二甲基丁酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 435 $(M+H)^+$
134		N-[4-(1-丁酰基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 407 $(M+H)^+$
135		N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 409 $(M+H)^+$
136		N-{4-[1-(环己基羰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 447 $(M+H)^+$
137		N-{4-[1-(3-甲基丁酰基)哌啶-4-		(ESI(+)) m/e 421 $(M+H)^+$

		基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		
138		N-{4-[1-(环戊基羰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 433 $(M+H)^+$
139		N-{4-[1-(2,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 435 $(M+H)^+$
149		N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 455 $(M+H)^+$
150		N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 473 $(M+H)^+$
151		N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 489 $(M+H)^+$
152		N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 473 $(M+H)^+$
153		N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 489 $(M+H)^+$
154		N-{4-[1-(3,5-二		(ESI(+))

		氯苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		m/e 523 $(M+H)^+$
155		N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 473 $(M+H)^+$
156		N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 489 $(M+H)^+$
157		1-(2-甲基吡啶-3-基)-N-(4-{1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 523 $(M+H)^+$
158		1-(2-甲基吡啶-3-基)-N-{4-[1-(噻嗪-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 457 $(M+H)^+$
159		1-(2-甲基吡啶-3-基)-N-[4-(1-戊酰基哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 435 $(M+H)^+$
160		N-{4-[1-(3-甲基戊酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 449 $(M+H)^+$
161		N-(4-{1-		(ESI(+))

		[(1S,4R)-双环[2.2.1]庚-2-基乙酰基]哌啶-4-基}苯基)-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		m/e 487 $(M+H)^+$
162		N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 461 $(M+H)^+$
163		N-(4-{1-[(2-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 433 $(M+H)^+$
164		1-(2-甲基吡啶-3-基)-N-{4-[1-(吗啉-4-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 478 $(M+H)^+$
165		N-{4-[1-(呋喃-3-基羰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 445 $(M+H)^+$
166		1-(2-甲基吡啶-3-基)-N-{4-[1-(吡咯烷-1-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 462 $(M+H)^+$
167		1-(2-甲基吡啶-3-基)-N-{4-[1-(5-氧代-D-脯氨酰)哌啶-4-基]苯基}		(ESI(+)) m/e 462 $(M+H)^+$

		氮杂环丁烷-3-甲酰胺		
168		N-{4-[1-(N,N-二甲基-β-丙氨酰)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 450 $(M+H)^+$
169		1-(2-甲基吡啶-3-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 461 $(M+H)^+$
170		N-(4-{1-[(1-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 433 $(M+H)^+$
171		1-(2-甲基吡啶-3-基)-N-(4-{1-[(3-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 475 $(M+H)^+$
172		1-(2-甲基吡啶-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 475 $(M+H)^+$
173		N-(4-{1-[(4-甲基哌嗪-1-基)乙酰基]哌啶-4-基}苯基)-1-(2-甲基吡啶-3-基)氮杂环		(ESI(+)) m/e 491 $(M+H)^+$

		丁烷-3-甲酰胺		
174		1-(2-甲基吡啶-3-基)-N-{4-[1-(5-氧代-L-脯氨酰)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 462 $(M+H)^+$
175		N-{4-[1-(3-乙氧基丙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 451 $(M+H)^+$
176		N-{4-[1-(4-甲基戊酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 449 $(M+H)^+$
177		N-(4-{1-[(1-甲基环己基)羰基]哌啶-4-基}苯基)-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 475 $(M+H)^+$
178		N-[4-(1-乙酰基哌啶-4-基)苯基]-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 393 $(M+H)^+$
179		N-{4-[1-(环己基乙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 475 $(M+H)^+$
180		N-{4-[1-(N-乙酰基-L-亮氨酰)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-		(ESI(+)) m/e 506 $(M+H)^+$

		3-甲酰胺		
181		1-(2-甲基吡啶-3-基)-N-[4-(1-丙酰基哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 407 $(M+H)^+$
182		1-(2-甲基吡啶-3-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 461 $(M+H)^+$
183		N-(4-{1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}苯基)-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 467 $(M+H)^+$
184		1-(2-甲基吡啶-3-基)-N-(4-{1-[3-(吗啉-4-基)丙酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 492 $(M+H)^+$
185		N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 435 $(M+H)^+$
186		1-(2-甲基吡啶-3-基)-N-(4-{1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 475 $(M+H)^+$
187		1-(2-甲基吡啶-3-		(ESI(+)) m/e 461

		基)-N-{4-[1-(噻吩-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺		$(M+H)^+$
188		1-(2-甲基吡啶-3-基)-N-(4-{1-[(1-甲基-1H-吡咯-2-基)羰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 458 $(M+H)^+$
189		N-{4-[1-(呋喃-2-基羰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 445 $(M+H)^+$
190		1-(2-甲基吡啶-3-基)-N-(4-{1-[3-(哌啶-1-基)丙酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 490 $(M+H)^+$
191		N-{4-[1-(乙氧基乙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 437 $(M+H)^+$
192		N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 449 $(M+H)^+$
193		N-{4-[1-(2,2-二甲基丁酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 449 $(M+H)^+$

194		N-[4-(1-丁酰基哌啶-4-基)苯基]-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 421 $(M+H)^+$
195		N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 423 $(M+H)^+$
196		N-{4-[1-(环己基羰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 461 $(M+H)^+$
197		N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 435 $(M+H)^+$
198		N-{4-[1-(2,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(2-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 449 $(M+H)^+$

[0371] 实施例 11

(3S)-1-(吡啶-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]氧基}苯基)吡咯烷-3-甲酰胺如实施例 1D-E 中所述制备标题化合物，用叔丁基 4-[4-({[(3S)-1-(吡啶-3-基)吡咯烷-3-基]羰基}氨基)苯氧基]哌啶-1-甲酸酯代替实施例 1D 中的叔丁基 4-(4-(1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯。

^1H NMR(300MHz, DMSO-d_6) δ ppm9.98(s,1H),7.99(d, J = 2.9Hz,1H),7.91(d, J = 4.8Hz,1H),7.50(s,2H),7.33(dd, J = 8.5,4.8Hz,1H),7.16-7.09(m,1H),6.97-6.89(m,2H),4.58-4.47(m,1H),3.95-3.65(m,4H),3.56(d, J = 8.6Hz,1H),3.50-3.32(m,6H),2.36-2.11(m,4H),2.01-1.79(m,3H),1.66-1.38(m,4H),1.32-1.08(m,3H) ;MS(ESI(+))m/e 493$(M+H)^+$.

[0372] 表 3.

以下实施例基本上如实施例 1D-E 中所述制备，用叔丁基 4-[4-({[(3S)-1-(吡啶-3-基)吡咯烷-3-基]羰基}氨基)苯氧基]哌啶-1-甲酸酯代替实施例 1D 中的叔丁基 4-(4-(1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯和用合适的羧酸代替实施例 1E 中 2-(四氢-2H-吡喃-4-基)乙酸。一些产物通过快速色谱纯化

而其他通过反向 HPLC 纯化。因此，一些实施例分离为三氟乙酸盐。

实施例	名称	^{1}H NMR	MS
12	(3S)-N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)吡咯烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.97 (s, 1H), 7.96 (d, J = 2.9 Hz, 1H), 7.86 (dd, J = 4.6, 1.3 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.19 (dd, J = 8.4, 4.6 Hz, 1H), 6.99 – 6.90 (m, 3H), 4.59 – 4.48 (m, 1H), 4.03 – 3.67 (m, 3H), 3.54 (d, J = 8.6 Hz, 1H), 3.47 – 3.38 (m, 2H), 3.35 (d, J = 7.4 Hz, 2H), 3.28 – 3.18 (m, 1H), 2.95 – 2.82 (m, 1H), 2.38 – 2.03 (m, 2H), 2.00 – 1.80 (m, 2H), 1.64 – 1.37 (m, 2H), 1.00 (d, J = 6.7 Hz, 6H)	(ESI(+)) m/e 437 $(M+H)^+$
13	(3S)-1-(吡啶-3-基)-N-[4-({1-[(2S)-四氢呋喃-2-基羰基]哌啶-4-基}氧基)苯基]吡咯烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.97 (s, 1H), 7.97 (d, J = 2.8 Hz, 1H), 7.88 (d, J = 5.1 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.33 – 7.19 (m, 1H), 7.05 – 6.88 (m, 3H), 4.67 (t, J = 6.5 Hz, 1H), 4.57 – 4.50 (m, 1H), 3.94 – 3.67 (m, 4H), 3.55 (d, J = 8.6 Hz, 1H), 3.47 – 3.38 (m, 4H), 2.38 – 2.12 (m, 2H), 2.07 – 1.74 (m, 7H), 1.65 – 1.00 (m, 3H)	(ESI(+)) m/e 465 $(M+H)^+$
14	(3S)-1-(吡啶-3-基)-N-[4-({1-[(2R)-四氢呋喃-2-基羰基]哌啶-4-基}氧基)苯基]吡咯烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.97 (s, 1H), 7.96 (d, J = 2.9 Hz, 1H), 7.87 (dd, J = 4.6, 1.2 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.21 (dd, J = 8.4, 4.6 Hz, 1H), 7.02 – 6.93 (m, 2H), 6.92 (s, 1H), 4.67 (t, J = 6.6 Hz, 1H), 4.57 – 4.50 (m, 1H), 3.94 – 3.62 (m, 4H), 3.54 (d, J = 8.6 Hz, 1H), 3.44 (d, J = 6.7 Hz, 2H), 3.41 (d, J = 5.4 Hz, 2H), 3.23 (d, J = 7.8 Hz, 1H), 2.36 – 2.07 (m, 3H), 2.09 – 1.76 (m, 6H), 1.65 – 1.39 (m, 2H)	(ESI(+)) m/e 465 $(M+H)^+$
15	(3S)-1-(吡啶-3-基)-N-(4-{[1-(四氢呋喃-3-基羰基)哌啶-4-基]氧基}苯基)吡咯烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.97 (s, 1H), 7.97 (d, J = 2.9 Hz, 1H), 7.88 (dd, J = 4.7, 1.2 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.25 (dd, J = 8.4, 4.7 Hz, 1H), 7.02 (dd, J = 8.5, 2.8 Hz, 1H), 6.97 – 6.90 (m, 2H), 4.60 – 4.48 (m, 1H), 3.98 – 3.61 (m, 7H), 3.55 (d, J = 8.6 Hz, 1H), 3.45 (d, J = 6.9 Hz, 2H), 3.44 – 3.39 (m, 2H), 3.38 – 3.32 (m, 2H), 2.38 – 2.09 (m, 2H), 2.10 – 1.81 (m, 4H), 1.65 – 1.40 (m, 2H)	(ESI(+)) m/e 465 $(M+H)^+$
16	(3S)-N-(4-{[1-(环丙基乙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.96 (s, 1H), 7.99 – 7.93 (m, 1H), 7.85 (dd, J = 4.6, 1.3 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.16 (dd, J = 8.4, 4.5 Hz, 1H), 6.98 – 6.87 (m, 3H), 4.59 – 4.47 (m, 1H), 3.92 – 3.80 (m, 1H), 3.73 – 3.61 (m, 1H),	(ESI(+)) m/e 449 $(M+H)^+$

		基)吡咯烷-3-甲酰胺	3.54 (d, J = 8.6 Hz, 1H), 3.47 – 3.37 (m, 2H), 3.26 – 3.07 (m, 3H), 2.27 (d, J = 6.8 Hz, 3H), 2.23 – 2.12 (m, 1H), 1.97 – 1.79 (m, 2H), 1.62 – 1.32 (m, 2H), 1.04 – 0.83 (m, 1H), 0.49 – 0.36 (m, 2H), 0.19 – 0.07 (m, 2H)	
17		(3S)-N-(4-{[1-(2-羟基-2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)吡咯烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.96 (s, 1H), 7.96 (d, J = 3.1 Hz, 1H), 7.87 (d, J = 4.7 Hz, 1H), 7.57 – 7.39 (m, 2H), 7.21 (dd, J = 8.4, 4.6 Hz, 1H), 7.03 – 6.88 (m, 3H), 5.38 (s, 1H), 4.59 – 3.79 (m, 3H), 3.65 – 3.38 (m, 4H), 2.35 – 2.10 (m, 2H), 1.99 – 1.84 (m, 2H), 1.63 – 1.34 (m, 3H), 1.35 – 1.19 (m, 7H)	(ESI(+)) m/e 453 $(M+H)^+$
18		(3S)-1-(吡啶-3-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)吡咯烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.96 (s, 1H), 7.95 (d, J = 2.9 Hz, 1H), 7.85 (dd, J = 4.6, 1.3 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.16 (dd, J = 8.4, 4.5 Hz, 1H), 6.98 – 6.88 (m, 3H), 4.55 (dq, J = 7.7, 3.8 Hz, 1H), 3.83 (ddd, J = 13.2, 6.8, 3.9 Hz, 1H), 3.74 – 3.49 (m, 5H), 3.48 – 3.38 (m, 2H), 2.38 – 2.06 (m, 3H), 2.02 – 1.80 (m, 2H), 1.71 – 1.36 (m, 3H)	(ESI(+)) m/e 477 $(M+H)^+$
19		(3S)-N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)苯基]-1-(吡啶-3-基)吡咯烷-3-甲酰胺	^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.96 (s, 1H), 7.95 (d, J = 2.9 Hz, 1H), 7.85 (d, J = 4.6 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.16 (dd, J = 8.4, 4.5 Hz, 1H), 6.98 – 6.88 (m, 3H), 4.60 – 4.48 (m, 1H), 4.03 – 3.69 (m, 2H), 3.54 (d, J = 8.6 Hz, 1H), 3.47 – 3.37 (m, 2H), 3.33 (d, J = 4.6 Hz, 1H), 3.27 – 3.17 (m, 1H), 2.72 (h, J = 6.7 Hz, 1H), 2.35 – 2.01 (m, 2H), 2.02 – 1.79 (m, 2H), 1.65 – 1.10 (m, 5H), 0.98 (d, J = 6.7 Hz, 3H), 0.81 (t, J = 7.4 Hz, 3H)	(ESI(+)) m/e 451 $(M+H)^+$

[0373] 实施例 21

N-[1-(吡啶 -3- 基)氮杂环丁烷 -3- 基]-4-{[1-(四氢 -2H- 吡喃 -4- 基乙酰基)哌啶 -4- 基]氧基}苯甲酰胺

实施例 21A

叔丁基 4-(4-(1-(苄基氧基羰基)氮杂环丁烷 -3- 基氨基甲酰基)苯氧基)哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物，用苄基 3- 氨基氮杂环丁烷 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基)哌啶 -1- 甲酸酯和用 4-(1-(叔丁氧基羰基)哌啶 -4- 基氧基)苯甲酸代替 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

[0374] 实施例 21B

苄基 3-(4-(哌啶 -4- 基氧基)苯甲酰氨基)氮杂环丁烷 -1- 甲酸酯

如实施例 1D 中所述制备标题化合物，用叔丁基 4-(4-(1-(苄基氧基羰基)氮杂环丁烷 -3- 基氨基甲酰基)苯氧基)哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基)氮杂环丁烷 -3- 甲酰胺基)苯氧基)哌啶 -1- 甲酸酯。

[0375] 实施例 21C

苄基 3-(4-(1-(2-(四氢 -2H- 吡喃 -4- 基)乙酰基)哌啶 -4- 基氧基)苯甲酰氨基)氮杂环丁烷 -1- 甲酸酯如实施例 1A 中所述制备标题化合物，用苄基 3-(4-(哌啶 -4- 基氧

基）苯甲酰氨基）氮杂环丁烷-1-甲酸酯代替叔丁基4-(4-氨基苯氧基）哌啶-1-甲酸酯和用2-(四氢-2H-吡喃-4-基）乙酸代替1-(苄基氧基羰基）氮杂环丁烷-3-甲酸。

[0376] 实施例21D

N-(氮杂环丁烷-3-基)-4-(1-(2-(四氢-2H-吡喃-4-基）乙酰基）哌啶-4-基氧基）苯甲酰胺

如实施例1B中所述制备标题化合物，用苄基3-(4-(1-(2-(四氢-2H-吡喃-4-基）乙酰基）哌啶-4-基氧基）苯甲酰氨基）氮杂环丁烷-1-甲酸酯代替叔丁基4-(4-(1-(苄基氧基羰基）氮杂环丁烷-3-甲酰胺基）苯氧基）哌啶-1-甲酸酯。

[0377] 实施例21E

N-[1-(吡啶-3-基）氮杂环丁烷-3-基]-4-{[1-(四氢-2H-吡喃-4-基乙酰基）哌啶-4-基]氧基}苯甲酰胺如实施例1C中所述制备标题化合物，用N-(氮杂环丁烷-3-基)-4-(1-(2-(四氢-2H-吡喃-4-基）乙酰基）哌啶-4-基氧基）苯甲酰胺代替叔丁基4-(4-(氮杂环丁烷-3-甲酰胺基）苯氧基）哌啶-1-甲酸酯。

^{1}H NMR(300MHz，DMSO-d_6) δ ppm 8.83(d，J = 6,8Hz,1H),7.93(d，J = 4.0Hz,1H),7.85(d，J = 8.4Hz,3H),7.27(s,2H),7.26-7.11(m,1H),7.05(d，J = 8.6Hz,2H),6.87(d，J = 8.1Hz,1H),4.86(d，J = 6.9Hz,1H),4.71(s,1H),4.28-4.19(m,2H),3.93-3.64(m,6H),2.30-2.23(m,2H),2.05-1.67(m,3H),1.52(t，J = 29.3Hz,5H),1.32-0.81(m,3H)；MS(ESI(+))m/e479(M+H)$^+$.

[0378] 实施例23

4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)-N-[1-(吡啶-3-基）氮杂环丁烷-3-基]苯甲酰胺

如实施例21中所述制备标题化合物，用(S)-2-甲基丁酸代替实施例21C中的2-(四氢-2H-吡喃-4-基）乙酸。

^{1}HNMR(300MHz，DMSO-d_6) δ ppm 8.84(d，J = 7.0Hz,1H),7.99-7.84(m,3H),7.83(s,1H),7.18(dd，J = 8.2,4.6Hz,1H),7.09-7.01(m,2H),6.87(ddd，J = 8.2,2.8,1.4Hz,1H),4.94-4.64(m,2H),4.24(t，J = 7.5Hz,2H),3.98-3.72(m,4H),2.73(h，J = 6.7Hz,1H),2.04-1.83(m,2H),1.67-1.20(m,4H),1.06-0.87(m,4H),0.87-0.77(m,4H)；MS(ESI(+))m/e437(M+H)$^+$.

[0379] 实施例24

4-{[1-(2-羟基-2-甲基丙酰基）哌啶-4-基]氧基}-N-[1-(吡啶-3-基）氮杂环丁烷-3-基]苯甲酰胺

如实施例21中所述制备标题化合物，用2-羟基-2-甲基丙酸代替实施例21C中的2-(四氢-2H-吡喃-4-基）乙酸。

^{1}H NMR(500MHz，DMSO-d_6) δ ppm 8.84(d，J = 7.0Hz,1H),7.93(dd，J = 4.6,1.3Hz,1H),7.87-7.86(m,1H),7.86(s,1H),7.84(s,1H),7.18(dd，J = 8.2,4.6Hz,1H),7.08-7.02(m,2H),6.87(ddd，J = 8.2,2.8,1.4Hz,1H),5.40(s,1H),4.92-4.81(m,1H),4.76-4.67(m,1H),4.24(t，J = 7.5Hz,3H),3.82(dd，J = 7.6,5.9Hz,3H),1.98-1.94(m,3H),1.72-1.41(m,3H),1.32(s,6H)；MS(ESI(+))m/e 439(M+H)$^+$.

[0380] 实施例27

叔丁基 4-(4-{[(3S)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 氨基甲酰基 } 苯氧基) 哌啶 -1- 甲酸酯

如实施例 21A、D 和 E 中所述制备标题化合物，用 (S)- 苄基 3- 氨基吡咯烷 -1- 甲酸酯代替实施例 21A 中的苄基 3- 氨基氮杂环丁烷 -1- 甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 8.43(d, J = 6.8Hz,1H),7.94(d, J = 2.9Hz,1H),7.87-7.80(m,3H),7.15(dd, J = 8.4,4.5Hz,1H),7.03(s,1H),7.00(s,1H),6.90(ddd, J = 8.4,3.0,1.3Hz,1H),4.71-4.55(m,2H),3.73-3.53(m,3H),3.44(t, J = 7.5Hz,1H),3.18(d, J = 13.4Hz,2H),3.17(d, J = 12.2Hz,2H),2.34-2.19(m,1H),2.14-1.97(m,1H),1.98-1.82(m,2H),1.63-1,43(m,2H),1.40(s,9H) ;MS(ESI(+))m/e467(M+H)$^+$.

[0381] 实施例 28

叔丁基 4-(4-{[(3R)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 氨基甲酰基 } 苯氧基) 哌啶 -1- 甲酸酯

如实施例 21A、D 和 E 中所述制备标题化合物，用 (R)- 苄基 3- 氨基吡咯烷 -1- 甲酸酯代替实施例 21A 中的苄基 3- 氨基氮杂环丁烷 -1- 甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 8.44(d, J = 6.8Hz,1H),7.94(d, J = 2.9Hz,1H),7.88-7.79(m,3H),7.15(dd, J = 8.3,4.5Hz,1H),7.06-6.98(m,2H),6.90(ddd, J = 8.4,3.0,1.4Hz,1H),4.72-4.54(m,2H),3.74-3.50(m,3H),3.51-3.39(m,1H),3.18(d. J = 13.6Hz,2H),3.16(d, J = 11.9Hz,1H),2.33-2.18(m,1H),2.07(dq, J = 12.9,6.5Hz,1H),2.00-1.82(m,2H),1.67-1.43(m,2H),1.40(s,9H) ;MS(ESI(+))m/e467(M+H)$^+$.

[0382] 实施例 74

N-(4-{[1-(环丙基甲基) 哌啶 -4- 基] 氧基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺在 20mL 小瓶中加入溶于甲醇 (2.0mL) 中的 N-(4-(哌啶 -4- 基氧基) 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺双 (2,2,2- 三氟乙酸酯)(67mg,0.12mmol)，随后加入溶于甲醇 (0.45mL) 中的环丙烷甲醛 (10mg,0.14mmol)，随后加入纯乙酸 (66μL,1.2mmol)。混合物在 70℃下摇动 1 小时。随后，加入 265mg 的 MP- 氰基硼氢化物树脂 (2-3mmol/g) 并将所获的混合物在 70℃下摇动过夜。将反应混合物过滤，通过 LC/MS 检查并浓缩至干燥。将残余物溶解于 1 ： 1DMSO/CH_3OH 并通过反向 HPLC 纯化。

^{1}H NMR(500MHz, 吡 啶 -d_5/D-$_2$0) δ ppm 8.20-8.25(m,1H)8.13(d, J = 2.75Hz,1H)7.98-8.03(m,2H)7.11(dd, J = 8.24,4.58Hz,1H)7.02-7.07(m,2H)6.72-6.78(m,1H)4.58(d,J = 2.75Hz,1H)4.34(t,J = 6.71Hz,2H)4.05(t,J = 7.63Hz,2H)3.80-3.92(m,1H)3.34(s,4H)2.92(d, J = 7.32Hz,2H)2.32-2.44(m,2H)2.12(s,2H)1.09-1.22(m,1H)0.51-0.58(m,2H)0.28-0.34(m,2H) ;MS(ESI(+))m/e 407(M+H).

[0383] 表 4.

以下实施例基本上如实施例 74 中所述制备，用合适的醛代替环丙烷甲醛。一些产物通过快速色谱纯化而其他通过反向 HPLC 纯化。因此，一些实施例分离为三氟乙酸盐。

实施例		名称	^{1}H NMR	MS
75		N-(4-{[1-(2-甲基戊基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O 温度=27 °C) δ ppm 8.23 (dd, J=4.58, 1.22 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.97 - 8.03 (m, 2 H) 7.06 - 7.13 (m, 3 H) 6.71 - 6.77 (m, 1 H) 4.44 (s, 1 H) 4.34 (t, J=6.56 Hz, 2 H) 4.00 - 4.08 (m, 2 H) 3.78 - 3.88 (m, 1 H) 2.96 (s, 2 H) 2.67 (s, 1 H) 2.34 - 2.48 (m, J=2.44 Hz, 3 H) 2.21 (s, 2 H) 1.97 (s, 2 H) 1.72 - 1.83 (m, 1 H) 1.15 - 1.45 (m, 3 H) 1.00 - 1.10 (m, 1 H) 0.96 (d, J=6.71 Hz, 3 H) 0.85 (t, J=7.17 Hz, 3 H)	(ESI(+)) m/e 437 $(M+H)^+$
76		N-(4-{[1-(2-甲基丙基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O 温度=27 °C) δ ppm 8.23 (dd, J=4.73, 1.37 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.97 - 8.04 (m, 2 H) 7.04 - 7.15 (m, 3 H) 6.72 - 6.76 (m, 1 H) 4.40 - 4.47 (m, 1 H) 4.34 (t, J=6.56 Hz, 2 H) 3.99 - 4.09 (m, 2 H) 3.79 - 3.89 (m, 1 H) 2.91 - 3.00 (m, 2 H) 2.61 - 2.82 (m, 2 H) 2.36 - 2.45 (m, 2 H) 2.13 - 2.26 (m, J=9.46 Hz, 2 H) 1.79 - 2.04 (m, 3 H) 0.92 (d, J=6.41 Hz, 6 H)	(ESI(+)) m/e 409 $(M+H)^+$
77		N-(4-{[1-(3-甲基丁基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O 温度=27 °C) δ ppm 8.21 - 8.26 (m, 1 H) 8.14 (d, J=3.05 Hz, 1 H) 7.98 - 8.03 (m, 2 H) 7.05 - 7.13 (m, 3 H) 6.71 - 6.77 (m, 1 H) 4.47 - 4.54 (m, 1 H) 4.34 (t, J=6.56 Hz, 2 H) 4.00 - 4.07 (m, 2 H) 3.80 - 3.89 (m, 1 H) 3.11 (s, 2 H) 2.87 - 3.06 (m, 2 H) 2.77 - 2.86 (m, 2 H) 2.22 - 2.33 (m, 2 H) 2.04 (s, 2 H) 1.47 - 1.61 (m, 3 H) 0.82 (d, J=6.41 Hz, 6 H)	(ESI(+)) m/e 423 $(M+H)^+$
78		N-(4-{[1-(2-乙基丁基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O 温度=27 °C) δ ppm 8.23 (dd, J=4.58, 1.22 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.98 - 8.03 (m, 2 H) 7.06 - 7.13 (m, 3 H) 6.71 - 6.76 (m, 1 H) 4.40 - 4.49 (m, 1 H) 4.34 (t, J=6.56 Hz, 2 H) 4.00 - 4.06 (m, 2 H) 3.78 - 3.88 (m, 1 H) 2.91 - 3.03 (m, 2 H) 2.57 - 2.77 (m, 2 H) 2.40 - 2.49 (m, J=4.27, 2.14 Hz, 2 H)	(ESI(+)) m/e 437 $(M+H)^+$

			2.14 - 2.28 (m, 2 H) 1.90 - 2.01 (m, J=14.04 Hz, 2 H) 1.58 (s, 1 H) 1.29 - 1.45 (m, 4 H) 0.84 (t, J=7.48 Hz, 6 H)	
79		N-(4-{[1-(2,2-二甲基丙基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O 温度=27 °C) δ ppm 8.23 (dd, J=4.58, 1.22 Hz, 1 H) 8.14 (d, J=2.75 Hz, 1 H) 7.99 - 8.01 (m, 2 H) 7.07 - 7.13 (m, 3 H) 6.74 (d, J=5.49 Hz, 1 H) 4.33 (t, J=6.56 Hz, 2 H) 4.00 - 4.06 (m, 2 H) 3.80 - 3.86 (m, 1 H) 2.73 - 2.81 (m, 2 H) 2.34 - 2.43 (m, 2 H) 1.93 - 2.03 (m, 4 H) 1.76 - 1.88 (m, 2 H) 1.24 - 1.34 (m, 1 H) 0.87 (s, 9 H)	(ESI(+)) m/e 423 $(M+H)^+$
80		N-(4-{[1-(2-甲基丁基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O 温度=27 °C) δ ppm 8.21 - 8.24 (m, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 8.00 (d, J=9.16 Hz, 2 H) 7.07 - 7.14 (m, 3 H) 6.70 - 6.77 (m, 1 H) 4.29 - 4.39 (m, 3 H) 3.97 - 4.06 (m, 2 H) 3.77 - 3.86 (m, 1 H) 2.75 - 2.88 (m, 2 H) 2.45 - 2.56 (m, 4 H) 2.04 - 2.25 (m, 3 H) 1.85 - 1.97 (m, 2 H) 1.38 - 1.64 (m, 2 H) 0.81 - 0.93 (m, 6 H)	(ESI(+)) m/e 423 $(M+H)^+$
81		N-{4-[(1-丙基哌啶-4-基)氧基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺		(ESI(+)) m/e 395 $(M+H)^+$
82		N-(4-{[1-(2-环丙基乙基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O 温度=27 °C) δ ppm 8.23 (dd, J=4.58, 1.53 Hz, 1 H) 8.14 (d, J=2.44 Hz, 1 H) 7.95 - 8.04 (m, 2 H) 7.05 - 7.14 (m, 3 H) 6.69 - 6.78 (m, 1 H) 4.42 - 4.51 (m, 1 H) 4.34 (t, J=6.56 Hz, 2 H) 3.95 - 4.11 (m, 2 H) 3.79 - 3.89 (m, J=8.24, 8.24 Hz, 1 H) 3.00 - 3.13 (m, 2 H) 2.73 - 2.93 (m, 3 H) 2.40 - 2.48 (m, 1 H) 2.15 - 2.30 (m, 2 H) 2.01 (s, 2 H) 1.50 - 1.61 (m, J=8.54 Hz, 2 H) 0.54 - 0.70 (m, 1 H) 0.33 - 0.42 (m, 2 H) 0.06 (t, J=4.73 Hz, 2 H)	(ESI(+)) m/e 421 $(M+H)^+$
83		1-(吡啶-3-基)-N-(4-{[1-(四氢呋喃-3-基甲基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O 温度=27 °C) δ ppm 8.23 (dd, J=4.58, 1.22 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.98 - 8.04 (m, 2 H) 7.03 - 7.15 (m, 3 H) 6.70 - 6.77 (m, 1 H) 4.44 - 4.53 (m, 1 H) 4.34 (t, J=6.56 Hz, 2 H) 3.96 - 4.09 (m, 3 H) 3.77 - 3.92 (m, 2 H) 3.55 - 3.74 (m, 2 H) 3.03 - 3.19 (m, 2 H) 2.86 - 3.04 (m, 2 H) 2.75 - 2.88 (m, 2 H) 2.57 - 2.72 (m, 1 H) 2.19 - 2.34 (m, 2 H) 1.94 - 2.08 (m, 3 H) 1.56 - 1.71 (m, 1 H)	(ESI(+)) m/e 437 $(M+H)^+$
84		N-(4-{[1-(2,2-二甲基丁基)哌啶-4-基]氧基}苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O 温度=27 °C) δ ppm 8.23 (dd, J=4.73, 1.37 Hz, 1 H) 8.14 (d, J=2.44 Hz, 1 H) 7.97 - 8.02 (m, 2 H) 7.07 - 7.13 (m, 3 H) 6.71 - 6.76 (m, 1 H) 4.28 - 4.38 (m, 2 H) 4.00 - 4.06 (m, 2 H) 3.82 (s, 1 H) 2.72 - 2.82 (m, 2 H) 2.29 - 2.43 (m, 2 H) 1.91 - 2.07 (m, 4 H) 1.75 - 1.88 (m, 2 H) 1.19 - 1.29 (m, J=7.22, 7.22, 7.22 Hz, 3 H) 0.72 - 0.86 (m, 9 H)	(ESI(+)) m/e 437 $(M+H)^+$

[0384] 实施例 85

N-{4-[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺如实施例 10 中所述制备标题化合物，用 4- 溴哒嗪代替实施例 10C 中的 3- 溴

吡啶和用 2- 羟基 -2- 甲基丙酸代替实施例 10E 中的 (S)- 四氢呋喃 -2- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 10.04(s,1H),8.60(d, J = -6.0Hz,1H),8.51(d, J = 3.0Hz,1H),7.57-7.50(m,2H),7.22-7.14(m,2H),6.54(dd, J = 6.0,3.0Hz,1H),5.36(s,1H),4.73(bs,2H),4.30-3.96(m,4H),3.87-3.60(m,1H),2.71(d, J = 11.9Hz,1H),1.82-1.72(m,2H),1.67-1.42(m,2H),1.35-1.31(m,8H) ;MS(ESI(+))m/e 424(M+H)$^+$.

[0385] 表 5.

以下实施例基本上如实施例 10 中所述制备,用 4- 溴哒嗪代替实施例 10C 中的 3- 溴吡啶和用合适的酸代替实施例 10E 中的 (S)- 四氢呋喃 -2- 甲酸。一些产物通过快速色谱纯化而其他通过反向 HPLC 纯化。因此,一些实施例分离为三氟乙酸盐。

实施例	名称	MS
140	N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
143	N-(4-{1-[(2S)-2-甲基丁酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
144	N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 448 $(M+H)^+$
145	1-(哒嗪-4-基)-N-{4-[1-(四氢-2H-吡喃-4-基乙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 464 $(M+H)^+$
146	1-(哒嗪-4-基)-N-{4-[1-(四氢-2H-吡喃-4-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 564 $(M+H)^+$
525	N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
526	1-(哒嗪-4-基)-N-{4-[1-(1,3-噻唑-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 449 $(M+H)^+$
527	N-{4-[1-(环丙基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 420 $(M+H)^+$
528	N-{4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 408 $(M+H)^+$
529	N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 460 $(M+H)^+$
530	1-(哒嗪-4-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}氮杂环	(ESI(+))

		丁烷-3-甲酰胺	m/e 448 (M+H)+
531		N-(4-{1-[(4-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 474 (M+H)+
532		N-(4-{1-[(3,5-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 492 (M+H)+
533		N-{4-[1-(3,4-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 (M+H)+
534		N-(4-{1-[(3-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 474 (M+H)+
535		1-(哒嗪-4-基)-N-(4-{1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 510 (M+H)+
536		N-(4-{1-[(2,4-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 492 (M+H)+
537		1-(哒嗪-4-基)-N-{4-[1-(1,3-噻唑-4-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 449 (M+H)+
538		1-(哒嗪-4-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 (M+H)+
539		N-(4-{1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 (M+H)+
540		N-(4-{1-[(2-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 474 (M+H)+
541		N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 406 (M+H)+
542		1-(哒嗪-4-基)-N-{4-[1-(四氢呋喃-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 (M+H)+
543		1-(哒嗪-4-基)-N-{4-[1-(吡啶-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 443 (M+H)+
544		N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 (M+H)+
545		N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 (M+H)+
546		N-{4-[1-(2-甲基-2-苯基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 484 (M+H)+
547		N-{4-[1-(2,4-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 (M+H)+
548		N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环	(ESI(+))

		丁烷-3-甲酰胺	m/e 410 $(M+H)^+$
549		1-(哒嗪-4-基)-N-{4-[1-(噻吩-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 448 $(M+H)^+$
550		1-(哒嗪-4-基)-N-[4-(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$
551		N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 460 $(M+H)^+$
552		N-{4-[1-(3,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 $(M+H)^+$
553		1-(哒嗪-4-基)-N-(4-{1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 510 $(M+H)^+$
554		N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 460 $(M+H)^+$
555		1-(哒嗪-4-基)-N-(4-{1-[4-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 526 $(M+H)^+$
556		N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
557		1-(哒嗪-4-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 448 $(M+H)^+$
558		N-(4-{1-[二氟(苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 492 $(M+H)^+$
559		N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
560		N-(4-{1-[(4,4-二氟环己基)羰基]哌啶-4-基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 484 $(M+H)^+$
561		1-(哒嗪-4-基)-N-[4-(1-{[4-(三氟甲氧基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 540 $(M+H)^+$
562		1-(哒嗪-4-基)-N-(4-{1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 526 $(M+H)^+$
563		1-(哒嗪-4-基)-N-[4-(1-{[4-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$

[0386] 实施例 86

N-{4-[1-(环己基甲基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺

如实施例 74 中所述制备标题化合物,用 N-(4-(哌啶-4-基)苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺代替 N-(4-(哌啶-4-基氧基)苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺和用环己烷甲醛代替环丙烷甲醛。

^1H NMR(500MHz, 吡啶-d_5/D_2O) δ ppm 8.23(dd, J = 4.58,1.22Hz,1H)8.13(d, J = 2.75Hz,1H)7.99(d, J = 8.54Hz,2H)7.31-7.36(m,2H)7.11(dd, J = 8.24,

4.27Hz,1H)6.71-6.75(m,1H)4.32(t,J = 6.56Hz,2H)3.98-4.05(m,2H)3.79-3.89(m,1H)3.62-3.71(m,2H)2.69-2.95(m,5H)2.37-2.49(m,2H)1.75-2.00(m,5H)1.46-1.65(m,3H)0.90-1.24(m,5H);(ESI(+))m/e 433(M+H).

[0387] 表6.

以下实施例基本上如实施例74中所述制备,用N-(4-(哌啶-4-基)苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺代替N-(4-(哌啶-4-基氧基)苯基)-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺和用合适的醛代替环丙烷甲醛。一些产物通过快速色谱纯化而其他通过反向HPLC纯化。因此,一些实施例分离为三氟乙酸盐。

实施例	名称	^{1}H NMR	MS
87	N-{4-[1-(3,3-二甲基丁基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶-d_5/D_2O) δ ppm 8.23 (dd, J=4.73, 1.37 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.98 (d, J=8.54 Hz, 2 H) 7.29 - 7.32 (m, 2 H) 7.11 (dd, J=7.93, 4.88 Hz, 1 H) 6.69 - 6.75 (m, 1 H) 4.32 (t, J=6.71 Hz, 2 H) 3.98 - 4.04 (m, 2 H) 3.79 - 3.87 (m, 1 H) 3.68 (s, 2 H) 3.08 - 3.15 (m, 2 H) 2.80 - 2.92 (m, 2 H) 2.71 - 2.79 (m, 1 H) 2.34 - 2.46 (m, 2 H) 1.90 - 1.99 (m, 2 H) 1.71 - 1.78 (m, 2 H) 0.87 (s, 9 H)	(ESI(+)) m/e 421 $(M+H)^+$
88	N-{4-[1-(环戊基甲基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶-d_5/D_2O) δ ppm 8.23 (dd, J=4.88, 1.22 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.31 - 7.35 (m, 2 H) 7.11 (dd, J=8.09, 4.73 Hz, 1 H) 6.70 - 6.75 (m, 1 H) 4.33 (t, J=6.56 Hz, 2 H) 3.97 - 4.05 (m, 2 H) 3.77 - 3.85 (m, 1 H) 3.56 - 3.71 (m, 2 H) 2.98 (d, J=6.71 Hz, 2 H) 2.69 - 2.86 (m, J=12.21, 12.21 Hz, 3 H) 2.34 - 2.49 (m, 2 H) 2.19 - 2.31 (m, 1 H) 1.78 - 1.97 (m, 4 H) 1.35 - 1.57 (m, 4 H) 1.17 - 1.28 (m, 2 H)	(ESI(+)) m/e 419 $(M+H)^+$
89	N-{4-[1-(2,2-二甲基丁基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶-d_5/D_2O) δ ppm 8.23 (dd, J=4.58, 1.22 Hz, 1 H) 8.14 (d, J=2.75 Hz, 1 H) 8.02 (d, J=8.54 Hz, 2 H) 7.32 (d, J=8.24 Hz, 2 H) 7.11 (dd, J=8.24, 4.58 Hz, 1 H) 6.71 - 6.75 (m, 1 H) 4.33 (t, J=6.56 Hz, 2 H) 3.99 - 4.05 (m, 2 H) 3.79 - 3.86 (m, 1 H) 2.89 - 2.97 (m, 2 H) 2.29 - 2.50 (m, J=59.51 Hz, 3 H) 2.14 (d, J=3.97 Hz, 2 H) 1.84 - 1.97 (m, 2 H) 1.71 - 1.78 (m, 2 H) 1.30 (q, J=7.63 Hz, 2 H) 0.88 (s, 6 H) 0.82 (t, J=7.48 Hz, 3 H)	(ESI(+)) m/e 421 $(M+H)^+$
90	N-{4-[1-(2-甲基戊基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶-d_5/D_2O) δ ppm 8.23 (dd, J=4.73, 1.37 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.30 - 7.37 (m, 2 H) 7.11 (dd, J=8.24, 4.27 Hz, 1 H) 6.69 - 6.77 (m, 1 H) 4.28 - 4.36 (m, 2 H) 3.96 - 4.06 (m, 2 H) 3.77 - 3.87 (m, 1 H) 3.53 (s, 2 H) 2.55 - 2.91 (m, 5 H) 2.23 - 2.42 (m, 2 H) 1.81 - 1.95 (m, J=6.71 Hz, 3 H) 1.04 - 1.47 (m, 4 H) 1.03 (t, J=6.41 Hz, 3 H) 0.85 (t, J=7.17 Hz, 3 H)	(ESI(+)) m/e 421 $(M+H)^+$

91		N-[4-(1-丁基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O) δ ppm 8.20 - 8.27 (m, 1 H) 8.13 (d, J=3.05 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.30 - 7.35 (m, 2 H) 7.08 - 7.12 (m, 1 H) 6.68 - 6.74 (m, 1 H) 4.32 (t, J=6.56 Hz, 2 H) 3.97 - 4.06 (m, 2 H) 3.78 - 3.86 (m, 1 H) 3.56 - 3.69 (m, 2 H) 2.92 - 3.03 (m, 2 H) 2.66 - 2.87 (m, 3 H) 2.29 - 2.45 (m, 2 H) 1.91 (d, J=13.73 Hz, 2 H) 1.65 - 1.77 (m, 2 H) 1.10 - 1.31 (m, 2 H) 0.79 (t, J=7.32 Hz, 3 H)	(ESI(+)) m/e 393 $(M+H)^+$
92		N-{4-[1-(2-乙基丁基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O) δ ppm 8.23 (d, J=4.58 Hz, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.33 (d, J=8.54 Hz, 2 H) 7.09 - 7.11 (m, 1 H) 6.70 - 6.74 (m, 1 H) 4.32 (t, J=6.56 Hz, 2 H) 3.97 - 4.05 (m, 2 H) 3.78 - 3.86 (m, 1 H) 3.43 - 3.61 (m, 2 H) 2.55 - 2.95 (m, 5 H) 2.22 - 2.43 (m, 2 H) 1.90 (d, J=13.12 Hz, 2 H) 1.67 - 1.78 (m, 1 H) 1.30 - 1.50 (m, 4 H) 0.85 (t, J=7.48 Hz, 6 H)	(ESI(+)) m/e 421 $(M+H)^+$
93		N-{4-[1-(3-甲基丁基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O) δ ppm 8.19 - 8.26 (m, 1 H) 8.13 (d, J=2.75 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.29 - 7.34 (m, 2 H) 7.11 (dd, J=8.24, 4.58 Hz, 1 H) 6.67 - 6.76 (m, 1 H) 4.32 (t, J=6.56 Hz, 2 H) 3.98 - 4.04 (m, 2 H) 3.77 - 3.87 (m, 1 H) 3.57 - 3.69 (m, 2 H) 2.95 - 3.05 (m, 2 H) 2.67 - 2.87 (m, 3 H) 2.29 - 2.44 (m, 2 H) 1.84 - 1.98 (m, 2 H) 1.60 - 1.71 (m, 2 H) 1.39 - 1.58 (m, 1 H) 0.82 (d, J=6.71 Hz, 6 H)	(ESI(+)) m/e 407 $(M+H)^+$
94		N-{4-[1-(2-甲基丙基)哌啶-4-基]苯基}-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O) δ ppm 8.21 - 8.27 (m, 1 H) 8.14 (d, J=2.75 Hz, 1 H) 7.99 (d, J=8.54 Hz, 2 H) 7.32 (d, J=8.54 Hz, 2 H) 7.11 (dd, J=8.09, 4.73 Hz, 1 H) 6.70 - 6.75 (m, 1 H) 4.33 (t, J=6.56 Hz, 2 H) 3.97 - 4.04 (m, 2 H) 3.78 - 3.87 (m, 1 H) 3.27 - 3.41 (m, 2 H) 2.62 (s, 1 H) 2.38 - 2.52 (m, 4 H) 2.10 - 2.26 (m, J=22.28 Hz, 2 H) 1.90 - 1.99 (m, 1 H) 1.81 - 1.88 (m, 2 H) 0.95 (d, J=6.41 Hz, 6 H)	(ESI(+)) m/e 393 $(M+H)^+$
95		N-[4-(1-丙基哌啶-4-基)苯基]-1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺	^{1}H NMR (500 MHz, 吡啶 -d_5/D_2O) δ ppm 8.21 - 8.25 (m, 1 H) 8.10 - 8.15 (m, 1 H) 7.98 (d, J=8.54 Hz, 2 H) 7.31 (d, J=8.54 Hz, 2 H) 7.11 (dd, J=8.24, 4.58 Hz, 1 H) 6.71 - 6.76 (m, 1 H) 4.32 (t, J=6.56 Hz, 2 H) 3.99 - 4.04 (m, 2 H) 3.77 - 3.89 (m, 1 H) 3.55 - 3.66 (m, 2 H) 2.86 - 2.98 (m, 2 H) 2.64 - 2.86 (m, 3 H) 2.30 - 2.46 (m, 2 H) 1.90 (d, J=14.04 Hz, 2 H) 1.70 - 1.81 (m, 2 H) 0.78 (t, J=7.32 Hz, 3 H)	(ESI(+)) m/e 379 $(M+H)^+$

[0388] 实施例 141

(3S)-N-{4-[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 吡咯烷 -3- 甲酰胺

实施例 141A

(S)- 叔丁基 4-(4-(1-((苄基氧基) 羰基) 吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯如实施例 1A 中所述制备标题化合物，用 (S)-1-((苄基氧基) 羰基) 吡咯烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸和用叔丁基 4-(4- 氨基苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯。

[0389] 实施例 141B

(S)- 叔丁基 4-(4-(吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 1B 中所述制备标题化合物，用 (S)- 叔丁基 4-(4-(1-((苄基氧基) 羰基) 吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0390] 实施例 141C

(S)- 叔丁基 4-(4-(1-(哒嗪 -4- 基) 吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 1C 中所述制备标题化合物，用 (S)- 叔丁基 4-(4-(吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯和用 4- 溴哒嗪代替 3- 溴吡啶。

[0391] 实施例 141D

(S)-N-(4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -4- 基) 吡咯烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物，用叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0392] 实施例 141E

(3S)-N-{4-[1-(2- 羟基 -2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 (S)-N-(4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -4- 基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 羟基 -2- 甲基丙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.07(s,1H),8.68-8.61(m,1H),8.61-8.50(m,1H),7.52(t, J = 6.8Hz,2H),7.17(d, J = 8.6Hz,2H),6.62(dd, J = 6.3,3.2Hz,1H),5.35(s,1H),3.73-3.34(m,8H),2.73(dd, J = 13.9,10.2Hz,2H),2.40-2.06(m,2H),1.76(d, J = 11.0Hz,2H),1.64-1.38(m,2H),1.33(s,6H) ;MS(ESI(+))m/e 438(M+H)$^+$.

[0393] 实施例 142

(3S)-N-{4-[1-(环戊基乙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 (S)-N-(4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -4- 基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用环戊基乙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.07(s,1H),8.64(dd, J = 3.1,0.9Hz,1H),8.57(dd, J = 6.2,0.9Hz,1H),7.54(s,1H),7.51(s,1H),7.21-7.13(m,2H),6.61(dd, J = 6.2,3.1Hz,1H),3.68-3.41(m,8H),3.18-3.00(m,1H),2.78-2.64(m,1H),2.42-2.06(m,5H),1.83-1.69(m,4H),1.65-1.20(m,6H),1.22-1.04(m,2H) ;MS(ESI(+))m/e 462(M+H)$^+$.

[0394] 实施例 147

N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 147A

叔丁基 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

在 50mL 圆底烧瓶中加入叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯 (918mg,2.55mmol) 和在乙醇 (10.6ml) 中的二异丙基乙胺 (0.558ml,3.19mmol)。加入以单独部分的作为固体的 3,6- 二氯哒嗪 (317mg,2.128mmol)。将反应物在 45℃下搅拌过夜 ;并将反应物冷却并浓缩。加入二氯甲烷和水并将层分离。用二氯甲烷将含水层萃取三次并将合并的有机物用硫酸镁干燥,过滤并通过旋转蒸发浓缩。将残余物通过常规相快速柱色谱 (regular phase flash column chromatography) 纯化来产生标题化合物。

[0395] 实施例 147B

叔丁基 4-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

向 50mL 圆底烧瓶中加入叔丁基 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯 (550mg,1.165mmol) 和 Pd/C(93mg,0.087mmol)。将烧瓶用氮气冲洗 10 分钟并加入乙醇 (11.7ml)。加入三乙胺 (0.162ml,1.165mmol) 和环己 -1,4- 二烯 (654mg,8.16mmol),并将反应物在 80℃下搅拌 1 小时,冷却并经硅藻土过滤。将滤液真空浓缩并将残余物通过常规相快速柱色谱纯化来产生标题化合物。

[0396] 实施例 147C

N-(4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用叔丁基 4-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0397] 实施例 147D

N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 甲基丙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz,DMSO-d_6) δ ppm10.03(s,1H),8.56(dd,J = 4.5,1.3Hz,1H),7.52(dd,J = 9.2,4.7Hz,2H),7.40(ddd,J = 13.5,7.9,2.8Hz,1H),7.18(d,J = 8.6Hz,2H),6.82(dd,J = 8.9,1.3Hz,1H),4.55(d,J = 12.0Hz,1H),4.32-3.90(m,5H),3.83-3.54(m,1H),3.10(t,J = 12.9Hz,1H),2.89(hept,J = 6.7Hz,1H),2.71(ddd,J = 28.5,16.0,11.7Hz,1H),1.77(d,J = 12.3Hz,2H),1.60-1.10(m,4H),1.01(t,J = 6.0Hz,6H) ;MS(ESI(+))m/e 408(M+H)$^+$.

[0398] 表 7.

以下实施例基本上如实施例 1A 中所述制备,用 N-(4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用合适的羧酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。一些产物通过快速色谱纯化而其他通过反向 HPLC 纯化。因此,一些实施例分离为三氟乙酸盐。

实施例		名称	MS
316		N-[4-(1-乙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 380 $(M+H)^+$
317		N-[4-(1-丁酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 408 $(M+H)^+$
318		N-[4-(1-戊酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
319		N-{4-[1-(2-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
320		N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
321		N-[4-(1-己酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
322		N-{4-[1-(2-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
323		N-{4-[1-(3-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
324		N-{4-[1-(4-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
325		N-{4-[1-(2,2-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436

			(M+H)+
326		N-{4-[1-(2,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 (M+H)+
327		N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 (M+H)+
328		N-{4-[1-(2-乙基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 (M+H)+
329		N-[4-(1-庚酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
330		N-{4-[1-(丁-3-烯酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 406 (M+H)+
331		N-{4-[1-(戊-4-烯酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 420 (M+H)+
332		1-(哒嗪-3-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 448 (M+H)+
333		N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 410 (M+H)+
334		N-(4-{1-[(甲基巯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 426 (M+H)+
335		N-(4-{1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 454 (M+H)+
336		N-{4-[1-(3-硝基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 439 (M+H)+
337		N-(4-{1-[3-(甲基巯基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 440 (M+H)+
338		N-{4-[1-(戊-4-炔酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 418 (M+H)+
339		N-{4-[1-(环己基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 448 (M+H)+
340		N-{4-[1-(环己基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 (M+H)+
341		N-{4-[1-(3-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 456 (M+H)+
342		N-{4-[1-(2-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 458 (M+H)+
343		N-{4-[1-(3-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 458

			$(M+H)^+$
344		N-{4-[1-(4-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 458 $(M+H)^+$
345		N-{4-[1-(2-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 472 $(M+H)^+$
346		N-{4-[1-(3-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 472 $(M+H)^+$
347		N-{4-[1-(4-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 472 $(M+H)^+$
348		N-{4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 460 $(M+H)^+$
349		N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 460 $(M+H)^+$
350		N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
351		N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
352		N-{4-[1-(3-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 467 $(M+H)^+$
353		N-{4-[1-(4-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 467 $(M+H)^+$
354		1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 510 $(M+H)^+$
355		1-(哒嗪-3-基)-N-(4-{1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 510 $(M+H)^+$
356		1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 526 $(M+H)^+$
357		N-{4-[1-(2,3-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 470 $(M+H)^+$
358		N-{4-[1-(2,4-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 470 $(M+H)^+$
359		N-{4-[1-(2,5-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 470 $(M+H)^+$
360		N-{4-[1-(3,4-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 470 $(M+H)^+$
361		N-{4-[1-(3,5-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 470

			$(M+H)^+$
362		N-{4-[1-(2,4-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 510 $(M+H)^+$
363		N-{4-[1-(2,5-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 510 $(M+H)^+$
364		N-{4-[1-(3,4-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 510 $(M+H)^+$
365		N-{4-[1-(3,5-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 510 $(M+H)^+$
366		N-(4-{1-[(2-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 474 $(M+H)^+$
367		N-(4-{1-[(3-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 474 $(M+H)^+$
368		N-(4-{1-[(4-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 474 $(M+H)^+$
369		N-(4-{1-[(2-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
370		N-(4-{1-[(4-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
371		1-(哒嗪-3-基)-N-[4-(1-{[4-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$
372		N-(4-{1-[(3,5-二甲基苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 484 $(M+H)^+$
373		N-(4-{1-[(2,5-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 492 $(M+H)^+$
374		N-(4-{1-[(3,4-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 525 $(M+H)^+$
375		N-{4-[1-(呋喃-3-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 432 $(M+H)^+$
376		1-(哒嗪-3-基)-N-{4-[1-(噻吩-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 448 $(M+H)^+$
377		N-(4-{1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 $(M+H)^+$
378		N-(4-{1-[(5-甲基吡嗪-2-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 458 $(M+H)^+$
379		N-(4-{1-[(1-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 420

			$(M+H)^+$
380		N-{4-[1-(3-乙氧基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$
381		N-(4-{1-[(1-苯基环丙基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 482 $(M+H)^+$
382		1-(哒嗪-3-基)-N-(4-{1-[(噻唑-2-基硫基)乙酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
383		N-(4-{1-[(1-乙酰基哌啶-4-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 491 $(M+H)^+$
384		N-(4-{1-[(3,5-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 492 $(M+H)^+$
385		N-{4-[1-(N-乙酰基-L-亮氨酰)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 493 $(M+H)^+$
386		N-{4-[1-(二苯基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 532 $(M+H)^+$
387		N-{4-[1-(3-氟-2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 474 $(M+H)^+$
388		N-{4-[1-(5-氟-2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 474 $(M+H)^+$
389		N-{4-[1-(3-氟-4-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 474 $(M+H)^+$
390		N-{4-[1-(2,3-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 $(M+H)^+$
391		N-{4-[1-(2,4-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 $(M+H)^+$
392		N-(4-{1-[4-(丙烷-2-基)苯甲酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 484 $(M+H)^+$
393		N-{4-[1-(4-叔丁基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 498 $(M+H)^+$
394		N-(4-{1-[2-氟-5-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 528 $(M+H)^+$
395		N-(4-{1-[2-氯-5-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 544 $(M+H)^+$
397		N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 448 $(M+H)^+$
398		N-(4-{1-[(4-甲基苯氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 486

			$(M+H)^+$
399		N-(4-{1-[(2S)-2-苯基丁酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 484 $(M+H)^+$
400		N-{4-[1-(3,5-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 $(M+H)^+$
401		N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
402		N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
403		1-(哒嗪-3-基)-N-{4-(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$
404		N-(4-{1-[(3-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
405		N-(4-{1-[(2,4-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$
406		N-{4-[1-(萘-1-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 492 $(M+H)^+$
407		N-(4-{1-[(2R)-2-甲氧基-2-苯基乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 486 $(M+H)^+$
408		N-(4-{1-[N-(呋喃-2-基羰基)甘氨酰]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 489 $(M+H)^+$
409		N-(4-{1-[(苄基氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 486 $(M+H)^+$
410		N-{4-[1-(萘-1-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 506 $(M+H)^+$
411		N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 406 $(M+H)^+$
412		1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
413		N-{4-[1-(N-苯甲酰基甘氨酰)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 499 $(M+H)^+$
414		1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
415		1-(哒嗪-3-基)-N-(4-{1-[4-(噻吩-2-基)丁酰基]哌啶-4-基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
416		N-{4-[1-(2,5-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478

			$(M+H)^+$
417		N-{4-[1-(环丁基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 420 $(M+H)^+$
418		N-[4-(1-{N-[(4-甲基苯基)磺酰基]甘氨酰}哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 549 $(M+H)^+$
419		N-(4-{1-[(2,3-二氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 492 $(M+H)^+$
420		N-(4-{1-[(2S)-2-甲氧基-2-苯基乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 486 $(M+H)^+$
421		N-{4-[1-(萘-2-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 506 $(M+H)^+$
422		N-{4-[1-(3-苯基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 470 $(M+H)^+$
423		N-(4-{1-[(2,6-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$
424		N-(4-{1-[3-(苯基磺酰基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 534 $(M+H)^+$
425		1-(哒嗪-3-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 448 $(M+H)^+$
426		N-(4-{1-[(2,5-二甲基呋喃-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 460 $(M+H)^+$
427		N-{4-[1-(环丙基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 420 $(M+H)^+$
428		N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 460 $(M+H)^+$
429		N-{4-[1-(2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 456 $(M+H)^+$
430		1-(哒嗪-3-基)-N-{4-[1-(1,3-噻唑-4-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 449 $(M+H)^+$
431		1-(哒嗪-3-基)-N-{4-[1-(1,3-噻唑-5-基羰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 449 $(M+H)^+$
432		N-{4-[1-(乙氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 $(M+H)^+$
433		1-(哒嗪-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 $(M+H)^+$
434		N-(4-{1-[(6-甲基吡啶-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 457

			$(M+H)^+$
435		N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 442 $(M+H)^+$
436		N-{4-[1-(呋喃-2-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 432 $(M+H)^+$
437		N-(4-{1-[(1-甲基环己基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 $(M+H)^+$
438		N-{4-[1-(2-氧代丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 408 $(M+H)^+$
439		N-{4-[1-(环戊基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 434 $(M+H)^+$
440		N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 394 $(M+H)^+$
441		N-{4-[1-(4-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 456 $(M+H)^+$

[0399] 实施例 148

N-{4-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 148A

4-(1- 异丁基 -1H- 吡唑 -4- 基) 苯胺

将 4- 溴苯胺 (406mg,2.362mmol)、1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑 (650mg,2.60mmol)、$PdCl_2$(dppf)- 二氯甲烷加合物 (57.9mg,0.071mmol) 和碳酸钠 (526mg,4.96mmol) 在四氢呋喃 / 甲醇 / 水 (12ml) 的 6 ： 2 ： 1 的混合物中的悬浮液进行三次真空 / 氮气吹扫循环 ;将反应混合物在油浴中在 85℃下加热过夜。将混合物用乙酸乙酯和水稀释 ;将分离的含水层用乙酸乙酯萃取,并将合并的有机层用盐水洗涤,用硫酸镁干燥,过滤并浓缩。将残余物通过正相色谱纯化以产生标题化合物。

[0400] 实施例 148B

苄基 3-((4-(1- 异丁基 -1H- 吡唑 -4- 基) 苯基) 氨基甲酰基) 氮杂环丁烷 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用 4-(1- 异丁基 -1H- 吡唑 -4- 基) 苯胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯。

[0401] 实施例 148C

N-(4-(1- 异丁基 -1H- 吡唑 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1B 中所述制备标题化合物,用苄基 3-((4-(1- 异丁基 -1H- 吡唑 -4- 基) 苯基) 氨基甲酰基) 氮杂环丁烷 -1- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0402] 实施例 148D

N-{4-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺如实施例 1C 中所述制备标题化合物,用 4- 溴哒嗪代替 3- 溴吡啶和用 N-(4-(1- 异丁

基-1H-吡唑-4-基)苯基)氮杂环丁烷-3-甲酰胺代替叔丁基4-(4-(氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.10(s,1H),8.61(d, J = 6.0Hz,1H),8.51(d, J = 3.0Hz,1H),8.08(s,1H),7.81(s,1H),7.64-7.56(m,2H),7.55-7.48(m,2H),6.55(dd, J = 6.0,3.0Hz,1H),4.31-3.96(m,4H),3.91(d, J = 7.1Hz,2H),3.74(s,1H),2.12(dd, J = 13.3,6.5Hz,1H),0.86(d,J = 6.7Hz,6H) ;MS(ESI(+))m/e 377(M+H)$^+$.

[0403] 实施例199

N-(4-{[1-(4-氟苯甲酰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺如实施例1中所述制备标题化合物,用叔丁基4-(4-氨基苯氧基)氮杂环丁烷基-1-甲酸酯代替实施例1A中的叔丁基4-(4-氨基苯氧基)哌啶-1-甲酸酯,用4-溴哒嗪代替实施例1C中的3-溴吡啶(bromopyridyl)和用4-氟苯甲酸代替实施例1E中的2-(四氢-2H-吡喃-4-基)乙酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.01(s,1H),8.67-8.44(m,1H),7.83-7.63(m,2H),7.62-7.43(m,2H),7.43-7.18(m,2H),6.90-6.77(m,2H),6.55(dd, J = 6.1,3.1Hz,1H),5.13-4.94(m,1H),4.61(d,J = 52.0Hz,2H),4.36-4.04(m,4H),3.99(s,1H),3.70(ddt,J = 33.0,30.2,15.0Hz,1H),1.21(t, J = 15.0Hz,3H) ;MS(ESI(+))m/e 448(M+H)$^+$.

[0404] 表8.

以下实施例基本上如实施例1中所述制备,用合适的胺代替实施例1A中的叔丁基4-(4-氨基苯氧基)哌啶-1-甲酸酯,用4-溴哒嗪代替实施例1C中的3-溴吡啶(bromopyridyl)和用合适的羧酸代替实施例1E中的2-(四氢-2H-吡喃-4-基)乙酸。一些产物通过快速色谱纯化而其他通过反向HPLC纯化。因此,一些实施例分离为三氟乙酸盐。

实施例	名称	MS
200	N-(4-{[1-(2,4-二氟苯甲酰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 466 (M+H)$^+$
201	N-[4-({1-[二氟(苯基)乙酰基]氮杂环丁烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 480 (M+H)$^+$

202		N-[4-({1-[(4,4-二氟环己基)羰基]氮杂环丁烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 472 $(M+H)^+$
203		N-[4-({1-[(4-氟苯基)乙酰基]氮杂环丁烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 $(M+H)^+$
205		1-(哒嗪-4-基)-N-[4-({1-[4-(三氟甲基)苯甲酰基]氮杂环丁烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 498 $(M+H)^+$
206		N-{4-[(1-苯甲酰基氮杂环丁烷-3-基)氧基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 430 $(M+H)^+$
207		N-(4-{[1-(2-羟基-2-甲基丙酰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 412 $(M+H)^+$
208		1-(哒嗪-4-基)-N-(4-{[1-(四氢呋喃-3-基羰基)氮杂环丁烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 $(M+H)^+$
209		N-(4-{[1-(呋喃-3-基羰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 420 $(M+H)^+$
210		N-{4-[(1-戊酰基氮杂环丁烷-3-基)氧基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 410 $(M+H)^+$
254		N-(4-{[1-(3,3-二甲基丁酰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 $(M+H)^+$
255		N-(4-{[1-(环己基羰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
256		1-(哒嗪-4-基)-N-(4-{[1-(四氢-2H-吡喃-4-基乙酰基)氮杂环丁烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 452 $(M+H)^+$
257		N-[4-({1-[(2-甲基环丙基)羰基]氮杂环丁烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 408 $(M+H)^+$
258		1-(哒嗪-4-基)-N-(4-{[1-(3,3,3-三氟丙酰基)氮杂环丁烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
259		N-(4-{[1-(环戊基羰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
260		N-(4-{[1-(3,3-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 452 $(M+H)^+$
261		N-(4-{[1-(环丁基羰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 408 $(M+H)^+$
262		1-(哒嗪-4-基)-N-(4-{[1-(四氢呋喃-2-基羰基)氮杂环丁烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 $(M+H)^+$
263		N-(4-{[1-(4-甲基戊酰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 $(M+H)^+$

264		N-(4-{[1-(2-甲基丙酰基)氮杂环丁烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 396 $(M+H)^+$
265		N-[4-({1-[(2S)-2-甲基丁酰基]氮杂环丁烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 410 $(M+H)^+$
266		N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$
267		N-(4-{[1-(甲氧基乙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 426 $(M+H)^+$
268		1-(哒嗪-4-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 464 $(M+H)^+$
269		N-[4-({1-[二氟(苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 508 $(M+H)^+$
270		N-[4-({1-[(4,4-二氟环己基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 500 $(M+H)^+$
271		N-(4-{[1-(4-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
272		1-(哒嗪-4-基)-N-(4-{[1-(1,3-噻唑-4-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 465 $(M+H)^+$
273		1-(哒嗪-4-基)-N-{4-[(1-{[4-(三氟甲基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 540 $(M+H)^+$
274		N-(4-{[1-(3,4-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 494 $(M+H)^+$
275		1-(哒嗪-4-基)-N-{4-[(1-{[4-(三氟甲氧基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 556 $(M+H)^+$
276		N-[4-({1-[(4-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
277		N-[4-({1-[(2,4-二氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 508 $(M+H)^+$
278		1-(哒嗪-4-基)-N-(4-{[1-(噻吩-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 464 $(M+H)^+$
279		N-(4-{[1-(2-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 492 $(M+H)^+$
280		N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$
281		N-(4-{[1-(2-甲基-2-苯基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 500 $(M+H)^+$

282		N-{4-[(1-乙酰基哌啶-4-基)氧基]苯基}-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 396 $(M+H)^+$
283		1-(哒嗪-4-基)-N-(4-{[1-(1,3-噻唑-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 465 $(M+H)^+$
284		N-(4-{[1-(2,4-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 494 $(M+H)^+$
285		1-(哒嗪-4-基)-N-[4-({1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 526 $(M+H)^+$
286		N-(4-{[1-(3-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
287		1-(哒嗪-4-基)-N-[4-({1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 526 $(M+H)^+$
288		N-[4-({1-[(3-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
289		N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
290		1-(哒嗪-4-基)-N-[4-({1-[4-(三氟甲氧基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 542 $(M+H)^+$
291		N-[4-({1-[(3,5-二氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 508 $(M+H)^+$
292		1-(哒嗪-4-基)-N-[4-({1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 542 $(M+H)^+$
293		N-(4-{[1-(环丙基乙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
294		N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 $(M+H)^+$
295		N-(4-{[1-(3-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 492 $(M+H)^+$
296		1-(哒嗪-4-基)-N-(4-{[1-(吡啶-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 459 $(M+H)^+$
297		N-(4-{[1-(4-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 492 $(M+H)^+$
298		1-(哒嗪-4-基)-N-(4-{[1-(四氢呋喃-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 452 $(M+H)^+$
299		N-(4-{[1-(3,5-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 494 $(M+H)^+$

300		N-(4-{[1-(2,2-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 452 $(M+H)^+$
301		N-(4-{[1-(环丙基羰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
302		1-(哒嗪-4-基)-N-(4-{[1-(四氢呋喃-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 452 $(M+H)^+$
303		1-(哒嗪-4-基)-N-(4-{[1-(噻吩-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 464 $(M+H)^+$
304		N-[4-({1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 $(M+H)^+$
305		1-(哒嗪-4-基)-N-{4-[(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 540 $(M+H)^+$
306		1-(哒嗪-4-基)-N-(4-{[1-(四氢-2H-吡喃-4-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 466 $(M+H)^+$
307		N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$
308		N-[4-({1-[(2-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
396		N-(4-{[(3R)-1-(4-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 $(M+H)^+$
442		N-(4-{[(3R)-1-(2-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 $(M+H)^+$
443		1-(哒嗪-4-基)-N-(4-{[(3R)-1-(1,3-噻唑-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 451 $(M+H)^+$
444		N-(4-{[(3R)-1-(环丙基乙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
445		N-[4-({(3R)-1-[(2S)-2-甲基丁酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 $(M+H)^+$
446		1-(哒嗪-4-基)-N-(4-{[(3R)-1-(四氢-2H-吡喃-4-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 452 $(M+H)^+$
447		1-(哒嗪-4-基)-N-(4-{[(3R)-1-{[4-(三氟甲氧基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 542 $(M+H)^+$
448		1-(哒嗪-4-基)-N-(4-{[(3R)-1-(噻吩-3-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 $(M+H)^+$
449		N-[4-({(3R)-1-[(4-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$

450		N-[4-({(3R)-1-[(3,5-二氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 494 $(M+H)^+$
451		N-(4-{[(3R)-1-(3,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 480 $(M+H)^+$
452		N-[4-({(3R)-1-[(3-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
453		1-(哒嗪-4-基)-N-[4-({(3R)-1-[3-(三氟甲基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 512 $(M+H)^+$
454		N-[4-({(3R)-1-[(2,4-二氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 494 $(M+H)^+$
455		1-(哒嗪-4-基)-N-(4-{[(3R)-1-{[4-(三氟甲基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 526 $(M+H)^+$
456		1-(哒嗪-4-基)-N-(4-{[(3R)-1-(1,3-噻唑-4-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 451 $(M+H)^+$
457		1-(哒嗪-4-基)-N-(4-{[(3R)-1-(四氢呋喃-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$
458		N-[4-({(3R)-1-[(5-甲基噻吩-2-基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 464 $(M+H)^+$
459		N-[4-({(3R)-1-[(2-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
460		N-(4-{[(3R)-1-(环丙基羰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 408 $(M+H)^+$
461		1-(哒嗪-4-基)-N-(4-{[(3R)-1-(四氢呋喃-3-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$
462		1-(哒嗪-4-基)-N-[4-({(3R)-1-[3-(三氟甲氧基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 528 $(M+H)^+$
463		1-(哒嗪-4-基)-N-(4-{[(3R)-1-(吡啶-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 445 $(M+H)^+$
464		N-(4-{[(3R)-1-(3-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 $(M+H)^+$
465		N-(4-{[(3R)-1-(4-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 $(M+H)^+$
466		N-(4-{[(3R)-1-(2-甲基-2-苯基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 486 $(M+H)^+$
467		N-(4-{[(3R)-1-(2,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 480 $(M+H)^+$

468		N-(4-{[(3R)-1-(甲氧基乙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 412 $(M+H)^+$
469		1-(哒嗪-4-基)-N-(4-{[(3R)-1-(噻吩-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 $(M+H)^+$
470		1-(哒嗪-4-基)-N-(4-{[(3R)-1-{[3-(三氟甲基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 526 $(M+H)^+$
471		N-(4-{[(3R)-1-(2-甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 410 $(M+H)^+$
472		N-(4-{[(3R)-1-(2-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 $(M+H)^+$
473		N-(4-{[(3R)-1-(2,2-二甲基丁酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$
474		N-(4-{[(3R)-1-(3,5-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 480 $(M+H)^+$
475		1-(哒嗪-4-基)-N-[4-({(3R)-1-[4-(三氟甲基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 512 $(M+H)^+$
476		N-(4-{[(3R)-1-(3-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 $(M+H)^+$
477		1-(哒嗪-4-基)-N-[4-({(3R)-1-[4-(三氟甲氧基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 528 $(M+H)^+$
478		N-(4-{[(3R)-1-(3-甲基丁酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 $(M+H)^+$
479		1-(哒嗪-4-基)-N-(4-{[(3R)-1-(3,3,3-三氟丙酰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 $(M+H)^+$
480		N-[4-({(3R)-1-[二氟(苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 494 $(M+H)^+$
481		N-(4-{[(3R)-1-(2,2-二甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 $(M+H)^+$
482		N-[4-({(3R)-1-[(4,4-二氟环己基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 486 $(M+H)^+$

[0405] 实施例 204

(3S)-N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(吡啶-3-基)吡咯烷-3-甲酰胺如实施例 1 中所述制备标题化合物,用 (S)-1-((苄基氧基)羰基)吡咯烷-3-甲酸代替 1-(苄基氧基羰基)氮杂环丁烷-3-甲酸和用叔丁基 4-(4-氨基苯基)哌啶-1-甲酸酯代替实施例 1A 中的叔丁基 4-(4-氨基苯氧基)哌啶-1-甲酸酯,和用环戊基苯甲酸代替实施例 1E 中的 2-(四氢-2H-吡喃-4-基)乙酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 10.03(s,1H),7.95(d, J = 2.8Hz,1H),7.85(dd, J = 4.6,1.2Hz,1H),7.55(t, J = 10.1Hz,2H),7.16(dd, J = 8.3,4.3Hz,3H),6.92(ddd, J = 8.4,2.9,1.3Hz,1H),4.54(d,J = 12.7Hz,1H),3.98(d,J = 13.7Hz,1H),3.64-3.48(m,1H),

3.48-3.38(m,1H),3.22-2.87(m,2H),2.68(dd,J = 24.3,12.3Hz,1H),2.41-2.01(m,6H),1.77(s,4H),1.68-1.04(m,9H);MS(ESI(+))m/e 461(M+H)$^+$.

[0406] 实施例 211

N-(4-{[1-(2- 氯苯甲酰基)哌啶 -4- 基]氧基}苯基)-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺

如实施例 147 中所述制备标题化合物,用叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基)苯氧基)哌啶 -1- 甲酸酯代替实施例 147A 中的 4-(4-(氮杂环丁烷 -3- 甲酰胺基)苯基)哌啶 -1- 甲酸酯和用 2- 氯苯甲酸代替实施例 147D 中的 2- 甲基丙酸。

^{1}H NMR(400MHz,DMSO/D_2O) δ ppm 8.51(dd,J = 4.4,1.2Hz,1H),7.78-7.66(m,1H),7.55-7.45(m,3H),7.45-7.37(m,2H),7.37-7.28(m,2H),7.01-6.89(m,2H),4.63-4.34(m,6H),4.03-3.86(m,1H),3.86-3.72(m,1H),3.63-3.43(m,1H),3.43-3.31(m,1H),3.26-3.07(m,1H),2.06-1.80(m,2H),1.80-1.53(m,2H),1.28-1.21(m,1H);MS(ESI(+))m/e 492(M+H)$^+$.

[0407] 表 9.

以下实施例基本上如实施例 147 中所述制备,代替实施例 147A 中的合适的胺和 147D 中合适的羧酸。一些产物通过快速色谱纯化而其他通过反向 HPLC 纯化。因此,一些实施例分离为三氟乙酸盐。

实施例	名称	MS
212	N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 (M+H)$^+$
213	1-(哒嗪-3-基)-N-(4-{[1-(1,3-噻唑-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 465 (M+H)$^+$
214	1-(哒嗪-3-基)-N-(4-{[1-(四氢-2H-吡喃-4-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 466 (M+H)$^+$
215	N-[4-({1-[二氟(苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 508 (M+H)$^+$
216	N-[4-({1-[(4,4-二氟环己基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 500 (M+H)$^+$
217	N-(4-{[1-(2-甲基-2-苯基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 500

			$(M+H)^+$
218		1-(哒嗪-3-基)-N-(4-{[1-(1,3-噻唑-4-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 465 $(M+H)^+$
219		N-[4-({1-[(5-甲基噻吩-2-基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 $(M+H)^+$
220		1-(哒嗪-3-基)-N-{4-[(1-{[4-(三氟甲基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 540 $(M+H)^+$
221		1-(哒嗪-3-基)-N-(4-{[1-(四氢呋喃-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 452 $(M+H)^+$
222		1-(哒嗪-3-基)-N-[4-({1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 526 $(M+H)^+$
223		1-(哒嗪-3-基)-N-(4-{[1-(噻吩-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 464 $(M+H)^+$
224		1-(哒嗪-3-基)-N-[4-({1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 542 $(M+H)^+$
225		N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$
226		1-(哒嗪-3-基)-N-(4-{[1-(四氢呋喃-3-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 452 $(M+H)^+$
227		N-[4-({1-[(3-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
228		N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
229		N-(4-{[1-(2,4-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 494 $(M+H)^+$
230		N-(4-{[1-(4-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
231		N-(4-{[1-(3-氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
232		N-[4-({1-[(4-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
233		N-(4-{[1-(环丙基乙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
234		N-(4-{[1-(3,4-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 494 $(M+H)^+$
235		1-(哒嗪-3-基)-N-[4-({1-[4-(三氟甲氧基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 542

			$(M+H)^+$
236		N-[4-({1-[(2,4-二氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 508 $(M+H)^+$
237		1-(哒嗪-3-基)-N-[4-({1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 526 $(M+H)^+$
238		1-(哒嗪-3-基)-N-{4-[(1-{[4-(三氟甲氧基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 556 $(M+H)^+$
239		N-[4-({1-[(3,5-二氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 508 $(M+H)^+$
240		1-(哒嗪-3-基)-N-{4-[(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)氧基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 540 $(M+H)^+$
241		N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$
242		1-(哒嗪-3-基)-N-(4-{[1-(吡啶-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 459 $(M+H)^+$
243		N-(4-{[1-(3,5-二氟苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 494 $(M+H)^+$
244		-{4-[(1-乙酰基哌啶-4-基)氧基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 396 $(M+H)^+$
245		N-(4-{[1-(4-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 492 $(M+H)^+$
246		N-(4-{[1-(甲氧基乙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 426 $(M+H)^+$
247		N-[4-({1-[(2-氟苯基)乙酰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
248		N-(4-{[1-(2,2-二甲基丁酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 452 $(M+H)^+$
249		1-(哒嗪-3-基)-N-(4-{[1-(噻吩-2-基羰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 464 $(M+H)^+$
250		N-(4-{[1-(3-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 492 $(M+H)^+$
251		N-(4-{[1-(环丙基羰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
252		1-(哒嗪-3-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 464 $(M+H)^+$
253		N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424

			$(M+H)^+$
483		N-(4-{[(3R)-1-(2-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 $(M+H)^+$
484		1-(哒嗪-3-基)-N-(4-{[(3R)-1-(1,3-噻唑-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 451 $(M+H)^+$
485		N-(4-{[(3R)-1-(环丙基乙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
486		N-[4-({(3R)-1-[(2S)-2-甲基丁酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 $(M+H)^+$
487		1-(哒嗪-3-基)-N-(4-{[(3R)-1-(四氢-2H-吡喃-4-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 452 $(M+H)^+$
488		1-(哒嗪-3-基)-N-(4-{[(3R)-1-{[4-(三氟甲氧基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 542 $(M+H)^+$
489		N-(4-{[(3R)-1-(4-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 $(M+H)^+$
490		1-(哒嗪-3-基)-N-(4-{[(3R)-1-(噻吩-3-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 $(M+H)^+$
491		N-[4-({(3R)-1-[(4-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
492		N-[4-({(3R)-1-[(3,5-二氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 494 $(M+H)^+$
493		N-(4-{[(3R)-1-(3,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 480 $(M+H)^+$
494		N-[4-({(3R)-1-[(3-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
495		1-(哒嗪-3-基)-N-[4-({(3R)-1-[3-(三氟甲基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 512 $(M+H)^+$
496		N-[4-({(3R)-1-[(2,4-二氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 494 $(M+H)^+$
497		1-(哒嗪-3-基)-N-(4-{[(3R)-1-{[4-(三氟甲基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 526 $(M+H)^+$
498		1-(哒嗪-3-基)-N-(4-{[(3R)-1-(1,3-噻唑-4-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 451 $(M+H)^+$
499		1-(哒嗪-3-基)-N-(4-{[(3R)-1-(四氢呋喃-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$
500		N-[4-({(3R)-1-[(5-甲基噻吩-2-基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 464

			(M+H)+
501		N-[4-({(3R)-1-[(2-氟苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 (M+H)+
502		N-(4-{[(3R)-1-(环丙基羰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 408 (M+H)+
503		1-(哒嗪-3-基)-N-(4-{[(3R)-1-(四氢呋喃-3-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 (M+H)+
504		1-(哒嗪-3-基)-N-[4-({(3R)-1-[3-(三氟甲氧基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 528 (M+H)+
505		1-(哒嗪-3-基)-N-(4-{[(3R)-1-(吡啶-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 445 (M+H)+
506		N-(4-{[(3R)-1-(3-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 (M+H)+
507		N-(4-{[(3R)-1-(4-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 (M+H)+
508		N-(4-{[(3R)-1-(2-甲基-2-苯基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 486 (M+H)+
509		N-(4-{[(3R)-1-(2,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 480 (M+H)+
510		N-(4-{[(3R)-1-(甲氧基乙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 412 (M+H)+
511		1-(哒嗪-3-基)-N-(4-{[(3R)-1-(噻吩-2-基羰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
512		1-(哒嗪-3-基)-N-(4-{[(3R)-1-{[3-(三氟甲基)苯基]乙酰基}吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 526 (M+H)+
513		N-(4-{[(3R)-1-(2-甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 410 (M+H)+
514		N-(4-{[(3R)-1-(2-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 (M+H)+
515		N-(4-{[(3R)-1-(2,2-二甲基丁酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 (M+H)+
516		N-(4-{[(3R)-1-(3,5-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 480 (M+H)+
517		1-(哒嗪-3-基)-N-[4-({(3R)-1-[4-(三氟甲基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 512 (M+H)+
518		N-(4-{[(3R)-1-(3-氯苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462

			(M+H)+
519		1-(哒嗪-3-基)-N-[4-({(3R)-1-[4-(三氟甲氧基)苯甲酰基]吡咯烷-3-基}氧基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 528 (M+H)+
520		N-(4-{[(3R)-1-(3-甲基丁酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 (M+H)+
521		1-(哒嗪-3-基)-N-(4-{[(3R)-1-(3,3,3-三氟丙酰基)吡咯烷-3-基]氧基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
522		N-[4-({(3R)-1-[二氟(苯基)乙酰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 494 (M+H)+
523		N-(4-{[(3R)-1-(2,2-二甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 (M+H)+
524		N-[4-({(3R)-1-[(4,4-二氟环己基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 486 (M+H)+

[0408] 实施例 309

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 呋喃 -2- 甲酰胺

实施例 309A

叔丁基 (1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 基) 氨基甲酸酯

叔丁基氮杂环丁烷 -3- 基氨基甲酸酯 (500mg,2.90mmol) 和 3,6- 二氯哒嗪 (454mg,3.05mmol) 在 DMSO(5mL) 和 N- 乙基 -N- 异丙基丙烷 -2- 胺 (563mg,4.35mmol) 中合并,并将混合物在 100℃下加热过夜。将混合物冷却至室温并用水稀释。过滤提供标题化合物。

[0409] 实施例 309B

叔丁基 (1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基) 氨基甲酸酯

将叔丁基 1-(6- 氯哒嗪 (chloropyridizan)-3- 基) 氮杂环丁烷 -3- 基氨基甲酸酯 (413mg,1.45mmol)、1,4- 环己二烯 (1.10mL,11.6mmol) 和三乙胺 (0.61mL,1.45mmol) 的混合物用氮气吹扫并加入在碳 (20mg) 上的 5% 钯。将反应混合物在 80℃下加热过夜,冷却至室温并经硅藻土过滤,用甲醇润洗。浓缩提供标题化合物。

[0410] 实施例 309C

1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 胺

将叔丁基 1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基氨基甲酸酯 • 三乙胺盐酸化物 (200mg,0.516mmol) 溶于甲醇 (1.5mL) 并逐滴加入 HCl 在二噁烷 (1.5mL,6.00mmol) 中的 4N 溶液。将反应混合物在室温下搅拌 1 小时,随后浓缩至干燥以产生标题化合物。

[0411] 实施例 309D

5-(1- 异丁基 -1H- 吡唑 -4- 基) 呋喃 -2- 甲酸

如实施例 148A 中所述制备标题化合物,用 5- 溴呋喃 -2- 甲酸代替 4- 溴苯胺。

[0412] 实施例 309E

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 呋喃 -2- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 胺代替叔丁

基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯并用 5-(1- 异丁基 -1H- 吡唑 -4- 基) 呋喃 -2- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz,DMSO-d_6) δ ppm 8.83(d,J = 7.5Hz,1H),8.57(dd,J = 4.5,1.3Hz,1H),8.15(d,J = 0.7Hz,1H),7.88(d,J = 0.7Hz,1H),7.39(dd,J = 8.9,4.5Hz,1H),7.16(d,J = 3.5Hz,1H),6.84(dd,J = 8.9,1.4Hz,1H),6.64(d,J = 3.5Hz,1H),4.97-4.84(m,1H),4.38(t,J = 8.1Hz,2H),4.06(dd,J = 8.6,5.7Hz,2H),3.95(d,J = 7.2Hz,2H),2.21-2.05(m,1H),0.85(d,J = 6.7Hz,6H) ;MS(ESI(+))m/e 367(M+H)$^+$.

[0413] 实施例 310

(3S)-N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 147 中所述制备标题化合物,用 (S)- 叔丁基 4-(4-(吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替实施例 147A 中的叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.06(s,1H),8.48(dd,J = 4.4,1.2Hz,1H),7.54(d,J = 8.5Hz,2H),7.43-7.25(m,1H),7.18(d,J = 8.6Hz,2H),6.87(dd,J = 9.2,1.2Hz,1H),4.64-4.48(m,1H),4.15-3.97(m,1H),3.76(dd,J = 10.4,8.0Hz,1H),3.69-3.54(m,2H),3.54-3.38(m,1H),3.20-3.03(m,1H),3.02-2.83(m,2H),2.79-2.64(m,1H),2.64-2.52(m,1H).2.37-2.13(m,2H),1.90-1.68(m,2H),1.59-1.29(m,2H),0.99(dt,J = 14.5,7.0Hz,6H) ;MS(ESI(+))m/e 422(M+H)$^+$.

[0414] 实施例 311

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 147 中所述制备标题化合物,用 (S)- 叔丁基 4-(4-(吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替实施例 147A 中的叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯和用苯甲酸代替实施例 147D 中的 2- 甲基丙酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.06(s,1H),8.48(dd,J = 4.4,1.3Hz,1H),7.55(d,J = 8.6Hz,1H),7.51-7.39(m,5H),7.34(dd,J = 9.1,4.5Hz,1H),7.25-7.19(m,2H),6.87(dd,J = 9.1,1.3Hz,1H),4.65-4.48(m,1H),3.84-3.53(m,4H),3.48(dt,J = 10.2,7.4Hz,1H),3.22-2.69(m,3H),2.36-2.13(m,2H),1.98-1.48(m,4H) ;MS(ESI(+))m/e 456(M+H)$^+$.

[0415] 实施例 312

(3S)-1-(哒嗪 -3- 基)-N-{4-[1-(四氢 -2H- 吡喃 -4- 基乙酰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺如实施例 147 中所述制备标题化合物,用 (S)- 叔丁基 4-(4-(吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替实施例 147A 中的叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯和用四氢 -2H- 吡喃 -4- 基乙酸代替实施例 147D 中的 2- 甲基丙酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.06(s,1H),8.48(dd,J = 4.4,1.2Hz,1H),7.54(d,J = 8.6Hz,2H),7.39-7.27(m,1H),7.17(d,J = 8.6Hz,2H),6.87(dd,J = 9.2,1.2Hz,1H),4.65-4.45(m,1H),4.07-3.92(m,1H),3.89-3.68(m,3H),3.68-3.54(m,2H),3.54-3.39(m,1H),3.22-2.93(m,2H),2.80-2.65(m,1H),2.64-2.52(m,1H),2.38-2.13(m,

4H),2.00-1.84(m,1H),1.80(dt,J = 27.7,7.7Hz,2H),1.68-1.14(m,7H);MS(ESI(+))m/e 478(M+H)$^+$.

[0416] 实施例 313

(3S)-N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺如实施例 147 中所述制备标题化合物,用 (S)-叔丁基 4-(4-(吡咯烷-3-甲酰胺基)苯基)哌啶-1-甲酸酯代替实施例 147A 中的叔丁基 4-(4-(氮杂环丁烷-3-甲酰胺基)苯基)哌啶-1-甲酸酯和用 2,2-二甲基丙酸代替实施例 147D 中的 2-甲基丙酸。

^{1}H NMR(400MHz,DMSO-d_6) δ ppm10.05(s,1H),8.47(dd,J = 4.4,1.0Hz,1H),7.52(d,J = 8.5Hz,2H),7.32(dd,J = 9.1,4.5Hz,1H),7.16(d,J = 8.5Hz,2H),6.86(dd,J = 9.2,1.0Hz,1H),4.39(d,J = 13.2Hz,2H),3.75(dd,J = 10.4,8.0Hz,1H),3.69-3.54(m,2H),3.46(dt,J = 10.1,7.5Hz,1H),3.27(dd,J = 14.8,7.4Hz,1H),2.96(dd,J = 12.8,7.0Hz,1H),2.84(dd,J = 22.1,9.6Hz,2H),2.78-2.64(m,1H),2.27(dt,J = 7.1,5.0Hz,1H),2.18(ddd,J = 14.3,11.6,7.3Hz,1H),1.77(d,J = 11.3Hz,2H),1.54-1.31(m,3H).1.18(d,J = 16.8Hz,9H);MS(ESI(+))m/e 436(M+H)$^+$.

[0417] 表 10.

以下实施例基本上如实施例 313 中所述制备,用合适的羧酸代替 2,2-二甲基丙酸。

实施例	名称	MS
630	(3S)-1-(哒嗪-3-基)-N-{4-[1-(1,3-噻唑-5-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺	(ESI(+)) m/e 463 (M+H)$^+$
631	(3S)-N-{4-[1-(4-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 470 (M+H)$^+$
632	(3S)-N-(4-{1-[(2S)-2-苯基丁酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)	(ESI(+))

		吡咯烷-3-甲酰胺	m/e 498 (M+H)+
633		(3S)-N-(4-{1-[(2S)-2-甲氧基-2-苯基乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 500 (M+H)+
634		(3S)-N-(4-{1-[(2R)-2-甲氧基-2-苯基乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 500 (M+H)+
635		(3S)-N-{4-[1-(乙氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 438 (M+H)+
636		(3S)-N-(4-{1-[(4-甲基苯氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 500 (M+H)+
637		(3S)-N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 474 (M+H)+
638		(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-3-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
639		(3S)-N-{4-[1-(萘-1-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 506 (M+H)+
640		(3S)-N-(4-{1-[(2,6-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 538 (M+H)+
641		(3S)-N-{4-[1-(萘-1-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 520 (M+H)+
642		(3S)-1-(哒嗪-3-基)-N-(4-{1-[4-(噻吩-2-基)丁酰基]哌啶-4-基}苯基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 504 (M+H)+
643		(3S)-N-{4-[1-(环丙基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 434 (M+H)+
644		(3S)-N-{4-[1-(环戊基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 462 (M+H)+
645		(3S)-N-{4-[1-(2,5-二氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 492 (M+H)+
646		(3S)-N-{4-[1-(萘-2-基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 520 (M+H)+
647		(3S)-N-(4-{1-[3-(苯基磺酰基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 548 (M+H)+
648		(3S)-1-(哒嗪-3-基)-N-[4-(1-{[3-(三氟甲基)苯基]乙酰基}哌啶-4-基)苯基]吡咯烷-3-甲酰胺	(ESI(+)) m/e 538 (M+H)+
649		(3S)-N-{4-[1-(呋喃-2-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 446 (M+H)+
650		(3S)-N-{4-[1-(N-苯甲酰基甘氨酰)哌啶-4-基]苯基}-1-(哒嗪-3-基)	(ESI(+))

		吡咯烷-3-甲酰胺	m/e 513 (M+H)+
651		(3S)-N-(4-{1-[(2,4-二氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 538 (M+H)+
652		(3S)-N-{4-[1-(2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 470 (M+H)+
653		(3S)-1-(哒嗪-3-基)-N-{4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺	(ESI(+)) m/e 476 (M+H)+
654		(3S)-N-(4-{1-[(1-甲基环己基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 476 (M+H)+
655		(3S)-1-(哒嗪-3-基)-N-{4-[1-(噻吩-3-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺	(ESI(+)) m/e 462 (M+H)+
656		(3S)-N-(4-{1-[(6-甲基吡啶-3-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 471 (M+H)+
657		(3S)-N-(4-{1-[(3-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 504 (M+H)+
658		(3S)-N-[4-(1-丙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 408 (M+H)+
659		(3S)-N-{4-[1-(3,5-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 492 (M+H)+
660		(3S)-N-{4-[1-(环戊基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 448 (M+H)+
661		(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢呋喃-2-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
662		(3S)-N-{4-[1-(环丙基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 420 (M+H)+
663		(3S)-N-{4-[1-(4-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 490 (M+H)+
669		(3S)-N-{4-[1-(2-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 490 (M+H)+
670		(3S)-N-{4-[1-(2-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
671		(3S)-N-{4-[1-(4-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
672		(3S)-N-{4-[1-(2,4-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 484 (M+H)+
673		(3S)-N-[4-(1-庚酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰	(ESI(+))

		胺	m/e 464 $(M+H)^+$
674		(3S)-N-{4-[1-(2,4-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$
675		(3S)-N-(4-{1-[(4-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 488 $(M+H)^+$
676		(3S)-N-{4-[1-(2,3-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 492 $(M+H)^+$
677		(3S)-N-{4-[1-(3-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 470 $(M+H)^+$
678		(3S)-N-[4-(1-己酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 450 $(M+H)^+$
679		(3S)-N-(4-{1-[(3-甲基噻吩-2-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
680		(3S)-N-{4-[1-(2,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 450 $(M+H)^+$
681		(3S)-N-[4-(1-丁酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
682		(3S)-N-{4-[1-(3-甲基戊酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 450 $(M+H)^+$
683		(3S)-N-(4-{1-[(3,5-二甲基苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 498 $(M+H)^+$
684		(3S)-N-{4-[1-(3,5-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$
685		(3S)-N-{4-[1-(3-氟-2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 488 $(M+H)^+$
686		(3S)-N-(4-{1-[(4-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 504 $(M+H)^+$
687		(3S)-N-{4-[1-(呋喃-3-基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 446 $(M+H)^+$
688		(3S)-N-{4-[1-(3,4-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 484 $(M+H)^+$
689		(3S)-N-{4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 474 $(M+H)^+$
690		(3S)-N-(4-{1-[2-氯-5-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 558 $(M+H)^+$
691		(3S)-N-[4-(1-乙酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰	(ESI(+))

		胺	m/e 394 $(M+H)^+$
692		(3S)-N-{4-[1-(2,4-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 492 $(M+H)^+$
693		(3S)-N-{4-[1-(3,5-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 484 $(M+H)^+$
694		(3S)-N-{4-[1-(3-乙氧基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 452 $(M+H)^+$
695		(3S)-N-{4-[1-(2,5-二氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$
696		(3S)-N-{4-[1-(2,5-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 484 $(M+H)^+$
697		(3S)-N-{4-[1-(5-氟-2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 488 $(M+H)^+$
698		(3S)-N-{4-[1-(二苯基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 546 $(M+H)^+$
699		(3S)-1-(哒嗪-3-基)-N-(4-{1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$
700		(3S)-N-{4-[1-(戊-4-烯酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 434 $(M+H)^+$
701		(3S)-1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲氧基)苯甲酰基]哌啶-4-基}苯基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 540 $(M+H)^+$
702		(3S)-N-(4-{1-[(1-苯基环丙基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 496 $(M+H)^+$
703		(3S)-N-(4-{1-[2-氟-5-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 542 $(M+H)^+$
704		(3S)-N-{4-[1-(环己基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
705		(3S)-N-{4-[1-(4-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 486 $(M+H)^+$
706		(3S)-N-{4-[1-(2-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
707		(3S)-N-{4-[1-(2-乙基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 450 $(M+H)^+$
708		(3S)-N-{4-[1-(4-叔丁基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 512 $(M+H)^+$
709		(3S)-N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯	(ESI(+))

		烷-3-甲酰胺	m/e 490 (M+H)+
710		(3S)-N-(4-{1-[(2-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 488 (M+H)+
711		(3S)-1-(哒嗪-3-基)-N-(4-{1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}苯基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 524 (M+H)+
712		(3S)-N-(4-{1-[(1-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 434 (M+H)+
713		(3S)-N-{4-[1-(戊-4-炔酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 432 (M+H)+
714		(3S)-N-(4-{1-[(3-氟苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 488 (M+H)+
715		(3S)-N-(4-{1-[3-(甲基硫基)丙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 454 (M+H)+
716		(3S)-N-(4-{1-[(1-乙酰基哌啶-4-基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 505 (M+H)+
717		(3S)-N-{4-[1-(丁-3-烯酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 420 (M+H)+
718		(3S)-N-{4-[1-(2,2-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
719		(3S)-N-{4-[1-(3-氟-4-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 488 (M+H)+
720		(3S)-N-{4-[1-(3-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 486 (M+H)+
721		(3S)-N-(4-{1-[(2-氯苯基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 504 (M+H)+
722		(3S)-N-(4-{1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 468 (M+H)+
723		(3S)-N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
724		(3S)-N-{4-[1-(N-乙酰基-L-亮氨酰)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 507 (M+H)+
725		(3S)-N-{4-[1-(3-氯苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 474 (M+H)+
726		(3S)-N-{4-[1-(4-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 481 (M+H)+
727		(3S)-N-{4-[1-(2-甲氧基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)	(ESI(+))

		吡咯烷-3-甲酰胺	m/e 486 (M+H)+
728		(3S)-N-{4-[1-(2,3-二甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 484 (M+H)+
729		(3S)-N-(4-{1-[4-(丙烷-2-基)苯甲酰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 498 (M+H)+
730		(3S)-N-{4-[1-(环己基羰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 462 (M+H)+
731		(3S)-1-(哒嗪-3-基)-N-{4-[1-(噻吩-2-基羰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺	(ESI(+)) m/e 462 (M+H)+
732		(3S)-N-{4-[1-(4-羟基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 472 (M+H)+
733		(3S)-N-{4-[1-(3-氰基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 481 (M+H)+
734		(3S)-1-(哒嗪-3-基)-N-{4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}吡咯烷-3-甲酰胺	(ESI(+)) m/e 462 (M+H)+
735		(3S)-N-{4-[1-(甲氧基乙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 424 (M+H)+
736		(3S)-N-{4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 436 (M+H)+

[0418] 实施例 314

叔丁基 4-(4-{[1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基]氨基甲酰基}苯基)哌啶 -1- 甲酸酯如实施例 1A 中所述制备标题化合物,用 1-(哒嗪 -3- 基)氮杂环丁烷 -3- 胺代替叔丁基 4-(4- 氨基苯氧基)哌啶 -1- 甲酸酯和用 4-(1-(叔丁氧基羰基)哌啶 -4- 基)苯甲酸代替 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6)d 8.96(d, J = 7.0Hz,1H),8.56(dd, J = 4.6,1.3Hz,1H),7.82(d, J = 8.3Hz,2H),7.41-7.31(m,3H),6.83(dd, J = 9.0,1.3Hz,1H),4.96-4.85(m,1H),4.37(t, J = 8.1Hz,2H),4.16-3.97(m,4H),2.88-2.65(m,3H),1.80-1.70(m,2H),1.60-1.43(m,2H),1.41(s,9H) ;MS (ESI(+))m/e 438(M+H)$^+$.

[0419] 实施例 315

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基]噻吩 -2- 甲酰胺

实施例 315A

5-(1- 异丁基 -1H- 吡唑 -4- 基)噻吩 -2- 甲酸

如实施例 148A 中所述制备标题化合物,用 5- 溴噻吩 -2- 甲酸代替 4- 溴苯胺。

[0420] 实施例 315B

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基]噻吩 -2- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 1-(哒嗪 -3- 基)氮杂环丁烷 -3- 胺代替叔丁基 4-(4- 氨基苯氧基)哌啶 -1- 甲酸酯和用 5-(1- 异丁基 -1H- 吡唑 -4- 基)噻吩 -2- 甲

酸代替 1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm8.99(d, J = 7.1Hz,1H),8.57(dd, J = 4.5,1.3Hz, 1H),8.14(d, J = 0.8Hz1H),7.81-7.79(m,1H),7.72(d, J = 3.9Hz,1H),7.39(dd, J = 8.9,4.5Hz,1H),7.21(d, J = 3.8Hz,1H),6.84(dd, J = 9.0,1.4Hz,1H),4.92-4.81(m, 1H),4.37(t, J = 8.1Hz,2H),4.03(dd, J = 8.6,5.5Hz,2H),3.92(d, J = 7.1Hz,2H), 2.19-2.04(m,1H),0.85(d,J = 6.7Hz,6H) ;MS(ESI(+))m/e 383(M+H)$^+$.

[0421] 实施例 564

N-(4-{[1-(3-氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺

实施例 564A

叔丁基 4-((4-(1-((苄基氧基)羰基)氮杂环丁烷-3-甲酰胺基)苯基)硫代)哌啶-1-甲酸酯

如实施例 1A 中所述制备标题化合物,用叔丁基 4-(4-氨基苯基硫代)哌啶-1-甲酸酯代替叔丁基 4-(4-氨基苯氧基)哌啶-1-甲酸酯和用 1-(苄基氧基羰基)氮杂环丁烷-3-甲酸代替 1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

[0422] 实施例 564B

叔丁基 4-((4-(1-((苄基氧基)羰基)氮杂环丁烷-3-甲酰胺基)苯基)磺酰基)哌啶-1-甲酸酯

向 20mL 小瓶中加入在二氯甲烷 (79ml) 中的叔丁基 4-((4-(1-((苄基氧基)羰基)氮杂环丁烷-3-甲酰胺基)苯基)硫代)哌啶-1-甲酸酯 (8.3g,15.79mmol)。将反应化合物在甲醇/干冰浴中冷却至 ca-20℃,用间氯过苯甲酸 (8.17g,47.4mmol) 处理,并允许缓慢加温至室温。当完成时,将反应混合物用 1N 含水氢氧化钠处理并用二氯甲烷萃取。将合并的有机物用硫酸钠干燥,过滤并通过旋转蒸发浓缩。将残余物通过常规相色谱纯化以产生标题化合物。

[0423] 实施例 564C

叔丁基 4-(4-(氮杂环丁烷-3-甲酰胺基)苯基磺酰基)哌啶-1-甲酸酯

将叔丁基 4-(4-(1-(苄基氧基羰基)氮杂环丁烷-3-甲酰胺基)苯基磺酰基)哌啶-1-甲酸酯 (7.94g,14.24mmol) 和乙醇 (160ml) 加入在 250mL SS 耐压瓶中的 20 % $Pd(OH)_2/C$(湿润的)(1.5g,1.089mmol),并将混合物在 30psi 和室温下搅拌 16 小时。将混合物经尼龙膜过滤并浓缩以产生标题化合物。

[0424] 实施例 564D

叔丁基 4-((4-(1-(6-氯哒嗪-3-基)氮杂环丁烷-3-甲酰胺基)苯基)磺酰基)哌啶-1-甲酸酯

如实施例 147A 中所述制备标题化合物,用叔丁基 4-(4-(氮杂环丁烷-3-甲酰胺基)苯基磺酰基)哌啶-1-甲酸酯代替叔丁基 4-(4-(氮杂环丁烷-3-甲酰胺基)苯基)哌啶-1-甲酸酯。

[0425] 实施例 564E

叔丁基 4-((4-(1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺基)苯基)磺酰基)哌啶-1-甲酸酯

如实施例 147B 中所述制备标题化合物，用叔丁基 4-((4-(1-(6- 氯哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺基）苯基）磺酰基）哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(6- 氯哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺基）苯基）哌啶 -1- 甲酸酯。

[0426] 实施例 564F

N-(4-(哌啶 -4- 基磺酰基）苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物，用叔丁基 4-((4-(1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺基）苯基）磺酰基）哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯。

[0427] 实施例 564G

N-(4-{[1-(3- 氯苯甲酰基）哌啶 -4- 基］磺酰基 } 苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(4-(哌啶 -4- 基磺酰基）苯基)-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯和用 3- 氯苯甲酸代替 1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO/D_2O) δ ppm8.53(dd, J = 4.4,1.2Hz,1H),7.93-7.84(m,2H),7.84-7.77(m,2H),7.72(dd, J = 9.3,4.4Hz,1H),7.58-7.38(m,2H),7.40-7.21(m,3H),4.58-4.37(m,5H),4.02(d, J = 31.5Hz,3H),3.88(tt, J = 8.8,5.9Hz,1H),3.48(ddd, J = 11.6,7.7,3.9Hz,1H),2.99(t, J = 11.9Hz,2H),1.92(d, J = 10.6Hz,2H),1.53(qd, J = 12.2,4.5Hz,3H) ;MS(ESI(+))m/e 540$(M+H)^+$.

[0428] 表 11.

以下实施例基本上如实施例 564 中所述制备，代替实施例 564F 中的合适的羧酸。一些产物通过快速色谱纯化而其他通过反向 HPLC 纯化。因此，一些实施例分离为三氟乙酸盐。

实施例		名称	MS
565		N-(4-{[1-(4-叔丁基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 562 $(M+H)^+$
566		N-(4-{[1-(4-甲氧基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 536 $(M+H)^+$
567		N-(4-{[1-(4-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 520 $(M+H)^+$
568		N-(4-{[1-(环己基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 512 $(M+H)^+$
569		N-(4-{[1-(环丙基乙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 484 $(M+H)^+$
570		N-(4-{[1-(2-甲氧基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 536 $(M+H)^+$
571		N-[4-({1-[(2S)-2-苯基丁酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 548 $(M+H)^+$
572		N-[4-({1-[4-(丙烷-2-基)苯甲酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 548 $(M+H)^+$
573		N-(4-{[1-(4-氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 540 $(M+H)^+$
574		N-{4-[(1-苯甲酰基哌啶-4-基)磺酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 506 $(M+H)^+$
575		1-(哒嗪-3-基)-N-(4-{[1-(4,4,4-三氟丁酰基)哌啶-4-基]磺酰基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 526 $(M+H)^+$
576		N-(4-{[1-(2,5-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 542 $(M+H)^+$
577		N-(4-{[1-(2-氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$
578		N-(4-{[1-(2-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 520 $(M+H)^+$
579		N-[4-({1-[(4-氯苯基)乙酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 538 $(M+H)^+$
580		N-(4-{[1-(3-甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 520 $(M+H)^+$
581		N-(4-{[1-(2,3-二甲基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 534

			$(M+H)^+$
582		N-[4-({1-[(3-氟苯基)乙酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 538 $(M+H)^+$
583		N-(4-{[1-(3-氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$
584		1-(哒嗪-3-基)-N-[4-({1-[3-(三氟甲基)苯甲酰基]哌啶-4-基}磺酰基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 575 $(M+H)^+$
585		N-[4-({1-[(3,5-二氟苯基)乙酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 556 $(M+H)^+$
586		N-(4-{[1-(2,4-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 542 $(M+H)^+$
587		1-(哒嗪-3-基)-N-[4-({1-[4-(三氟甲基)苯甲酰基]哌啶-4-基}磺酰基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 574 $(M+H)^+$
588		N-(4-{[1-(4-氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 524 $(M+H)^+$
589		N-(4-{[1-(2,3-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 542 $(M+H)^+$
590		N-(4-{[1-(2,4-二氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 574 $(M+H)^+$
591		N-(4-{[1-(萘-1-基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 556 $(M+H)^+$
592		N-(4-{[1-(环丙基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 470 $(M+H)^+$
593		N-(4-{[1-(3,5-二氟苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 542 $(M+H)^+$
594		N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 486 $(M+H)^+$
595		N-(4-{[1-(3,3-二甲基丁酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 500 $(M+H)^+$
596		N-(4-{[1-(3-甲氧基苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 536 $(M+H)^+$
597		N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 486 $(M+H)^+$
598		N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 472 $(M+H)^+$
599		N-(4-{[1-(环戊基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 498

			$(M+H)^+$
600		N-(4-{[1-(苯基乙酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 520 $(M+H)^+$
601		N-[4-({1-[(1-苯基环丙基)羰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 546 $(M+H)^+$
611		N-(4-{[1-(2-氯苯甲酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 540 $(M+H)^+$
612		N-(4-{[1-(4-甲基戊酰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 500 $(M+H)^+$
613		N-[4-({1-[(2-氯苯基)乙酰基]哌啶-4-基}磺酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 538 $(M+H)^+$

[0429] 实施例 602

N-{4-[1-(2- 甲基丙氨酰) 哌啶 -4- 基] 苯基 }-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(4-(哌啶 -4- 基) 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 甲基丙氨酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。^{1}H NMR(400MHz,DMSO-d_6) δ ppm10.14(s, 1H),8.18-8.11(m,4H),8.07(d, J = 2.5Hz,1H),7.74(dd, J = 8.6,5.4Hz,1H),7.55(d, J = 8.5Hz,2H),7.52(dd, J = 8.7,2.3Hz,1H),7.21(d, J = 8.5Hz,2H),4.41-3.68(m,7H), 3.10-2.89(m,2H),2.89-2.74(m,1H),1.85(d, J = 12.3Hz,2H),1.58(s,6H),1.52-1.37(m, 2H) ;MS(ESI(+))m/e 422$(M+H)^+$.

[0430] 实施例 603

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺

实施例 603A

(R)- 叔丁基 3-(5-(1- 异丁基 -1H- 吡唑 -4- 基) 噻吩 -2- 甲酰胺基) 吡咯烷 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物，用 (R)- 叔丁基 3- 氨基吡咯烷 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 5-(1- 异丁基 -1H- 吡唑 -4- 基) 噻吩 -2- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0431] 实施例 603B

(R)-5-(1- 异丁基 -1H- 吡唑 -4- 基)-N-(吡咯烷 -3- 基) 噻吩 -2- 甲酰胺

如实施例 1D 中所述制备标题化合物，用 (R)- 叔丁基 3-(5-(1- 异丁基 -1H- 吡唑 -4- 基) 噻吩 -2- 甲酰胺基) 吡咯烷 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0432] 实施例 603C

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(吡啶 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺

如实施例 1C 中所述制备标题化合物，用 (R)-5-(1- 异丁基 -1H- 吡唑 -4- 基)-N-(吡

咯烷 -3- 基) 噻吩 -2- 甲酰胺代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

^{1}H NMR(300MHz,DMSO-d_6) δ ppm0.85(d,J＝6.78Hz,6H)1.90-2.38(m,3H)3.16-3.66(m,4H)3.92(d,J ＝ 7.12Hz,2H)4.59(d,J ＝ 5.76Hz,1H)6.92(dd,J ＝ 8.48,1.70Hz,1H)7.08-7.27(m,2H)7.72(d,J＝3.73Hz,1H)7.79(s,1H)7.85(d,J＝3.73Hz,1H)7.95(d,J＝2.71Hz,1H)8.13(s,1H)8.54(d,J＝7.12Hz,1H) ;MS(ESI(+))m/e 396(M+H)$^+$.

[0433] 实施例 604

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -4- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺

如实施例 1C 中所述制备标题化合物,用 4- 溴哒嗪代替 3- 溴吡啶和用 (R)-5-(1- 异丁基 -1H- 吡唑 -4- 基)-N-(吡咯烷 -3- 基) 噻吩 -2- 甲酰胺代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

^{1}H NMR(300MHz,DMSO-d_6) δ ppm0.85(d,J＝6.44Hz,6H)1.90-2.39(m,3H)3.38-3.75(m,4H)3.92(d,J ＝ 7.12Hz,2H)4.43-4.71(m,1H)6.62(dd,J ＝ 6.44,3.05Hz,1H)7.19(d,J ＝ 3.73Hz,1H)7.71(d,J ＝ 4.07Hz,1H)7.79(s,1H)8.13(s,1H)8.55(dd,J ＝ 8.99,6.95Hz,2H)8.64(d,J ＝ 2.71Hz,1H) ;MS(ESI(+))m/e 397(M+H)$^+$.

[0434] 实施例 605

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺

实施例 605A

(R)-N-(1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基)-5-(1- 异丁基 -1H- 吡唑 -4- 基) 噻吩 -2- 甲酰胺

如实施例 147A 中所述制备标题化合物,用 (R)-5-(1- 异丁基 -1H- 吡唑 -4- 基)-N-(吡咯烷 -3- 基) 噻吩 -2- 甲酰胺代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0435] 实施例 605B

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺

如实施例 1B 中所述制备标题化合物,用 (R)-N-(1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基)-5-(1- 异丁基 -1H- 吡唑 -4- 基) 噻吩 -2- 甲酰胺代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

^{1}H NMR(400MHz,DMSO-d_6) δ ppm0.85(d,J ＝ 6.71Hz6H)1.94-2.38(m,3H)3.39-3.84(m,4H)3.92(d,J＝7.32Hz,2H)4.45-4.66(m,1H)6.88(d,J＝8.24Hz,1H)7.19(d,J＝3.97Hz,1H)7.34(dd,J＝9.00,4.43Hz,1H)7.73(d,J＝3.97Hz,1H)7.80(s,1H)8.14(s,1H)8.49(d,J＝3.66Hz,1H)8.56(d,J ＝ 6.71Hz,1H) ;MS(ESI(+))m/e 397(M+H)$^+$.

[0436] 实施例 606

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺

实施例 606A

(S)-叔丁基 3-(5-(1-异丁基-1H-吡唑-4-基)噻吩-2-甲酰胺基)吡咯烷-1-甲酸酯

如实施例 1A 中所述制备标题化合物,用 (S)-叔丁基 3-氨基吡咯烷-1-甲酸酯代替叔丁基 4-(4-氨基苯氧基)哌啶-1-甲酸酯和用 5-(1-异丁基-1H-吡唑-4-基)噻吩-2-甲酸代替 1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

[0437] 实施例 606B

(S)-5-(1-异丁基-1H-吡唑-4-基)-N-(吡咯烷-3-基)噻吩-2-甲酰胺

如实施例 1D 中所述制备标题化合物,用 (S)-叔丁基 3-(5-(1-异丁基-1H-吡唑-4-基)噻吩-2-甲酰胺基)吡咯烷-1-甲酸酯代替叔丁基 4-(4-(1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯。

[0438] 实施例 606C

(S)-N-(1-(6-氯哒嗪-3-基)吡咯烷-3-基)-5-(1-异丁基-1H-吡唑-4-基)噻吩-2-甲酰胺

如实施例 147A 中所述制备标题化合物,用 (S)-5-(1-异丁基-1H-吡唑-4-基)-N-(吡咯烷-3-基)噻吩-2-甲酰胺代替叔丁基 4-(4-(氮杂环丁烷-3-甲酰胺基)苯基)哌啶-1-甲酸酯。

[0439] 实施例 606D

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺

如实施例 1B 中所述制备标题化合物,用 (S)-N-(1-(6-氯哒嗪-3-基)吡咯烷-3-基)-5-(1-异丁基-1H-吡唑-4-基)噻吩-2-甲酰胺代替叔丁基 4-(4-(1-(苄基氧基羰基)氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯。

^{1}H NMR(300MHz,DMSO-d_6) δ ppm0.85(d,J=6.78Hz,6H)1.91-2.42(m,3H)3.49-3.88(m,4H)3.87-4.07(m,2H)4.30-4.81(m,1H)7.20(d,J = 3.73Hz,1H)7.68(d,J = 8.82Hz,1H)7.74-7.94(m,3H)8.14(s,1H)8.58(d,J = 3.05Hz,1H)8.71(d,J = 6.44Hz,1H);MS(ESI(+))m/e 397$(M+H)^+$.

[0440] 实施例 607

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(哒嗪-4-基)吡咯烷-3-基]噻吩-2-甲酰胺如实施例 1C 中所述制备标题化合物,用 4-溴哒嗪代替 3-溴吡啶和用 (S)-5-(1-异丁基-1H-吡唑-4-基)-N-(吡咯烷-3-基)噻吩-2-甲酰胺代替叔丁基 4-(4-(氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm0.75-0.98(m,6H)1.98-2.44(m,3H)3.67-4.18(m,6H)4.66(s,1H)7.15(dd,J = 7.12,3.05Hz,1H)7.21(d,J = 3.73Hz,1H)7.54-7.91(m,2H)8.14(s,1H)8.56-8.95(m,3H);MS(ESI(+))m/e 397$(M+H)^+$.

[0441] 实施例 608

5-[1-(2-甲基丙基)-1H-吡唑-4-基]-N-[(3S)-1-(吡啶-3-基)吡咯烷-3-基]噻吩-2-甲酰胺

如实施例 1C 中所述制备标题化合物,用 (S)-5-(1-异丁基-1H-吡唑-4-基)-N-(吡咯烷-3-基)噻吩-2-甲酰胺代替叔丁基 4-(4-(氮杂环丁烷-3-甲酰胺基)苯氧基)哌

啶 -1- 甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 0.85(d, J = 6.78Hz,6H)1.88-2.38(m, 3H)3.11-3.67(m,4H)3.92(d, J = 7.46Hz,2H)4.45-4.76(m,1H)6.75-7.01(m, 1H)7.03-7.25(m,2H)7.73(d, J = 4.07Hz,1H)7.79(s,1H)7.81-7.93(m,1H)7.95(d, J = 2.71Hz,1H)8.13(s,1H)8.54(d,J = 7.12Hz,1H) ;MS(ESI(+))m/e 396(M+H)$^+$.

[0442] 实施例 609

叔丁基 4-(2- 甲基 -1- 氧代 -1-{4-[4-({[1-(吡啶 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基] 哌啶 -1- 基 } 丙烷 -2- 基) 哌嗪 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用 N-(4-(哌啶 -4- 基) 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2-(4-(叔丁氧基羰基) 哌嗪 -1- 基)-2- 甲基丙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

$_1$H NMR(300MHz, DMSO-d_6) δ ppm10.00(s,1H),7.93(dd, J = 4.6,1.4Hz,1H),7.85(d, J = 2.5Hz,1H),7.53(d, J = 8.6Hz,2H),7.23-7.13(m,3H),6.86(ddd, J = 8.3,2.9,1.4Hz, 1H),5.43(bs,1H),4.59(bs,1H),4.15-4.03(m,2H),4.02-3.90(m,2H),3.71(tt, J = 8.3, 6.1Hz,1H),3.42-3.32(m,4H),3.04(bs,1H),2.80-2.62(m,2H),2.39(bs,4H),1.78(d, J = 11.1Hz,2H),1.57-1.42(m,2H),1.39(s,9H),1.17(s,6H) ;MS(ESI(+))m/e 591(M+H)$^+$.

[0443] 实施例 610

N-(4-{1-[2- 甲基 -2-(哌嗪 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺如实施例 1D 中所述制备标题化合物,用叔丁基 4-(2- 甲基 -1- 氧代 -1-{4-[4-({[1-(吡啶 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基] 哌啶 -1- 基 } 丙烷 -2- 基) 哌嗪 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.08(s,1H),8.52(s,1H),8.14(d, J = 5.2Hz, 1H),8.07(d, J = 2.6Hz,1H),7.76(dd, J = 8.7,5.4Hz,1H),7.54(d, J = 8.6Hz,2H), 7.20(d, J = 8.6Hz,2H),4.88(bs,4H),4.23(t, J = 8.4Hz,2H),4.12(dd, J = 7.9, 5.9Hz,2H),3.87-3.66(m,1H),3.10(bs,4H),2.85-2.54(m,5H),1.79(d, J = 13.1Hz,2H), 1.61-1.32(m,2H),1.21(s,6H) ;MS(ESI(+))m/e 491(M+H)$^-$.

[0444] 实施例 614

N-(4-{[1-(2- 甲基丙酰基) 哌啶 -4- 基] 磺酰基 } 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 614A

叔丁基 4-((4-(1-(5,6- 二氯哒嗪 -4- 基) 氮杂环丁烷 -3 甲酰胺基) 苯基) 磺酰基) 哌啶 -1- 甲酸酯向在 0℃下的在 50mL N, N- 二甲基甲酰胺中的 3,4,5- 三氯哒嗪 (1.624g, 8.85mmol) 和 N- 乙基 -N- 异丙基丙烷 -2- 胺 (2.289g,17.71mmol) 中逐滴加入在 10ml N, N- 二甲基甲酰胺中的叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基磺酰基) 哌啶 -1- 甲酸酯 (2.5g,5.90mmol)。将反应混合物从 0℃至室温搅拌过夜,用水稀释,并用乙酸乙酯萃取。将有机层用硫酸镁干燥,过滤,浓缩并通过快速色谱纯化以产生标题化合物。

[0445] 实施例 614B

叔丁基 4-((4-(1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 磺酰基) 哌啶 -1- 甲

酸酯

如实施例 1B 中所述制备标题化合物，用叔丁基 4-((4-(1-(5,6- 二氯哒嗪 -4- 基）氮杂环丁烷 -3 甲酰胺基）苯基）磺酰基）哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基）氮杂环丁烷 -3 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯。

[0446] 实施例 614C

N-(4-(哌啶 -4- 基磺酰基）苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物，用叔丁基 4-((4-(1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺基）苯基）磺酰基）哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯。

[0447] 实施例 614D

N-(4-{[1-(2- 甲基丙酰基）哌啶 -4- 基］磺酰基｝苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(4-(哌啶 -4- 基磺酰基）苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯和用异丁酸代替 1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.70(s,1H),8.79(d, J = 7.2Hz,1H),8.55(d, J = 3.1Hz,1H),7.93-7.86(m,2H),7.85-7.78(m,2H),7.00(dd, J = 7.2,3.1Hz,1H),4.65-4.36(m,5H),4.09-3.82(m,2H),3.35-2.67(m,4H),1.95-1.76(m,2H),1.48-0.99(m,2H),0.95(d, J = 6.7Hz,6H) ;MS(ESI(+))m/e 472(M+H)$^+$.

[0448] 实施例 615

N-{4-[(1- 苯甲酰基哌啶 -4- 基）磺酰基］苯基｝-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(4-(哌啶 -4- 基磺酰基）苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.70(s,1H),8.79(d, J = 7.2Hz,1H),8.55(d, J = 3.3Hz,1H),7.93-7.86(m,2H),7.85-7.78(m,2H),7.49-7.29(m,5H),7.00(dd, J = 7.2,3.1Hz,1H),4.65-4.35(m,4H),3.99-3.83(m,1H),3.73-3.50(m,1H),3.28-2.65(m,4H),2.37-1.59(m,2H),1.56-1.06(m,2H) ;MS(ESI(+))m/e 506(M+H)$^+$.

[0449] 实施例 616

N-(4-{[1-(4- 氟苯甲酰基）哌啶 -4- 基］磺酰基｝苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(4-(哌啶 -4- 基磺酰基）苯基)-1-(哒嗪 -4- 基）氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯和用 4- 氟苯甲酸代替 1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.70(s,1H),8.79(d, J = 6.9Hz,1H),8.55(d, J = 3.1Hz,1H),7.93-7.86(m,2H),7.85-7.78(m,2H),7.52-7.38(m,2H),7.31-7.20(m,2H),7.00(dd, J-7.2,3.1Hz,1H),4.63-4.19(m,4H),3.99-3.83(m,1H),3.73-3.46(m,2H),3.23-2.65(m,3H),2.37-1.60(m,2H),1.56-1.06(m,2H) ;MS(ESI(+))m/e 524(M+H)$^-$.

[0450] 实施例 617

N-(4-{[1-(环戊基羰基)哌啶-4-基]磺酰基}苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(哌啶-4-基磺酰基)苯基)-1-(哒嗪-4-基)氮杂环丁烷-3-甲酰胺代替叔丁基 4-(4-氨基苯氧基)哌啶-1-甲酸酯和用环戊烷羧酸代替 1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.69(s,1H),8.79(d, J = 7.2Hz,1H),8.55(d, J = 3.1Hz,1H),7.97-7.77(m,4H),7.00(dd, J = 7.2,3.1Hz,1H),4.67-4.37(m,5H),4.11-4.01(m,1H),3.99-3.84(m,1H),3.35-2.71(m,4H),1.95-1.06(m,10H),1.07-0.97(m,2H);MS(ESI(+))m/e 498(M+H)$^+$.

[0451] 实施例 618

N-[(3R)-1-(5,6-二氯哒嗪-4-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-2-甲酰胺将 3,4,5-三氯哒嗪 (269mg,1.464mmol) 溶于 5ml N,N-二甲基甲酰胺并加入三乙胺 (370mg,3.66mmol)。当逐滴加入在 N,N-二甲基甲酰胺中的 (R)-5-(1-异丁基-1H-吡唑-4-基)-N-(吡咯烷-3-基)噻吩-2-甲酰胺双三氟乙酸酯 (400mg,0.732mmol) 时,将溶液用冰浴冷却。将反应混合物从 0℃至室温搅拌过夜,用水稀释并用乙酸乙酯萃取。将有机层用硫酸镁干燥,过滤,浓缩并通过快速色谱纯化以产生标题化合物。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 8.66(s,1H),8.49(d, J = 6.5Hz,1H),8.14(s,1H),7.79(s,1H),7.70(d,J = 3.9Hz,1H),7.20(d,J = 3.8Hz,1H),4.59-4.45(m,1H),4.05(dd, J = 11.0,6.4Hz,1H),4.01-3.66(m,5H),2.30-1.94(m,3H),0.85(d, J = 6.7Hz,6H);MS(ESI(+))m/e 465(M+H)$^+$.

[0452] 实施例 619

N-[(3R)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-2-甲酰胺

如实施例 147A 中所述制备标题化合物,用 (R)-5-(1-异丁基-1H-吡唑-4-基)-N-(吡咯烷-3-基)噻吩-2-甲酰胺代替叔丁基 4-(4-(氮杂环丁烷-3-甲酰胺基)苯基)哌啶-1-甲酸酯。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 8.55(d, J = 6.6Hz,1H),8.14(s,1H),7.80(s,1H),7.72(d, J = 3.9Hz,1H),7.49(d, J = 9.4Hz,1H),7.20(d, J = 3.8Hz,1H),7.03(d, J = 9.4Hz,1H),4.64-4.52(m,1H),3.92(d, J = 7.2Hz,2H),3.76(dd, J = 11.0,6.6Hz,1H),3.69-3.41(m,3H),2.34-2.21(m,1H),2.19-2.02(m,2H),0.85(d, J = 6,7Hz,6H);MS(ESI(+))m/e 431(M+H)$^+$.

[0453] 实施例 620

N-[(3S)-1-(5,6-二氯哒嗪-4-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-2-甲酰胺

如实施例 618 中所述制备标题化合物,用 (S)-5-(1-异丁基-1H-吡唑-4-基)-N-(吡咯烷-3-基)噻吩-2-甲酰胺代替 (R)-5-(1-异丁基-1H-吡唑-4-基)-N-(吡咯烷-3-基)噻吩-2-甲酰胺。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 8.70(s,1H),8.55(d, J = 6.5Hz,1H),8.19(s,1H),7.85(s,1H),7.75(d, J = 3.9Hz,1H),7.25(d, J = 3.8Hz,1H),4.64-4.47(m,1H),4.1(dd, J = 10.9,6.4Hz,1H),4.07-3.67(m,5H),2.32-2.02(m,3H),0.94-0.75(m,6H) ;MS(ESI(+)) m/e 465(M+H)$^+$.

[0454] 实施例 621

N-[(3S)-1-(6-氯哒嗪-3-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-2-甲酰胺

如实施例 147A 中所述制备标题化合物,用 (S)-5-(1-异丁基-1H-吡唑-4-基)-N-(吡咯烷-3-基)噻吩-2-甲酰胺代替叔丁基 4-(4-(氮杂环丁烷-3-甲酰胺基)苯基)哌啶-1-甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm8.54(d, J = 6.7Hz,1H),8.13(d, J = 0.8Hz,1H),7.79(d, J = 0.8Hz,1H),7.72(d, J = 3.9Hz,1H),7.49(d, J = 9.4Hz,1H),7.19(d, J = 3.8Hz,1H),7.03(d, J = 9.4Hz,1H),4.63-4.53(m,1H),3.92(d, J = 7.2Hz,2H),3.76(dd, J = 11.0,6.6H z,1H),3.71-3.39(m,3H),2.37-2.00(m,3H),0.85(d, J = 6.7Hz,6H) ; MS(ESI(+))m/e 431(M+H)$^+$.

[0455] 实施例 622

N-[(3R)-1-(5,6-二氯哒嗪-4-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-3-甲酰胺

实施例 622A

5-(1-异丁基-1H-吡唑-4-基)噻吩-3-甲酸

标题化合物如实施例 148A 中所述进行制备,用 5-溴噻吩-3-甲酸代替 4-溴苯胺。

[0456] 实施例 622B

(R)-叔丁基 3-(5-(1-异丁基-1H-吡唑-4-基)噻吩-3-甲酰胺基)吡咯烷-1-甲酸酯

如实施例 1A 中所述制备标题化合物,用 (R)-叔丁基 3-氨基吡咯烷-1-甲酸酯代替叔丁基 4-(4-氨基苯氧基)哌啶-1-甲酸酯和用 5-(1-异丁基-1H-吡唑-4-基)噻吩-3-甲酸代替 1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

[0457] 实施例 622B

(R)-5-(1-异丁基-1H-吡唑-4-基)-N-(吡咯烷-3-基)噻吩-3-甲酰胺

如实施例 1D 中所述制备标题化合物,用 (R)-叔丁基 3-(5-(1-异丁基-1H-吡唑-4-基)噻吩-3-甲酰胺基)吡咯烷-1-甲酸酯代替叔丁基 4-(4-(1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯。

[0458] 实施例 622C

N-[(3R)-1-(5,6-二氯哒嗪-4-基)吡咯烷-3-基]-5-[1-(2-甲基丙基)-1H-吡唑-4-基]噻吩-3-甲酰胺如实施例 618 中所述制备标题化合物,用 (R)-5-(1-异丁基-1H-吡唑-4-基)-N-(吡咯烷-3-基)噻吩-3-甲酰胺代替 (R)-5-(1-异丁基-1H-吡唑-4-基)-N-(吡咯烷-3-基)噻吩-2-甲酰胺。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 8.66(s,1H),8.37(d, J = 6.5Hz,1H),8.08(d, J = 0.8Hz,1H),7.94(d, J = 1.4Hz,1H),7.74(d, J = 0.8Hz,1H),7.51(d, J = 1.4Hz,1H),

4.53(q, J = 5.4Hz,1H),4.06(dd, J = 10.9,6.4Hz,1H),3.98-3.66(m,5H),2.30-1.96(m,3H),0.85(d, J = 6.7Hz,6H) ;MS(ESI(+))m/e 465(M+H)$^+$.

[0459] 实施例 623

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -3- 甲酰胺

实施例 623A

(R)-N-(1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基)-5-(1- 异丁基 -1H- 吡唑 -4- 基) 噻吩 -3- 甲酰胺

如实施例 147A 中所述制备标题化合物,用 (R)-5-(1- 异丁基 -1H- 吡唑 -4- 基)-N-(吡咯烷 -3- 基) 噻吩 -3- 甲酰胺代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0460] 实施例 623B

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -3- 甲酰胺

如实施例 147B 中所述制备标题化合物,用 (R)-N-(1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基)-5-(1- 异丁基 -1H- 吡唑 -4- 基) 噻吩 -3- 甲酰胺代替 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 8.49(dd, J = 4.5,1.3Hz,1H),8.41(d, J = 6.7Hz,1H),8.08(s,1H),7.96(d, J = 1.4Hz,1H),7.73(s,1H),7.54(d, J = 1.4Hz,1H),7.37(dd, J = 9.1,4.4Hz,1H),6.92(d, J = 9.1Hz,1H),4.67-4.55(m,1H),3.92(d, J = 7.2Hz,2H),3.78(dd, J = 10.9,6.6Hz,1HL3.72-3.41(m,3H),2.40-1.98(m,3H),0.85(d, J = 6.7Hz,6H) ;MS(ESI(+))m/e 397(M+H)$^+$.

[0461] 实施例 624

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3R)-1-(哒嗪 -4- 基) 吡咯烷 -3- 基] 噻吩 -3- 甲酰胺

如实施例 1B 中所述制备标题化合物,用 N-[(3R)-1-(5,6- 二氯哒嗪 -4- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 噻吩 -3- 甲酰胺代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm8.86-8.69(m,2H),8.58(d, J = 6.6Hz,1H),8.08(d, J = 0.8Hz,1H),8.01(d, J = 1.4Hz,1H),7.74(d, J = 0.8Hz,1H), 7.55(d, J = 1.4Hz,1H),7.15(dd, J = 7.3,3.1Hz,1H),4.72-4.59(m,1H),4.08-3.47(m,6H),2.37-1.97(m,3H),0.85(d, J = 6.7Hz,6H) ;MS(ESI(+))m/e397(M+H)$^+$.

[0462] 实施例 625

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基}-1-(哒嗪 -3- 基) 哌啶 -4- 甲酰胺

实施例 625A

苄基 4-((4-(1-(叔丁氧基羰基) 哌啶 -4- 基) 苯基) 氨基甲酰基) 哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用叔丁基 4-(4- 氨基苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(苄基氧基羰基) 哌啶 -4- 甲酸代替

1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

[0463] 实施例 625B

叔丁基 4-(4-(哌啶-4-甲酰胺基)苯基)哌啶-1-甲酸酯

如实施例 1B 中所述制备标题化合物,用苄基 4-((4-(1-(叔丁氧基羰基)哌啶-4-基)苯基)氨基甲酰基)哌啶-1-甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基)氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯。

[0464] 实施例 625C

叔丁基 4-(4-(1-(6-氯哒嗪-3-基)哌啶-4-甲酰胺基)苯基)哌啶-1-甲酸酯

如实施例 147A 中所述制备标题化合物,用叔丁基 4-(4-(哌啶-4-甲酰胺基)苯基)哌啶-1-甲酸酯代替叔丁基 4-(4-(氮杂环丁烷-3-甲酰胺基)苯基)哌啶-1-甲酸酯。

[0465] 实施例 625D

叔丁基 4-(4-(1-(哒嗪-3-基)哌啶-4-甲酰胺基)苯基)哌啶-1-甲酸酯

如实施例 147B 中所述制备标题化合物,用叔丁基 4-(4-(1-(6-氯哒嗪-3-基)哌啶-4-甲酰胺基)苯基)哌啶-1-甲酸酯代替 4-(4-(1-(6-氯哒嗪-3-基)氮杂环丁烷-3-甲酰胺基)苯基)哌啶-1-甲酸酯。

[0466] 实施例 625E

N-(4-(哌啶-4-基)苯基)-1-(哒嗪-3-基)哌啶-4-甲酰胺

如实施例 1D 中所述制备标题化合物,用叔丁基 4-(4-(1-(哒嗪-3-基)哌啶-4-甲酰胺基)苯基)哌啶-1-甲酸酯代替叔丁基 4-(4-(1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯。

[0467] 实施例 625F

N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)哌啶-4-甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(哌啶-4-基)苯基)-1-(哒嗪-3-基)哌啶-4-甲酰胺代替叔丁基 4-(4-氨基苯氧基)哌啶-1-甲酸酯和用 2,2-二甲基丙酸代替 1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 9.86 (s.1H),8.51(d, J = 3.6Hz,1H),7.53-7.47(m,2H),7.43-7.31(m,1H),7.26(d, J = 8.6Hz,1H),7.17-7.11(m,2H),4.45-4.34(m,4H),2.94(t,J = 11.6Hz,1H),2.82(t,J = 12.5Hz,1H),2.66(dddd,J = 33.0,15.2,8.0,3.6Hz,1H),1.89-1.81(m,2H),1.80-1.71(m,2H),1.70-1.53(m,2H),1.51-1.33(m,2H),1.20(s,9H),MS(ESI(+))m/e 450$(M+H)^+$.

[0468] 实施例 626

N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)哌啶-4-甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(哌啶-4-基)苯基)-1-(哒嗪-3-基)哌啶-4-甲酰胺代替叔丁基 4-(4-氨基苯氧基)哌啶-1-甲酸酯和用苯甲酸代替 1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 9.87(s,1H),8.51(d, J = 4.8Hz,1H),7.54-7.48(m,2H),7.47-7.36(m,5H),7.35(dd, J = 9.3,4.4Hz,1H),7.26(d, J = 8.7Hz,1H),7.21-7.15(m,2H),4.60(s,1H),4.46-4.37(m,2H),3.63(s,1H),3.24-2.56(m,6H),

1.89-1.80(m,2H),1.80-1.46(m,5H),MS(ESI(+))m/e470(M+H)$^+$.

[0469] 实施例 627

N-{4-[1-(2- 氟苯甲酰基)哌啶 -4- 基]苯基}-1-(哒嗪 -3- 基)哌啶 -4- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(哌啶 -4- 基)苯基)-1-(哒嗪 -3- 基)哌啶 -4- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基)哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 9.87(s, 1 H),8.51(d, J = 4.4Hz,1H),7.56-7.38(m,4H),7.35(dd,J = 9.3,4.4Hz,1H),7.32-7.21(m,3H),7.16(d,J = 8.5Hz,2H),4.64(d,J = 13.1Hz,1H),4.41(d,J = 13.3Hz,2H),3.15(1,J = 12.3Hz,1H),2.93(dd,J = 18.0,7.3Hz,2H),2.70(dddd,J = 15.1,11.4,10.1,7.0Hz,3H),1.86(t,J = 13.8Hz,3H),1.76-1.39(m,5H) ;MS(ESI(+))m/e 488(M+H)$^+$.

[0470] 实施例 628

1-(哒嗪 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基)哌啶 -4- 基]苯基}哌啶 -4- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(哌啶 -4- 基)苯基)-1-(哒嗪 -3- 基)哌啶 -4- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基)哌啶 -1- 甲酸酯和用 4,4,4- 三氟丁酸代替 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 9.86(s,1H),8.51(d, J = 4.3Hz,1H),7.49(t, J = 8.9Hz,2H),7.41-7.30(m,1H),7.25(d,J = 9.3Hz,1H),7.14(d,J = 8.5Hz,2H),4.51(d,J = 13.0Hz,1H),4.41(d,J = 13.3Hz,2H),3.94(d,J = 13.4Hz,1H),3.07(t,J = 12.0Hz,1H),2.94(dd,J = 18.1,7.3Hz,2H),2.77-2.40(m,9H),1.93-1.80(m,2H),1.71(d,J = 25.3Hz,2H),1.58(dqd,J = 29.0,12.7,4.0Hz,3H),1.39(qd,J = 12.7,4.1Hz,1H) ;MS(ESI(+))m/e 490(M+H)$^+$.

[0471] 实施例 629

N-[(3S)-1-(6- 氯哒嗪 -3- 基)吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]噻吩 -3- 甲酰胺

如实施例 147A 中所述制备标题化合物,用 (S)-5-(1- 异丁基 -1H- 吡唑 -4- 基)-N-(吡咯烷 -3- 基)噻吩 -3- 甲酰胺代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基)苯基)哌啶 -1- 甲酸酯。

^{1}H NMR(500MHz, DMSO-d_6) δ ppm 8.42(d, J = 6.7Hz,1H),8.08(s,1H),7.96(d, J = 1.3Hz,1H),7.74(d, J = 0.5Hz,1H),7.54(d, J = 1.3Hz,1H),7.49(d, J = 9.5Hz,1H),7.02(d, J = 9.5Hz,1H),4.87-4.44(m,1H),3.92(d,2H),3.94-3.38(m,4H),2.50-1.87(m,3H),0.85(d,J = 6.7Hz,6H) ;MS(ESI(+))m/e 431(M+H)$^+$.

[0472] 实施例 664

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基)吡咯烷 -3- 基]噻吩 -3- 甲酰胺

如实施例 147B 中所述制备标题化合物,用 N-[(3S)-1-(6- 氯哒嗪 -3- 基)吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]噻吩 -3- 甲酰胺代替 4-(4-(1-(6- 氯哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺基)苯基 1 哌啶 -1- 甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 8.58(dd, J = 4.3,1.2Hz,2H),8.08(d, J = 0.8Hz, 1H),8.02(d, J = 1.4Hz,1H),7.86(dd, J = 9.5,4.3Hz,1H),7.77-7.66(m,2H),7.57(d, J = 1.4Hz,1H),4.70-4.61(m,1H),3.92(d,J = 7.2Hz,2H),3.67-2.93(m,4H),2.41-2.00(m, 3H),0.88-0.81(m,6H) ;MS(ESI(+))m/e397(M+H)$^+$.

[0473] 实施例 665

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 氟 -5- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 665A

苄基 3-((4-(哌啶 -4- 基) 苯基) 氨基甲酰基) 氮杂环丁烷 -1- 甲酸酯

如实施例 1D 中所述制备标题化合物,用叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0474] 实施例 665B

苄基 3-((4-(1- 苯甲酰基哌啶 -4- 基) 苯基) 氨基甲酰基) 氮杂环丁烷 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用苄基 3-((4-(哌啶 -4- 基) 苯基) 氨基甲酰基) 氮杂环丁烷 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0475] 实施例 665C

N-(4-(1- 苯甲酰基哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1B 中所述制备标题化合物,用苄基 3-((4-(1- 苯甲酰基哌啶 -4- 基) 苯基) 氨基甲酰基) 氮杂环丁烷 -1- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0476] 实施例 665D

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 氟 -5- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1C 中所述制备标题化合物,用 3- 溴 -6- 氟 -5- 甲基吡啶代替 3- 溴吡啶和用 N-(4-(1- 苯甲酰基哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

^{1}H NMR(400MHz, DMSO-d_6/D_2O) δ ppm7.55-7.34(m,7H),7.26-7.14(m,3H), 6.98-6.86(m.1H),4.21-4.01(m,3H),3.95(dd, J = 8.8,4.6Hz,2H),3.69(ddd, J = 8.5,7.4,4.3Hz,1H),3.09-2.95(m,2H),2.80(d, J = 0.6Hz,1H),2.23-2.14(m,3H), 1.87-1.75(m,2H),1.58(tt, J = 12.8,6.1Hz,2H),1.11-1.01(m,1H) ;MS(ESI(+))m/e 473(M+H)$^+$.

[0477] 表 12.

以下实施例基本上如实施例 665 中所述制备,代替实施例 665D 中合适的溴杂环。

实施例		名称	MS
666		N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-氟吡啶-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 459 $(M+H)^+$
668		N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-氟-6-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 473 $(M+H)^+$
737		N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(2-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 466 $(M+H)^+$
738		N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(4-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 466 $(M+H)^+$
739		N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(6-氟-4-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 473 $(M+H)^+$
740		N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-氰基吡啶-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 466 $(M+H)^+$
741		N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(5-甲基吡啶-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 455 $(M+H)^+$

[0478] 实施例 667

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 667A

叔丁基 4-(4-(1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 1C 中所述制备标题化合物,用 3- 溴 -6- 甲基哒嗪代替 3- 溴吡啶和用叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0479] 实施例 667B

1-(6- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用叔丁基 4-(4-(1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0480] 实施例 667C

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 1-(6- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d6) δ 10.02(s,1H),7.54(d, J = 8.5Hz,2H),7.49-7.39(m,5H),7.28(d, J = 9.1Hz,1H),7.22(d, J = 8.5Hz,2H),6.79(d, J = 9.0Hz,1H),4.72-4.51(m,1H),4.19(t, J = 8.2Hz,2H),4.10(dd, J = 7.8,6.2Hz,2H),3.71(tt, J = 8.5,6.1Hz,

2H),3.21-2.95(m,1H),2.95-2.64(m,2H),2.44(s,3H),1.93-1.46(m,4H);(ESI(+))m/e 456(M+H)$^+$.

[0481] 表 13.

以下实施例基本上如实施例 667 中所述制备,代替实施例 667C 中的合适的羧酸。

实施例		名称	MS
851		N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 474 (M+H)$^+$
852		N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]苯基}-1-(6-甲基哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 (M+H)$^+$

[0482] 实施例 742

2-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基]-1,3- 噻唑 -5- 甲酰胺

实施例 742A

2-(1- 异丁基 -1H- 吡唑 -4- 基) 噻唑 -5- 甲酸

如实施例 148A 中所述制备标题化合物,用 2- 溴噻唑 -5- 甲酸代替 4- 溴苯胺。

[0483] 实施例 742B

(S)- 叔丁基 3-(2-(1- 异丁基 -1H- 吡唑 -4- 基) 噻唑 -5- 甲酰胺基) 吡咯烷 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用 (S)- 叔丁基 3- 氨基吡咯烷 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2-(1- 异丁基 -1H- 吡唑 -4- 基) 噻唑 -5- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0484] 实施例 742C

(S)-2-(1- 异丁基 -1H- 吡唑 -4- 基)-N-(吡咯烷 -3- 基) 噻唑 -5- 甲酰胺

如实施例 1D 中所述制备标题化合物,用 (S)- 叔丁基 3-(2-(1- 异丁基 -1H- 吡唑 -4- 基) 噻唑 -5- 甲酰胺基) 吡咯烷 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0485] 实施例 742D

(S)-N-(1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基)-2-(1- 异丁基 -1H- 吡唑 -4- 基) 噻唑 -5- 甲酰胺

如实施例 147A 中所述制备标题化合物,用 (S)-2-(1- 异丁基 -1H- 吡唑 -4- 基)-N-(吡咯烷 -3- 基) 噻唑 -5- 甲酰胺代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0486] 实施例 742E

2-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基]-1,3- 噻唑 -5- 甲酰胺

如实施例 147B 中所述制备标题化合物,用 (S)-N-(1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基)-2-(1- 异丁基 -1H- 吡唑 -4- 基) 噻唑 -5- 甲酰胺代替 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm8.80(d,1H),8.41(d, J = 0.8Hz,1H),8.30(s,1H),8.28(s,1H),7.90(s,1H),7.34(dd, J = 9.1,4.5Hz,1H),6.88(dd, J = 9.1,1.3Hz,1H),4.67-4.52(m,1H),4.03-3.93(m,2H),3.90-3.40(m,4H),2.36-2.02(m,3H),0.89-0.82(m,6H);MS(ESI(+))m/e 398(M+H)$^+$.

[0487] 实施例 743

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(2- 甲基吡啶 -3- 基) 吡咯烷 -3- 甲酰胺

实施例 743A

(S)- 叔丁基 4-(4-(1-((苄基氧基) 羰基) 吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用叔丁基 4-(4- 氨基苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 (S)-1-((苄基氧基) 羰基) 吡咯烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0488] 实施例 743B

(S)- 叔丁基 4-(4-(吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 1B 中所述制备标题化合物,用 (S)- 叔丁基 4-(4-(1-((苄基氧基) 羰基) 吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0489] 实施例 743C

(S)- 叔丁基 4-(4-(1-(2- 甲基吡啶 -3- 基) 吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 1C 中所述制备标题化合物,用 3- 溴 -2- 甲基吡啶代替 3- 溴吡啶和用 (S)- 叔丁基 4-(4-(吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0490] 实施例 743D

(S)-1-(2- 甲基吡啶 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 吡咯烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用 (S)- 叔丁基 4-(4-(1-(2- 甲基吡啶 -3- 基) 吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0491] 实施例 743E

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(2- 甲基吡啶 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (S)-1-(2- 甲基吡啶 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 9.98(s,1H),7.97(ddd, J = 5.1,2.2,1.3Hz,2H),7.69(dt, J = 8.4,0.9Hz,1H),7.56-7.51(m,2H),7.47-7.41(m,5H),7.24-7.18(m,3H),7.09(dd, J = 8.0,4.7Hz,1H),4.62(s,1H),3.65(s,1H),3.19(ddd, J = 14.2,10.1,6.4Hz,4H),2.76(t, J = 11.9Hz,2H),2.47(s,3H),2.26-2.06(m,2H),1.93-1.49(m,4H),1.23(s,

1H), MS(ESI(+))m/e 469.3(M+H)$^+$.

[0492] 实施例 744

(3S)-N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(2- 甲基吡啶 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 (S)-1-(2- 甲基吡啶 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 9.98(s,1H), 8.01-7.93(m,2H), 7.58-7.45(m,2H), 7.44-7.37(m,1H), 7.30(tdd, J = 6.6,3.7,2.8Hz,2H), 7.20(dd, J = 11.4,4.7Hz,2H), 7.09(dd, J = 8.1,4.6Hz,1H), 4.66(d, J = 13.1Hz,1H), 3.49-3.14(m,8H), 2.90-2.69(m,2H), 2.47(s,3H), 2.31-2.06(m,2H), 1.92-1.80(m,1H), 1.70(s,1H), 1.64-1.41(m,2H) ; MS(ESI(+))m/e 487.3(M+H)$^+$.

[0493] 实施例 745

(3S)-1-(2- 甲基吡啶 -3- 基)-N-{4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 } 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 (S)-1-(2- 甲基吡啶 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 4,4,4- 三氟丁酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 9.97(s,1H), 7.97(dd, J = 4.8,3.6Hz,2H), 7.53(d, J = 8.3Hz,3H), 7.24-7.13(m,3H), 4.53(d, J = 12.9Hz,1H), 3.97(d, J = 13.3Hz,1H), 3.39(d, J = 7.5Hz,3H), 3.36-3.29(m,2H), 3.25-3.16(m,2H), 3.11(dd, J = 24.4,11.8Hz,1H), 2.70(ddd, J = 15.1,11.8,8.3Hz,1H), 2.67-2.57(m,3H), 2.47(s,3H), 2.27-2.07(m,2H), 1.75(s,2H), 1.56(dt, J = 12.5,8.7Hz,1H), 1.41(qd, J = 12.8,4.3Hz,1H), MS(ESI(+))m/e 489.3(M+H)$^+$.

[0494] 实施例 746

N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 呋喃 -2- 甲酰胺

实施例 746A

5-(1- 异丁基 -1H- 吡唑 -4- 基) 呋喃 -2- 甲酸

如实施例 148A 中所述制备标题化合物，用 5- 溴呋喃 -2- 甲酸代替 4- 溴苯胺。

[0495] 实施例 746B

(S)- 叔丁基 3-(5-(1- 异丁基 -1H- 吡唑 -4- 基) 呋喃 -2- 甲酰胺基) 吡咯烷 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物，用 (S)- 叔丁基 3- 氨基吡咯烷 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 5-(1- 异丁基 -1H- 吡唑 -4- 基) 呋喃 -2- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0496] 实施例 746C

(S)-5-(1- 异丁基 -1H- 吡唑 -4- 基)-N-(吡咯烷 -3- 基) 呋喃 -2- 甲酰胺

如实施例 1D 中所述制备标题化合物，用 (S)- 叔丁基 3-(5-(1- 异丁基 -1H- 吡

唑 -4- 基) 呋喃 -2- 甲酰胺基) 吡咯烷 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0497] 实施例 746D

N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 呋喃 -2- 甲酰胺

如实施例 147A 中所述制备标题化合物,用 (S)-5-(1- 异丁基 -1H- 吡唑 -4- 基)-N-(吡咯烷 -3- 基) 呋喃 -2- 甲酰胺代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 8.37(d, J = 6.9Hz,1H),8.14(s,1H),7.87(s,1H),7.49(d, J = 9.4Hz,1H),7.17(d, J = 3.5Hz,1H),7.03(d, J = 9.4Hz,1H),6.63(d, J = 3.5Hz,1H),4.69-4.54(m,1H),3.95(d, J = 7.2Hz,2H),3.79(dd, J = 11.0,6.8Hz,1H),3.72-3.58(m,1H),3.60-3.39(m,2H),2.36-2.19(m,1H),2.22-2.03(m,2H),0.85(d, J = 6.7Hz,6H) ;MS(ESI(+))m/e415(M+H)$^+$.

[0498] 实施例 747

5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 呋喃 -2- 甲酰胺

如实施例 147B 中所述制备标题化合物,用 N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-5-[1-(2- 甲基丙基)-1H- 吡唑 -4- 基] 呋喃 -2- 甲酰胺代替 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

^{1}H NMR(300MHz,DMSO-d_6) δ ppm8.49(dd,J = 4.5,1.2Hz,1H),8.38(d,J = 7.0Hz,1H),8.15(s,1H),7.87(s,1H),7.34(dd,J = 9.1,4.4Hz,1H),7.17(d,J = 3.5Hz,1H),6.88(dd,J = 9.1,1.3Hz,1H),6.63(d, J = 3.5Hz,1H),4.70-4.54(m,1H),3.95(d, J = 7.2Hz,2H),3.79(dd, J = 10.8,6.9Hz,1H),3.75-3.61(m,1H),3.61-3.39(m,2H),2.37-2.01(m,3H),0.85(d,J = 6.7Hz,6H) ;MS(ESI(+))m/e 381(M+H)$^+$.

[0499] 实施例 748

N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 748A

1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸

如实施例 147A 中所述制备标题化合物,用氮杂环丁烷 -3- 甲酸代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0500] 实施例 748B

1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸

如实施例 147B 中所述制备标题化合物,用 1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0501] 实施例 748C

N-(4- 溴苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 4- 溴苯胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环

丁烷 -3- 甲酸。

[0502] 实施例 748D

N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 148A 中所述制备标题化合物,用 1-((4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基)-4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑和用 N-(4- 溴苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替 4- 溴苯胺。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.09(s,1H),8.56(dd, J = 4.5,1.2Hz,1H),8.06(s,1H),7.82(s,1H),7.61(d, J = 8.7Hz,2H),7.52(d, J = 8.6Hz,2h),7.38(dd, J = 9.0,4.5Hz,1H),6.83(dd, J = 9.0,1.2Hz,1H),4.25(t, J = 8.3Hz,2H),4.16(dd, J = 8.0,6.0Hz,2H),4.02(s,2H),3.84-3.62(m,3H),3.52(ddd, J = 11.8,9.2,3.0Hz,2H),1.51(ddd, J = 13.3,9.0,4.2Hz,2H),1.32-1.17(m,2H),0.97(s,3H) ;MS(ESI(+))m/e 433(M+H)$^+$.

[0503] 实施例 749

N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯甲酰胺

实施例 749A

(S)- 叔丁基 (1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基) 氨基甲酸酯

如实施例 147A 中所述制备标题化合物,用 (S)- 叔丁基吡咯烷 -3- 基氨基甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0504] 实施例 749B

(S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 胺

如实施例 1D 中所述制备标题化合物,用 (S)- 叔丁基 (1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基) 氨基甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0505] 实施例 749C

N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯甲酰胺

如实施例 1A 中所述制备标题化合物,用 (S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 4-(1- 异丁酰基哌啶 -4- 基) 苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm8.53(d, J = 6.6Hz,1H),7.83-7.76(m,2H),7.48(d, J = 9.4Hz,1H),7.37-7.30(m,2H),7.01(d,J = 9.5Hz,1H),4.68-4.49(m,2H),4.12-4.00(m,1H),3.77(dd, J = 11.0,6.6Hz,1H),3.68-3.39(m,3H),3.19-3.00(m,1H),3.02-2.50(m,3H),2.35-2.19(m,1H),2.08(dq, J = 12.5,6.3Hz,1H),1.91-1.70(m2H),1.65-1.07(m,2H).1.05-0.88(m,6H) ;MS(ESI(+))m/e 456(M+H)$^+$.

[0506] 实施例 750

N-(4-{1-[2-(哌嗪 -1- 基) 乙基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环

丁烷 -3- 甲酰胺

实施例 750A

叔丁基 4-(2-(4-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-1H- 吡唑 -1- 基) 乙基) 哌嗪 -1- 甲酸酯

如实施例 148A 中所述制备标题化合物，用叔丁基 4-(2-(4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑 -1- 基) 乙基) 哌嗪 -1- 甲酸酯代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑和用 N-(4- 溴苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替 4- 溴苯胺。

[0507] 实施例 750B

N-(4-{1-[2-(哌嗪 -1- 基) 乙基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物，用叔丁基 4-(2-(4-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-1H- 吡唑 -1- 基) 乙基) 哌嗪 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.20(s,1H),8.71(s,2H),8.57(dd, J = 4.3, 1.0Hz,1H),8.14(s,1H),7.86(s,1H),7.80(dd, J = 9.4,4.4Hz,1H),7.66-7.58(m,2H), 7.57-7.49(m,2H),7.45(d, J = 9.2Hz,1H),4.56-4.36(m,4H),4.31(t, J = 6.3Hz,2H), 3.91-3.73(m,1H),3.25-3.09(m,4H),3.04(t, J = 6.1Hz,2H),2.83(s,4H) ;MS(ESI(+))m/e 433$(M+H)^+$.

[0508] 实施例 751

N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 148A 中所述制备标题化合物，用 1- 新戊基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑和用 N-(4- 溴苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替 4- 溴苯胺。

^{1}H NMR(500MHz, DMSO-d_6) δ ppm 10.14(s,1H),8.57(dd, J = 4.5,1.2Hz,1H),8.05(s, 1H),7.82(s,1H),7.66-7.58(m,2H),7.55-7.51(m,2H),7.48(dd, J = 9.1,4.5Hz,1H), 6.98(dd, J = 9.1,1.1Hz,1H),4.30(t, J = 8.6Hz,2H),4.22(dd, J = 8.4,6.0Hz,2H), 3.90(s,2H),3.77(tt, J = 8.6,5.9Hz,1H),0.92(s,9H) ;MS(ESI(+))m/e 391$(M+H)^+$.

[0509] 实施例 752

4-[1-(2- 甲基丙酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 苯甲酰胺

如实施例 147B 中所述制备标题化合物，用 N-[(3S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基]-4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯甲酰胺代替 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

^{1}H NMR(400MHz,DMSO-d_6) δ ppm8.69(d, J = 6.6Hz,1H),8.57(dd, J = 4.3,1.2Hz,1H), 8.16-7.75(m,3H),7.69(dd, J = 9.5,1.2Hz,1H),7.37-7.31(m,2H),4.90-4.41(m,2H), 4.33-3.60(m,5H),3.20-2.50(m,4H),2.37-2.14(m,2H),1.87-1.74(m,2H),1.63-1.20(m,

2H),1.02(bs,J = 7.4Hz,6H) ;MS(ESI(+)) m/e 422(M+H)$^+$.

[0510] 实施例 753

N-{4-[1-(2- 羟基 -2- 甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 148A 中所述制备标题化合物,用 2- 甲基 -1-(4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑 -1- 基) 丙 -2- 醇代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑和用 N-(4- 溴苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替 4- 溴苯胺。

^{1}H NMR(300MHz,DMSO-d_6) δ ppm10.09(s,1H,8.56(dd,J = 4.5,1.3Hz,1H),8.01(s,1H),7.81(s,1H),7.69-7.57(m,2H),7.57-7.44(m,2H),7.38(dd, J = 9.0,4.5Hz,1H),6.83(dd, J = 9.0,1.3Hz,1H),4.70(s,1H),4.25(t, J = 8.4Hz,2H),4.16(dd, J = 8.0,6.0Hz,2H),4.01(s,2H),3.74(tt, J = 8.5,6.0Hz,1H),1.08(s,6H) ;MS(ESI(+))m/e 393(M+H)$^+$.

[0511] 实施例 754

5-[1-(3- 氟苯甲酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺

实施例 754A

(S)- 叔丁基 (1-(哒嗪 -3- 基) 吡咯烷 -3- 基) 氨基甲酸酯

如实施例 147B 中所述制备标题化合物,用 (S)- 叔丁基 (1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基) 氨基甲酸酯代替 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0512] 实施例 754B

(S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 胺

如实施例 1D 中所述制备标题化合物,用 (S)- 叔丁基 (1-(哒嗪 -3- 基) 吡咯烷 -3- 基) 氨基甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0513] 实施例 754C

5-(1-(叔丁氧基羰基)-1,2,3,6- 四氢吡啶 -4- 基) 噻吩 -2- 甲酸

如实施例 148A 中所述制备标题化合物,用叔丁基 4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-5,6- 二氢吡啶 -1(2H)- 甲酸酯代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑和用 5- 溴噻吩 -2- 甲酸代替 4- 溴苯胺。

[0514] 实施例 754D

5-(1-(叔丁氧基羰基) 哌啶 -4- 基) 噻吩 -2- 甲酸

如实施例 1B 中所述制备标题化合物,用 5-(1-(叔丁氧基羰基)-1,2,3,6- 四氢吡啶 -4- 基) 噻吩 -2- 甲酸代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0515] 实施例 754E

(S)- 叔丁基 4-(5-((1-(哒嗪 -3- 基) 吡咯烷 -3- 基) 氨基甲酰基) 噻吩 -2- 基) 哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用 (S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 胺代替叔

丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 5-(1-(叔丁氧基羰基) 哌啶 -4- 基) 噻吩 -2- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0516] 实施例 754F

(S)-5-(哌啶 -4- 基)-N-(1-(哒嗪 -3- 基) 吡咯烷 -3- 基) 噻吩 -2- 甲酰胺

如实施例 1D 中所述制备标题化合物，用 (S)- 叔丁基 4-(5-((1-(哒嗪 -3- 基) 吡咯烷 -3- 基) 氨基甲酰基) 噻吩 -2- 基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0517] 实施例 754G

5-[1-(3- 氟苯甲酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 噻吩 -2- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 (S)-5-(哌啶 -4- 基)-N-(1-(哒嗪 -3- 基) 吡咯烷 -3- 基) 噻吩 -2- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 3- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 8.63-8.44(m,2H),7.66(d, J = 3.8Hz,1H), 7.58-7.44(m,1H),7.41-7.19(m,4H),6.95(d, J = 3.8Hz,1H),6.87(dd, J = 9.1, 1.4Hz,1H),4.66-4.19(m,2H),3.85-3.38(m,5H),3.20-2.72(m,3H),2.34-2.15(m,1H), 2.17-1.78(m,3H),1.72-1.46(m,2H) ;MS(ESI(+))m/e 480(M+H)$^+$.

[0518] 表 14.

以下实施例基本上如实施例 754 中所述制备，代替实施例 754G 中的合适的羧酸。

实施例		名称	MS
755		5-[1-(4-氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 480 (M+H)+
758		N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(四氢-2H-吡喃-4-基羰基)哌啶-4-基]噻吩-2-甲酰胺	(ESI(+)) m/e 470 (M+H)+
760		5-[1-(2-甲基丙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 428 (M+H)+
761		5-[1-(2,4-二氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 498 (M+H)+
762		5-[1-[(2-甲基环丙基)羰基]哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 440 (M+H)+
763		5-[1-(2-氟苯甲酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 480 (M+H)+
764		5-(1-苯甲酰基哌啶-4-基)-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 462 (M+H)+
765		N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(四氢呋喃-3-基羰基)哌啶-4-基]噻吩-2-甲酰胺	(ESI(+)) m/e 456 (M+H)+
766		N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-{1-[(2R)-四氢呋喃-2-基羰基]哌啶-4-基}噻吩-2-甲酰胺	(ESI(+)) m/e 456 (M+H)+
767		5-[1-[(1-甲基哌啶-4-基)乙酰基]哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 498 (M+H)+
768		N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(1,3-噻唑-4-基羰基)哌啶-4-基]噻吩-2-甲酰胺	(ESI(+)) m/e 469 (M+H)+
1013		5-[1-(2,2-二甲基丙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 442 (M+H)+
1014		5-[1-(3,3-二甲基丁酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 456 (M+H)+
1015		5-[1-(2,2-二甲基丁酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 456 (M+H)+
1016		5-[1-[(1-甲基环丙基)羰基]哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 440 (M+H)+
1017		N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]-5-[1-(3,3,3-三氟丙酰基)哌啶-4-基]噻吩-2-甲酰胺	(ESI(+)) m/e 468 (M+H)+
1018		5-[1-(环丙基乙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 440 (M+H)+
1019		5-[1-(双环[2.2.1]庚-2-基乙酰基)哌啶-4-基]-N-[(3S)-1-(哒嗪-3-基)吡咯烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 494 (M+H)+

[0519] 实施例 756

(3S)-N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

实施例 756A

(S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 甲酸

如实施例 147A 中所述制备标题化合物，用 (S)- 吡咯烷 -3- 甲酸代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0520] 实施例 756B

(S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酸

如实施例 147B 中所述制备标题化合物，用 (S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 甲酸代替 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0521] 实施例 756C

(S)-N-(4- 溴苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 4- 溴苯胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 (S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0522] 实施例 756D

(3S)-N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 148A 中所述制备标题化合物，用 1-((4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基)-4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑和用 (S)-N-(4- 溴苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺代替 4- 溴苯胺。

^1H

NMR(300MHz, DMSO-d_6) δ ppm10.11(s,1H),8.48(dd, J = 4.5,1.2Hz,1H),8.07(s,1H), 7.82(s,1H),7.64-7.58(m,2H),7.54-7.49(m,2H),7.34(dd, J = 9.1,4.4Hz,1H),6.88(dd, J = 9.2,1.3Hz,1H),4.02(s,2H),3.78(dd, J = 10.5,7.9Hz,1H),3.72-3.58(m,4H), 3.56-3.45(m,3H),3.37-3.32(m,1H),2.42-209(m,2H),1.51(ddd, J = 13.4,9.1,4.2Hz, 2H),1.32-1.12(m,2H),0.97(s,3H) ;MS(ESI(+))m/e 447$(M+H)^+$。

[0523] 表 15.

以下实施例基本上如实施例 756 中所述制备，代替实施例 756D 中的合适的硼酸盐。

实施例		名称	MS
757		(3S)-N-{4-[1-(2-羟基-2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 407 $(M+H)^+$
759		(3S)-N-{4-[1-(2,2-二甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 405 $(M+H)^+$
769		(3S)-N-{4-[1-(2-甲基丙基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 391 $(M+H)^+$
770		(3S)-N-{4-[1-(丙烷-2-基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 377 $(M+H)^+$
771		(3S)-N-{4-[1-(环丙基甲基)-1H-吡唑-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 389 $(M+H)^+$
772		(3S)-1-(哒嗪-3-基)-N-{4-[1-(四氢-2H-吡喃-2-基甲基)-1H-吡唑-4-基]苯基}吡咯烷-3-甲酰胺	(ESI(+)) m/e 433 $(M+H)^+$
773		(3S)-N-[4-(1-叔丁基-1H-吡唑-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 391 $(M+H)^+$

[0524] 实施例 774

(3S)-N-(4-{[(3R)-1- 苯甲酰基吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

实施例 774A

(R)- 叔丁基 3-(4-((S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺基) 苯氧基) 吡咯烷 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用 (R)- 叔丁基 3-(4- 氨基苯氧基) 吡咯烷 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 (S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0525] 实施例 774B

(S)-1-(哒嗪 -3- 基)-N-(4-((R)- 吡咯烷 -3- 基氧基) 苯基) 吡咯烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用 (R)- 叔丁基 3-(4-((S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺基) 苯氧基) 吡咯烷 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0526] 实施例 774C

(3S)-N-(4-{[(3R)-1- 苯甲酰基吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (S)-1-(哒嗪 -3- 基)-N-(4-((R)- 吡咯烷 -3- 基氧基) 苯基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.03(d, J = 18.3Hz,1H),8.51(d, J = 4.2Hz,1H),7.46(tdt,J = 21.9,19.2,10.8Hz,8H),7.13-7.02(m,1H),6.96(d,J = 8.9Hz,1H),6.86(d, J = 8.9Hz,1H),5.00(d, J = 34.1Hz,1H),3.88-3.74(m,2H),3.65(dd, J = 12.1,7.4Hz,

4H),3.51(d,J = 7.3Hz,2H),2.37-1.98(m,4H),MS(ESI(+))m/e 458(M+H)$^+$.

[0527] 表 16.

以下实施例基本上如实施例 774 中所述制备,代替实施例 774C 中的合适的羧酸。

实施例		名称	MS
775		(3S)-N-(4-{[(3R)-1-(2-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 476 (M+H)$^+$
776		(3S)-N-(4-{[(3R)-1-(3-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 476 (M+H)$^+$
777		(3S)-N-(4-{[(3R)-1-(4-氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 476 (M+H)$^+$
778		(3S)-N-(4-{[(3R)-1-(3,5-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 494 (M+H)$^+$
779		(3S)-N-(4-{[(3R)-1-(2-甲基苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 472 (M+H)$^+$
780		(3S)-N-(4-{[(3R)-1-(2,2-二甲基丙酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 438 (M+H)$^+$
781		(3S)-N-[4-({(3R)-1-[(4,4-二氟环己基)羰基]吡咯烷-3-基}氧基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 500 (M+H)$^+$
782		(3S)-1-(哒嗪-3-基)-N-(4-{[(3R)-1-(4,4,4-三氟丁酰基)吡咯烷-3-基]氧基}苯基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 478 (M+H)$^+$
783		(3S)-N-(4-{[(3R)-1-(2,4-二氟苯甲酰基)吡咯烷-3-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 494 (M+H)$^+$

[0528] 实施例 784

N-[4-(5-丙基-1,2,4-氧杂二唑-3-基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺

如实施例 806 中所述制备标题化合物,用丁酰氯代替实施例 806A 中的 3,3-二甲基丁酰氯。

^{1}H NMR(300 MHz,DMSO-d_6) δ ppm 10.39(s,1H),8.57(dd,J = 4.5,1.3Hz,1H),8.04-7.89(m,2H),7.89-7.74(m,2H),7.38(dd,J = 9.0,4.5Hz,1H),6.84(dd,J = 8.9,1.4Hz,1H),4.26(t,J = 8.4Hz,2H),4.18(dd,J = 8.2,5.9Hz,2H),3.79(tt,J = 8.6,5.9Hz,1H),2.96(t,J = 7.4Hz,2H),1.81(h.J = 7.4Hz,2H),0.99(t,J = 7.4Hz,3H);MS(ESI(+))m/e 365(M+H)$^+$.

[0529] 实施例 785

(3S)-N-{4-[1-(2-氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺

实施例 785A

(S)-叔丁基 3-(4-(1-(哒嗪-3-基)吡咯烷-3-甲酰胺基)苯基)氮杂环丁烷-1-甲酸酯

如实施例 1A 中所述制备标题化合物，用叔丁基 3-(4- 氨基苯基）氮杂环丁烷 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯和用 (S)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酸代替 1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酸。

[0530] 实施例 785B

(S)-N-(4-(氮杂环丁烷 -3- 基）苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物，用 (S)- 叔丁基 3-(4-(1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺基）苯基）氮杂环丁烷 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯。

[0531] 实施例 785C

(3S)-N-{4-[1-(2- 氟苯甲酰基）氮杂环丁烷 -3- 基] 苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 (S)-N-(4-(氮杂环丁烷 -3- 基）苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酸。

^{1}H NMR(500 MHz, DMSO-d_6) δ ppm10.15(bs,1H),8.51-8.46(m,1H),7.67-7.40(m,4H),7.40-7.24(m,5H),6.90-6.85(m,1H),4.50-4.42(m,1H),4,41-4.34(m,1H),4.02-3.96(m,2H),3.93-3.83(m,1H),3.81-3.73(m,1H),3.67-3.58(m,2H),3.53-3.44(m,1H),3.40-3.30(m,1H),2.43-2.12(m,2H) ;MS(ESI(+))m/e 446$(M+H)^+$.

[0532] 表 17.

以下实施例基本上如实施例 785 中所述制备，代替实施例 785C 中的合适的羧酸。

实施例		名称	MS
786		(3S)-N-{4-[1-(3-氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 446 $(M+H)^+$
787		(3S)-N-{4-[1-(4-氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 446 $(M+H)^+$
788		(3S)-N-[4-(1-苯甲酰基氮杂环丁烷-3-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 428 $(M+H)^+$
789		(3S)-N-{4-[1-(2,2-二甲基丙酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 408 $(M+H)^+$
790		(3S)-N-{4-[1-(3,5-二氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 464 $(M+H)^+$
791		3S)-N-{4-[1-(2-甲基苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 442 $(M+H)^+$
792		(3S)-N-{4-[1-(2,4-二氟苯甲酰基)氮杂环丁烷-3-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 464 $(M+H)^+$

[0533] 实施例 793

(3R)-N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

实施例 793A

(R)-1-(6-氯哒嗪-3-基)吡咯烷-3-甲酸

如实施例147A中所述制备标题化合物,用(R)-吡咯烷-3-甲酸代替叔丁基4-(4-(氮杂环丁烷-3-甲酰胺基)苯基)哌啶-1-甲酸酯。

[0534] 实施例793B

(R)-1-(哒嗪-3-基)吡咯烷-3-甲酸

如实施例147B中所述制备标题化合物,用(R)-1-(6-氯哒嗪-3-基)吡咯烷-3-甲酸代替4-(4-(1-(6-氯哒嗪-3-基)氮杂环丁烷-3-甲酰胺基)苯基)哌啶-1-甲酸酯。

[0535] 实施例793C

(R)-叔丁基4-(4-(1-(哒嗪-3-基)吡咯烷-3-甲酰胺基)苯基)哌啶-1-甲酸酯

如实施例1A中所述制备标题化合物,用叔丁基4-(4-氨基苯基)哌啶-1-甲酸酯代替叔丁基4-(4-氨基苯氧基)哌啶-1-甲酸酯和用(R)-1-(哒嗪-3-基)吡咯烷-3-甲酸代替1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

[0536] 实施例793D

(R)-N-(4-(哌啶-4-基)苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺

如实施例1D中所述制备标题化合物,用(R)-叔丁基4-(4-(1-(哒嗪-3-基)吡咯烷-3-甲酰胺基)苯基)哌啶-1-甲酸酯代替叔丁基4-(4-(1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯。

[0537] 实施例793E

(3R)-N-[4-(1-苯甲酰基哌啶-4-基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺

如实施例1A中所述制备标题化合物,用(R)-N-(4-(哌啶-4-基)苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺代替叔丁基4-(4-氨基苯氧基)哌啶-1-甲酸酯和用苯甲酸代替1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.06(s,1H),8.48(dd, J = 4.4,0.9Hz,1H),7.54(t, J = 6.3Hz,2H),7.47-7.40(m,5H),7.35(dd, J = 9.1,4.5Hz,1H),7.22(d, J = 8.6Hz,2H),6.89(dd, J = 9.2,1.1Hz,1H),4.62(s,1H),3.75(dt, J = 25.9,12.9Hz,1H),3.62(td, J = 10.2,5.8Hz,3H),3.55-3.41(m,1H),3.13(s,1H),2.98-2.69(m,2H),2.39-2.11(m,2H),1.90-1.48(m,4H),MS(ESI(+))m/e456$(M+H)^+$.

[0538] 实施例794

(3R)-N-{4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺

如实施例1A中所述制备标题化合物,用(R)-N-(4-(哌啶-4-基)苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺代替叔丁基4-(4-氨基苯氧基)哌啶-1-甲酸酯和用2-氟苯甲酸代替1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.06(s,1H),8.48(dd, J = 4.5,1.2Hz,1H),7.59-7.40(m,4H),7.41-7.23(m,3H),7.19(d, J = 8.5Hz,2H),6.89(dd, J = 9.2,1.2Hz,1H),4.66(d, J = 13.1Hz,1H),3.77(dd, J = 10.5,7.9Hz,1H),3.73-3.56(m,2H),3.48(dt, J = 10.2,7.4Hz,2H),3.17(t, J = 12.1Hz,1H),2.82(dt, J = 24.1,11.3Hz,2H),2.38-2.09(m,2H),1.97-1.79(m,1H),1.69(t, J = 17,4Hz,1H),1.52(ddd. J = 20.9,12.0,6.1Hz,2H),MS(ESI(+))m/e 474$(M+H)^+$.

[0539] 实施例 795

(3R)-N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (R)-N-(4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2,2- 二甲基丙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}HNMR(300MHz,DMSO-d_6) δ ppm10.04(s,1H),8.48(dd,J = 4.5,1.3Hz,1H),7.54(t,J = 6.4Hz,1H),7.34(dd,J = 9.1,4.5Hz,1H),7.21-7,14(m,2H),6.87(dd,J = 9.1,1.3Hz,1H),4.46-4.35(m,2H),3.76(dd, J = 10.5,7.9Hz,1H),3.69-3.54(m,2H),3.48(dt, J = 10.2,7.4Hz,1H),2.94-2.63(m,3H),2.39-2.07(m,2H),1.83-1.73(m,2H),1.50(s,1H),1.22(s,9H),MS(ESI(+))m/e 436$(M+H)^+$.

[0540] 实施例 796

(3S)-N-(4-{[1-(环己基羰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

实施例 796A

(S)- 叔丁基 4-(4-(1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 (S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0541] 实施例 796B

(S)-N-(4-(哌啶 -4- 基氧基) 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用 (S)- 叔丁基 4-(4-(1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0542] 实施例 796C

(3S)-N-(4-{[1-(环己基羰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (S)-N-(4-(哌啶 -4- 基氧基) 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用环己烷羧酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm9.97(s,1H),8.48(dd, J = 4.5,1.3Hz,1H),7.55-7.48(m,2H),7.34(dd, J = 9.1,4,4Hz,1H),6.97-6.84(m,3H),4.58-4.47(m,1H),3.88-3.40(m,6H),3.40-3.200m,2H),2.60-2.50(m,1H),2.41-2.08(m,2H),2.00-1.80(m,2H),1.77-1.07(m,13H) ;MS(ES)(+))m/e478$(M+H)^+$.

[0543] 表 18.

以下实施例基本上如实施例 796 中所述制备,代替实施例 796C 中的合适的羧酸。

实施例		名称	MS
797		(3S)-N-(4-{[1-(2-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
798		(3S)-N-(4-{[1-(3-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
799		(3S)-N-{4-[(1-苯甲酰基哌啶-4-基)氧基]苯基}-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 472 $(M+H)^+$
800		(3S)-N-(4-{[1-(4-氯苯甲酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 490 $(M+H)^+$
801		(3S)-N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]氧基}苯基)-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 452 $(M+H)^+$
802		(3S)-N-[4-({1-[(2-甲基环丙基)羰基]哌啶-4-基}氧基)苯基]-1-(哒嗪-3-基)吡咯烷-3-甲酰胺	(ESI(+)) m/e 450 $(M+H)^+$

[0544] 实施例 803

N-{4-[5-(2,2- 二甲基丙基)-1,3,4- 氧杂二唑 -2- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 803A

N′ -(3,3- 二甲基丁酰基)-4- 硝基苯酰肼

将 4- 硝基苯酰肼 (0.500g,2.76mmol) 和 4- 甲基吗啉 (0.455ml,4.14mmol) 的悬浮液在二氯甲烷 (20ml) 中搅拌。加入 3,3- 二甲基丁酰氯 (0.422ml,3.04mmol) 并将反应混合物搅拌 2 小时。粗反应混合物的正相色谱产生标题化合物。

[0545] 实施例 803B

2- 新戊基 -5-(4- 硝基苯基)-1,3,4- 噁二唑

将 N′ -(3,3- 二甲基丁酰基)-4- 硝基苯酰肼 (0.556g,1.991mmol) 和甲基 N-(三乙基铵磺酰基) 氨基甲酸酯 (0.572g,2.389mmol) 在四氢呋喃 (10ml) 中的混合物在微波炉中加热至 120℃ 45 分钟。将粗反应混合物浓缩并通过正相色谱纯化以产生标题化合物。

[0546] 实施例 803C

4-(5- 新戊基 -1,3,4- 氧杂二唑 -2- 基) 苯胺

如实施例 1B 中所述制备标题化合物,用 2- 新戊基 -5-(4- 硝基苯基)-1,3,4- 噁二唑代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0547] 实施例 803D

N-{4-[5-(2,2- 二甲基丙基)-1,3,4- 氧杂二唑 -2- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 4-(5- 新戊基 -1,3,4- 氧杂二唑 -2- 基) 苯胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^1H NMR(300MHz, DMSO-d_6) δ ppm10.45(s,1H),8.57(dd, J = 4.5,1.3Hz,1H),

7.97-7.91(m,2H),7.88-7.82(m,2H),7.39(dd,J = 9.0,4.5Hz,1H),6.84(dd,J = 9.0,1.4Hz,1H),4,26(t,J = 8.4Hz,2H),4,18(dd,J = 8.2,5.9Hz,2H),3.79(tt,J = 8.6,5.9Hz,1H),2.82(s,2H),1.03(s,9H) ;MS(ESI(+))m/e393(M+H)$^+$.

[0548] 实施例 804

N-{4-[1-(2,2- 二甲基丙基)-1H- 咪唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 804A

1- 新戊基 -4-(4- 硝基苯基)-1H- 咪唑

向 4-(4- 硝基苯基)-1H- 咪唑 (0.500g,2.64mmol) 在 N, N- 二甲基甲酰胺 (10ml) 中的溶液中加入碳酸铯 (1.292g,3.96mmol) 随后加入 1- 溴 -2,2- 二甲基丙烷 (0.366ml,2.91mmol)。在 85° 加热过夜后,将反应混合物冷却至室温,用乙酸乙酯稀释,用水和盐水洗涤,用硫酸镁干燥,过滤并浓缩。正向色谱产生标题化合物。

[0549] 实施例 804B

4-(1- 新戊基 -1H- 咪唑 -4- 基) 苯胺

如实施例 1B 中所述制备标题化合物,用 1- 新戊基 -4-(4- 硝基苯基)-1H- 咪唑代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0550] 实施例 804C

N-{4-[1-(2,2- 二甲基丙基)-1H- 咪唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 4-(1- 新戊基 -1H- 咪唑 -4- 基) 苯胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.08(s,1H),8.56(dd,J = 4.6,1.3Hz,1H),7.73-7.66(m,2H),7.64-7.58(m,2H),7.57(d,J = 1.2Hz,1H),7.49(d,J = 1.1Hz,1H),7.38(dd,J = 9.0,4.5Hz,1H),6.83(dd,J = 9.0,1.4Hz,1H),4.25(t,J = 8.3Hz,2H),4.16(dd,J = 8.1,6.0Hz,2H),3.77(s,2H),3.77-3.69(m,1H),0.91(s,9H) ;MS(ESI(+))m/e391(M+H)$^+$.

[0551] 实施例 805

N-[4-(3- 环丙基 -1- 甲基 -1H- 吡唑 -5- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 805A

3- 环丙基 -1-(4- 硝基苯基) 丙 -2- 炔 -1- 酮将 250-mL 圆底烧瓶装有双 (三苯基膦) 二氯化钯 (151mg,0.216mmol) 和碘化亚铜 (82mg,0.431mmol),并将烧瓶用氮气脱气。将四氢呋喃 (40mL) 经隔片加入,并将氮气经混合物发泡 30 分钟。向其中逐滴加入 4- 硝基苯甲酰氯 (2g,10.8mmol)、乙炔基环丙烷 (784mg,11.9mmol) 和三乙胺 (1.31g,12.9mmol) 在四氢呋喃 (15mL) 中的经氮气脱气的溶液。将反应混合物在室温搅拌 2 小时并随后浓缩至干燥。将残余物通过正向色谱纯化以产生标题化合物。

[0552] 实施例 805B

3- 环丙基 -1- 甲基 -5-(4- 硝基苯基)-1H- 吡唑

将 3- 环丙基 -1-(4- 硝基苯基) 丙 -2- 炔 -1- 酮 (500mg,2.323mmol) 溶解于 N, N- 二甲基甲酰胺 (7.75mL) 中,并将溶液冷却至 0℃。逐滴加入甲基肼 (118mg,2.56mmol)。将混合物在室温搅拌过夜随后用水 (25mL) 稀释并搅拌 45 分钟。通过过滤收集产生的沉淀物以得到标题化合物。

[0553] 实施例 805C

4-(3- 环丙基 -1- 甲基 -1H- 吡唑 -5- 基) 苯胺

如实施例 1B 中所述制备标题化合物,用 3- 环丙基 -1- 甲基 -5-(4- 硝基苯基)-1H- 吡唑代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0554] 实施例 805D

N-[4-(3- 环丙基 -1- 甲基 -1H- 吡唑 -5- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 4-(3- 环丙基 -1- 甲基 -1H- 吡唑 -5- 基) 苯胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz,DMSO-d_6)d 10.11(s,1H),8.56(dd,J = 4.5,1.3Hz,1H),7.69-7.58(m,4H),7.38(dd,J = 9.0,4.5Hz,1H),6.83(dd,J = 9.0,1.3Hz,1H),6.28(s,1H),4.25(t,J = 8.3Hz,2H),4.16(dd,J = 8.1,6.0Hz,2H),3.84(s,3H),3.75(dq,J = 8.3,5.9Hz,1H),1.95-1.82(m,1H),1.02-0.92(m,2H),0.71-0.62(m,2H) ;MS(ESI(+))m/e 375(M+H)$^+$.

[0555] 实施例 806

N-{4-[5-(2,2- 二甲基丙基)-1,2,4- 氧杂二唑 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 806A

5- 新戊基 -3-(4- 硝基苯基)-1,2,4- 噁二唑

向 (Z)-N′ -羟基 -4- 硝基苯甲脒 (0.500g,2.76mmol) 在二氯甲烷 (6ml) 中的悬浮液中加入 4- 甲基吗啉 (0.455ml,4.14mmol) 随后加入 3,3- 二甲基丁酰氯 (0.422ml,3.04mmol)。1 小时后,将粗反应混合物通过正向色谱纯化并将收集的中间产物溶解于二氯甲烷 (8ml) 中,并用四丁基氟化铵 (1.0M 于 THF 中)(8.28ml,8.28mmol) 处理。在室温 3 小时后,将混合物用乙酸乙酯稀释,用水洗涤,用硫酸镁干燥,过滤并浓缩。正相色谱产生标题化合物。

[0556] 实施例 806B

4-(5- 新戊基 -1,2,4- 氧杂二唑 -3- 基) 苯胺

如实施例 1B 中所述制备标题化合物,用 5- 新戊基 -3-(4- 硝基苯基)-1,2,4- 噁二唑代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0557] 实施例 806C

N-{4-[5-(2,2- 二甲基丙基)-1,2,4- 氧杂二唑 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 4-(5- 新戊基 -1,2,4- 氧杂二唑 -3- 基) 苯胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲

酸代替 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.40(s,1H),8.57(dd, J = 4.6,1.3Hz,1H),8.05-7.89(m,2H),7.89-7.75(m,2H),7.38(dd, J = 9.0,4.5Hz,1H),6.84(dd, J = 9.0,1.3Hz,1H),4.26(t, J = 8.4Hz,2H),4.18(dd, J = 8.1,5.9Hz,2H),3.79(tt, J = 8.5,5.9Hz,1H),2.90(s,2H),1.04(s,9H) ;MS(ESI(+))m/e393(M+H)$^+$.

[0558] 实施例 807

N-{4-[3- 环丙基 -1-(2- 甲氧基乙基)-1H- 吡唑 -5- 基]苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺如实施例 805 中所述制备标题化合物,用 (2- 甲氧基乙基)肼代替实施例 805B 中的甲基肼。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.20(s,1H),8.56(d, J = 4.5Hz,1H),7.72-7.57(m,4H),7.55-7.48(m,1H),7.07-6.99(m,1H),6.28(s,1H),4.38-4.18(m,6H),3.83-3.69(m,3H),3.25(s,3H),1.98-1.87(m,1H),1.00-0.91(m,2H),0.67(d, J = 2.3Hz,2H) :MS(ESI(+))m/e 419(M+H)$^+$.

[0559] 实施例 808

叔丁基 4-(5-{[1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基]氨基甲酰基}噻吩 -2- 基)哌啶 -1- 甲酸酯

实施例 808A

叔丁基 (1-(6- 氯哒嗪 -3- 基)氮杂环丁烷 -3- 基)氨基甲酸酯

如实施例 147A 中所述制备标题化合物,用叔丁基氮杂环丁烷 -3- 基氨基甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基)苯基)哌啶 -1- 甲酸酯。

[0560] 实施例 808B

叔丁基 (1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基)氨基甲酸酯

如实施例 147B 中所述制备标题化合物,用叔丁基 (1-(6- 氯哒嗪 -3- 基)氮杂环丁烷 -3- 基)氨基甲酸酯代替 4-(4-(1-(6- 氯哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺基)苯基)哌啶 -1- 甲酸酯。

[0561] 实施例 808C

1-(哒嗪 -3- 基)氮杂环丁烷 -3- 胺

如实施例 1D 中所述制备标题化合物,用叔丁基 (1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基)氨基甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基)氮杂环丁烷 -3- 甲酰胺基)苯氧基)哌啶 -1- 甲酸酯。

[0562] 实施例 808D

叔丁基 4-(5-{[1-(哒嗪 -3- 基)氮杂环丁烷 -3- 基]氨基甲酰基}噻吩 -2- 基)哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用 1-(哒嗪 -3- 基)氮杂环丁烷 -3- 胺代替叔丁基 4-(4- 氨基苯氧基)哌啶 -1- 甲酸酯和用 5-(1-(叔丁氧基羰基)哌啶 -4- 基)噻吩 -2- 甲酸代替 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 8.95(d, J = 7.2Hz,1H),8.56(dd, J = 4.5,1.3Hz,1H),7.65(d, J = 3.8Hz,1H),7.38(dd, J = 8.9,4.5Hz,1H),6.95(dd, J = 3.8,0.8Hz,1H),6.83(dd, J = 9.0,1.4Hz,1H),4.92-4.77(m,1H),4.36(t, J = 8.1Hz,2H),4.05-3.97(m,

4H),3.09-2.66(m,3H),1.98-1.88(m,2H).1.40(s,11H);MS(ESI(+))m/e 444(M+H)⁻.

[0563] 实施例 809

叔丁基 4- 氟 -4-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基] 哌啶 -1- 甲酸酯

实施例 809A

叔丁基 4-(4- 氨基苯基)-4- 羟基哌啶 -1- 甲酸酯

将在四氢呋喃 (100mL) 中的 N-(4- 溴苯基)-1,1,1- 三甲基 -N-(三甲基甲硅烷基) 硅烷胺 (7g,22.12mmol) 用正丁基锂 (1M,22mL) 的溶液在 -78℃处理。将反应混合物在 -78℃下再搅拌 1 小时,并随后用叔丁基 4- 氧代哌啶 -1- 甲酸酯 (3.97g,19.91mmol) 在四氢呋喃 (20mL) 中的溶液处理。将反应混合物在 -78℃下搅拌 30 分钟并随后加温至室温。通过加入饱和的氯化铵溶液 (100mL) 将反应停止 (quenched) 并用乙酸乙酯萃取。将合并的有机物用水、盐水洗涤,用硫酸镁干燥,过滤并浓缩。将粗叔丁基 4-(4-(双 (三甲基甲硅烷基) 氨基) 苯基)-4- 羟基哌啶 -1- 甲酸酯用四丁基氟化铵的溶液 (1M THF,40mL) 在室温处理 1 小时。将反应混合物用水稀释并用乙酸乙酯萃取。将有机物用水和盐水洗涤,用硫酸镁干燥,过滤并浓缩。通过正相色谱纯化产生标题化合物。

[0564] 实施例 809B

叔丁基 4-(4-(1-((苄基氧基) 羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-4- 羟基哌啶 -1- 甲酸酯如实施例 1A 中所述制备标题化合物,用叔丁基 4-(4- 氨基苯基)-4- 羟基哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-((苄基氧基) 羰基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0565] 实施例 809C

叔丁基 4-(4-(1-((苄基氧基) 羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-4- 氟哌啶 -1- 甲酸酯

将在 50mL 二氯甲烷中的叔丁基 4-(4-(1-((苄基氧基) 羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-4- 羟基哌啶 -1- 甲酸酯 (2.5g,4.91mmol) 冷却至 -78℃并经注射器逐滴加入三氟化二乙氨基硫。将反应混合物在 -78℃下再搅拌 1 小时并加温至 0℃。允许反应在 0℃下搅拌 1 小时并冷却降回 -78℃。将反应混合物用 50mL 二氯甲烷稀释随后用 10mL 甲醇停止。将溶液用饱和的碳酸氢钠和盐水洗涤,用硫酸镁干燥并过滤。浓缩和正相色谱产生标题化合物。

[0566] 实施例 809D

叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基)-4- 氟哌啶 -1- 甲酸酯

如实施例 1B 中所述制备标题化合物,用叔丁基 4-(4-(1-((苄基氧基) 羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-4- 氟哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0567] 实施例 809E

叔丁基 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-4- 氟哌啶 -1- 甲酸酯

如实施例 147A 中所述制备标题化合物,用叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基)-4- 氟哌啶 -1- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲

酸酯。

[0568] 实施例 809F

叔丁基 4- 氟 -4-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基] 哌啶 -1- 甲酸酯

如实施例 147B 中所述制备标题化合物，用叔丁基 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-4- 氟哌啶 -1- 甲酸酯代替 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -]- 甲酸酯。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.18-10.08(m,1H),8.55(dd, J = 4.5,1.4Hz,1H), 7.65-7.56(m,2H),7.40-7.33(m,3H),6.82(dd, J = 8.9,1.4Hz,1H),4.23(t, J = 8.3Hz, 2H),4.14(dd, J = 8.2,5.7Hz,2H),4.08-3.91(m,2H),3.81-3.68(m,1H),3.17-2.70(m, 2H),2.07-1.82(m,3H),1.42-1.35(s,10H) ;MS(ESI(+))m/e 456(M+H)$^+$.

[0569] 实施例 810

5-(1- 苯甲酰基哌啶 -4- 基)-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺

实施例 810A

5-(哌啶 -4- 基)-N-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基) 噻吩 -2- 甲酰胺

如实施例 1D 中所述制备标题化合物，用叔丁基 4-(5-{[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 氨基甲酰基 } 噻吩 -2- 基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0570] 实施例 810B

5-(1- 苯甲酰基哌啶 -4- 基)-N-[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 噻吩 -2- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 5-(哌啶 -4- 基)-N-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基) 噻吩 -2- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 8.96(d, J = 7.2Hz,1H),8.56(dd, J = 4.5,1.3Hz, 1H),7.66(d, J = 3.8Hz,1H),7.51-7.34(m,6H),6.98(dd, J = 3.8,0.8Hz,1H),6.84(dd, J = 9.0,1.4Hz,1H),4.92-4.77(m,1H),4.6(bs,1H),4.36(t, J = 8.1Hz,2H),4.01(dd, J = 8.6,5.6Hz,2H),3.64(bs,1H),3.23-2.83(m,3H),2.10-1.84(m,2H),1.67-1.48(m,2H) : MS(ESI(+))m/e 448(M+H)$^+$.

[0571] 表 19.

以下实施例基本上如实施例 810 中所述制备，代替实施例 810B 中的合适的羧酸。

实施例		名称	MS
811		5-[1-(2-氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 466 $(M+H)^+$
812		5-[1-(2-甲基苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 462 $(M+H)^+$
813		5-[1-(2,4-二氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 484 $(M+H)^+$
814		5-[1-(3-氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 466 $(M+H)^+$
815		5-[1-(4-氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 466 $(M+H)^+$
816		5-[1-(3,5-二氟苯甲酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 484 $(M+H)^+$
847		5-[1-(2,2-二甲基丙酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 428 $(M+H)^+$
848		5-{1-[(1-甲基环丙基)羰基]哌啶-4-基}-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 426 $(M+H)^+$
849		N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]-5-[1-(3,3,3-三氟丙酰基)哌啶-4-基]噻吩-2-甲酰胺	(ESI(+)) m/e 454 $(M+H)^+$
850		5-[1-(2,2-二甲基丁酰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 442 $(M+H)^+$
855		N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]-5-[1-(4,4,4-三氟丁酰基)哌啶-4-基]噻吩-2-甲酰胺	(ESI(+)) m/e 468 $(M+H)^+$
856		5-[1-(环丙基羰基)哌啶-4-基]-N-[1-(哒嗪-3-基)氮杂环丁烷-3-基]噻吩-2-甲酰胺	(ESI(+)) m/e 412 $(M+H)^+$

[0572] 实施例 817

N-{4-[3- 环丙基 -1-(2- 羟基乙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺如实施例 805 中所述制备标题化合物，用 2- 肼基乙醇代替 805B 中的甲基肼。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.14(s,1H),8.56(dd, J = 4.5,1.3Hz,1H),7.72-7.58(m,4H),7.38(dd, J = 9.0,4.5Hz,1H),6.83(dd, J = 9.0,1.4Hz,1H),6.27(s,1H),4.90(brs,1H),4.31-4.08(m,6H),3.84-3.69(m,3H),2.01-1.88(m,1H),1.01-0.89(m,2H),0.72-0.62(m,2H) ;MS(ESI(+))m/e 405$(M+H)^+$.

[0573] 实施例 818

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 818A

叔丁基 4-(4-(1-((苄基氧基) 羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物，用叔丁基 4-(4- 氨基苯基）哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯和用 1-((苄基氧基）羰基）氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酸。

[0574] 实施例 818B

叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基）苯基）哌啶 -1- 甲酸酯

如实施例 1B 中所述制备标题化合物，用叔丁基 4-(4-(1-((苄基氧基）羰基）氮杂环丁烷 -3- 甲酰胺基）苯基）哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯。

[0575] 实施例 818C

叔丁基 4-(4-(1-(6- 氟哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺基）苯基）哌啶 -1- 甲酸酯

如实施例 147A 中所述制备标题化合物，用叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基）苯基）哌啶 -1- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基）苯基）哌啶 -1- 甲酸酯和用 3,6- 二氟哒嗪代替 3,6- 二氯哒嗪。

[0576] 实施例 818D

1-(6- 氟哒嗪 -3- 基）-N-(4-(哌啶 -4- 基）苯基）氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物，用叔丁基 4-(4-(1-(6- 氟哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺基）苯基）哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基）氮杂环丁烷 -3- 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯。

[0577] 实施例 818E

N-[4-(1- 苯甲酰基哌啶 -4- 基）苯基]-1-(6- 氟哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 1-(6- 氟哒嗪 -3- 基）-N-(4-(哌啶 -4- 基）苯基）氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.03(s,1H),7.54(d, J = 8.6Hz,2H),7.49-7.38(m,6H),7.22(d, J = 8.6Hz,2H),7.12(dd, J = 9.5,6.8Hz,1H),4.23(t, J = 8.3Hz,2H),4.14(dd, J = 8.0,6.0Hz,2H),3.71(ddd, J = 14.4,8.4,5.9Hz,2H),2.86(dd, J = 67.9,55.9Hz,3H),2.04-1.43(m,4H) ;MS(ESI(+))m/e 460(M+H)$^+$.

[0578] 实施例 819

N-{4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(6- 氟哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 1-(6- 氟哒嗪 -3- 基）-N-(4-(哌啶 -4- 基）苯基）氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.04(s,1H),7.58-7.34(m,5H),7.35-7.25(m,2H),7.23-7.17(m,2H),7.12(dd, J = 9.4,6.7Hz,1H),4.70-4.61(m,1H),4.23(t, J = 8.3Hz,2H),4.14(d, J = 13.9Hz,2H),3.77-3.66(m,1H),3.50-3.41(m,1H),3.23-3.09(m,1H),2.95-2.72(m,2H),1.91-1.82(m,1H),1.79-1.42(m,3H) ;MS(ESI(+))m/e 478(M+H)$^+$.

[0579] 实施例 820

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 1-(6- 氟哒嗪 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2,2- 二甲基丙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.03(s,1H),7.57-7.50(m,2H),7.41(dd, J = 9.4, 1.9Hz,1H),7.22-7.15(m,2H),7.12(dd, J = 9.4,6.7Hz,1H),4.45-4.36(m,2H),4.23(t, J = 8.3Hz,2H),4.14(dd, J = 8.0,5.9Hz,2H),3.77-3.66(m,1H),2.93-2.66(m,3H), 1.82-1.74(m,2H),1.52-1.35(m,2H),1.22(s,9H) ;MS(ESI(+))m/e 440(M+H)$^+$.

[0580] 实施例 821

1-(6- 氟哒嗪 -3- 基)-N-{4-[1-(2- 甲基丙酰基) 哌啶 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 1-(6- 氟哒嗪 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用异丁酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.03(s,1H),7.54(d, J = 8.5Hz,2H),7.41(dd, J = 9.5,1.9Hz,1H),7.18(d, J = 8.5Hz,2H),7.12(dd, J = 9.5,6.8Hz,1H),4.62-4.45(m,1H), 4.23(t, J = 8.3Hz,2H),4.14(dd, J = 7.9,6.1Hz,2H),4.10-3.97(m,1H),3.72(ddd, J = 8.4,7.2,4.2Hz,1H),3.10(s,1H),2.89(dt, J = 13.4,6.7Hz,1H),2.81-2.64(m,1H), 2.57(s,1H),1.79(ddd, J = 16.4,10.0,2.9Hz,2H),1.58-1.25(m,2H),1.12-0.92(m,6H) ; MS(ESI(+))m/e 426(M+H)$^+$.

[0581] 实施例 822

N-{4-[1-(2- 乙基丁酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 1-(6- 氟哒嗪 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 乙基丁酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.03(s,1H),7.57-7.51(m,2H),7.41(dd, J = 9.4, 1.9Hz,1H),7.21-7.08(m,3H),4.68-4.59(m,1H),4.31-4.06(m,1H),3.77-3.66(m, 1H),3.15-3.04(m,1H),2.66(ddt, J = 25.3,20.0,12.2Hz,1H),1.87-1.74(m,2H), 1.64-1.27(m,6H),0.87-0.76(m,6H) ;MS(ESI(+))m/e 454(M+H)$^+$.

[0582] 实施例 823

N-{4-[1-(4- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 氟哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 1-(6- 氟哒嗪 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 4- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.04(s,1H),7.59-7.46(m,4H),7.41(dd, J = 9.4, 1.9Hz,1H),7.32-7.17(m,4H),7.13(dd, J = 9.4,6.7Hz,1H),4.70-4.48(m,1H),4.24(t,

J = 8.3Hz,2H),4.14(dd,J = 8.0,5.9Hz,2H),4.06-3.53(m,2H),3.22-2.68(m,3H),2.04-1.50(m,4H);MS(ESI(+))m/e478(M+H)$^+$.

[0583] 实施例 824

(3S)-N-(4-{[(3S)-1- 苯甲酰基吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

实施例 824A

(S)- 叔丁基 3-(4-((S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺基) 苯氧基) 吡咯烷 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用 (R)- 叔丁基 3-(4- 氨基苯氧基) 吡咯烷 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 (S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0584] 实施例 824B

(S)-1-(哒嗪 -3- 基)-N-(4-((S)- 吡咯烷 -3- 基氧基) 苯基) 吡咯烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用 (S)- 叔丁基 3-(4-((S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺基) 苯氧基) 吡咯烷 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0585] 实施例 774C

(3S)-N-(4-{[(3S)-1- 苯甲酰基吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (S)-1-(哒嗪 -3- 基)-N-(4-((S)- 吡咯烷 -3- 基氧基) 苯基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz,DMSO-d_6) δ ppm10.04-9.95(m,1H),8.51-8.45(m,1H),7.61-7.37(m,7H),7.37-7.30(m,1H),6.99-6.92(m,1H),6.90-6.83(m,2H),5.07-4.92(m,1H),3.88-3.70(m,2H),3.71-3.38(m,6H),2.37-1.97(m,4H);MS(ESI(+))m/e 458(M+H)$^-$.

[0586] 实施例 825

(3S)-N-(4-{[(3S)-1-(2- 氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (S)-1-(哒嗪 -3- 基)-N-(4-((S)- 吡咯烷 -3- 基氧基) 苯基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MH,DMSO-d_6) δ ppm10.04-9.96(m,1H),8.48(d,J = 4.5Hz,1H),7.59-7.37(m,4H),7.37-7.22(m,3H),6.94(d,J = 8.7Hz,1H),6.87(dd,J = 8.9,4.4Hz,2H),3.86-3.52(m,5H),3.54-3.37(m,2H),2.37-1.97(m,4H);MS(ESI(+))m/e 476(M+H)$^+$.

[0587] 实施例 826

(3S)-N-(4-{[(3S)-1-(3,5- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基 } 苯基)-1-(哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺如实施例 1A 中所述制备标题化合物,用 (S)-1-(哒嗪 -3- 基)-N-(4-((S)- 吡咯烷 -3- 基氧基) 苯基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2,4- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲

酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.07-9.93(m,1H),8.47(t, J = 4.6Hz,1H),7.54(dt, J = 12.8,10.3Hz,2H),7.44-7.18(m,4H),7.02-6.80(m,3H),5.16-4.85(m,1H),3.91-3.70(m,2H),3.70-3.35(m,7H),2.43-1.97(m,4H) ;MS(ESI(+))m/e 494(M+H)$^+$.

[0588] 实施例 827

(3S)-N-(4-{[(3S)-1-(2,2- 二甲基丙酰基）吡咯烷 -3- 基］氧基} 苯基)-1-(哒嗪 -3- 基）吡咯烷 -3- 甲酰胺如实施例 1A 中所述制备标题化合物，用 (S)-1-(哒嗪 -3- 基)-N-(4-((S)- 吡咯烷 -3- 基氧基）苯基）吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯和用 2,2- 二甲基丙酸代替 1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 9.99(s,1H),8.48(dd, J = 4.5,1.3Hz,1H),7.57-7.50(m,2H),7.33(dd, J = 9.1,4.5Hz,1H),6.95-6.83(m,4H),4.95(bs,1H),3.86-3.39(m,8H),2.39-1.92(m,4H),1.15(s,9H) ;MS(ESI(+))m/e 438.(M+H)$^+$.

[0589] 实施例 828

N-{2- 氟 -4-[1-(2- 氟苯甲酰基）哌啶 -4- 基］苯基}-1-(哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺

实施例 828A

叔丁基 4-(4- 氨基 -3- 氟苯基)-5,6- 二氢吡啶 -1(2H)- 甲酸酯

如实施例 148A 中所述制备标题化合物，用叔丁基 4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-5,6- 二氢吡啶 -1(2H)- 甲酸酯代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑和用 4- 溴 -2- 氟苯胺代替 4- 溴苯胺。

[0590] 实施例 828B

叔丁基 4-(4- 氨基 -3- 氟苯基）哌啶 -1- 甲酸酯

如实施例 1B 中所述制备标题化合物，用叔丁基 4-(4- 氨基 -3- 氟苯基)-5,6- 二氢吡啶 -1(2H)- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯。

[0591] 实施例 828C

叔丁基 4-(4-(1-((苄基氧基）羰基）氮杂环丁烷 -3- 甲酰胺基)-3- 氟苯基）哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物，用叔丁基 4-(4- 氨基 -3- 氟苯基）哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基）哌啶 -1- 甲酸酯和用 1-((苄基氧基）羰基）氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酸。

[0592] 实施例 828D

叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基)-3- 氟苯基）哌啶 -1- 甲酸酯

如实施例 1B 中所述制备标题化合物，用叔丁基 4-(4-(1-((苄基氧基）羰基）氮杂环丁烷 -3- 甲酰胺基)-3- 氟苯基）哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基）氮杂环丁烷 -3- 甲酰胺基）苯氧基）哌啶 -1- 甲酸酯。

[0593] 实施例 828E

叔丁基 4-(4-(1-(6- 氯哒嗪 -3- 基）氮杂环丁烷 -3- 甲酰胺基)-3- 氟苯基）哌

啶 -1- 甲酸酯

如实施例 147A 中所述制备标题化合物，用叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基)-3- 氟苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0594] 实施例 828F

叔丁基 4-(3- 氟 -4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 147B 中所述制备标题化合物，用叔丁基 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基)-3- 氟苯基) 哌啶 -1- 甲酸酯代替 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0595] 实施例 828G

N-(2- 氟 -4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物，用叔丁基 4-(3- 氟 -4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0596] 实施例 828H

N-{2- 氟 -4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(2- 氟 -4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 9.86(s,1H),8.56(dd, J = 4.5,1.3Hz,1H),7.79(t, J = 8.3Hz,1H),7.58-7.41(m,2H),7.42-7.25(m,3H),7.23-7.14(m,1H),7.11-7.03(m, 1H),6.83(dd, J = 9.0,1.4Hz,1H),4.70-4.61(m,1H),4.24(t, J = 8.3Hz,2H),4.14(dd, J = 8.1,5.8Hz,2H),3.92-3.81(m,1H),3.51-3.42(m,1H),3.23-3.10(m,1H),2.92-2.76(m, 2H),1.94-1.81(m,1H),1.83-1.44(m,3H) ;MS(ESI(+))m/e 478(M+H)$^+$.

[0597] 表 20.

以下实施例基本上如实施例 828 中所述制备，代替实施例 828H 中的合适的羧酸。

实施例		名称	MS
829		N-[4-(1-苯甲酰基哌啶-4-基)-2-氟苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 460 $(M+H)^+$
830		N-{2-氟-4-[1-(3-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 $(M+H)^+$
831		N-{2-氟-4-[1-(2-甲基苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 474 $(M+H)^+$
832		N-{2-氟-4-[1-(4-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 $(M+H)^+$
833		N-{4-[1-(2,4-二氟苯甲酰基)哌啶-4-基]-2-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 496 $(M+H)^+$
834		N-{4-[1-(3,5-二氟苯甲酰基)哌啶-4-基]-2-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 460 $(M+H)^+$
835		N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]-2-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 454 $(M+H)^+$
858		N-{2-氟-4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 426 $(M+H)^+$
859		N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]-2-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 440 $(M+H)^+$
860		N-{4-[1-(环丙基羰基)哌啶-4-基]-2-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 424 $(M+H)^+$
861		N-(2-氟-4-{1-[(1-甲基环丙基)羰基]哌啶-4-基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$
862		N-{4-[1-(环丙基乙酰基)哌啶-4-基]-2-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$

[0598] 实施例 836

(3S)-N-(4-{[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺实施例 836A

(S)- 叔丁基 4-(4-(1-((苄基氧基) 羰基) 吡咯烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物，用 (S)-1- 苄基 3- 叔丁基吡咯烷 -1,3- 二甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0599] 实施例 836B

(S)- 叔丁基 4-(4-(吡咯烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯

如实施例 1B 中所述制备标题化合物，用 (S)- 叔丁基 4-(4-(1-((苄基氧基) 羰基) 吡咯烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂

环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0600] 实施例 836C

(S)- 叔丁基 4-(4-(1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯

如实施例 1C 中所述制备标题化合物,用 3- 溴 -6- 甲基哒嗪代替 3- 溴吡啶和用 (S)- 叔丁基 4-(4-(吡咯烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0601] 实施例 836D

(S)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基氧基) 苯基) 吡咯烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用 (S)- 叔丁基 4-(4-(1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0602] 实施例 836E

(3S)-N-(4-{[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (S)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基氧基) 苯基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 9.98(s,1H),7.57-7.45(m,3H),7.42(td, J = 7.2, 1.8Hz,1H),7.35-7.20(m,3H),6.98-6.91(m,2H),6.83(d, J = 9.1Hz,1H),4.63-4.54(m, 1H),4.05-3.95(m,1H),3.74(dd, J = 10.3,7.9Hz,1H),3.64-3.42(m,3H),3.31-3.03(m, 3H),2.40(s,3H),2.36-2.08(m,2H),2.07-1.76(m,2H),1.78-1.19(m,4H) ;MS(ESI(+))m/e 504(M+H)$^+$.

[0603] 实施例 837

(3S)-N-{4-[(1- 苯甲酰基哌啶 -4- 基) 氧基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (S)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基氧基) 苯基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 9.98(s,1H),7.55-7.48(m,2H),7.48-7.37(m,5H), 7.23(d, J = 9.1Hz,1H),6.97-6.91(m,2H),6.83(d, J = 9.1Hz,1H),4.57(dq, J = 7.7, 3.8Hz,1H),4.04-3.42(m,8H),3.26(p, J = 7.4Hz,1H),2.41(s,3H),2.35-2.08(m,2H), 2.09-1.84(m,2H),1.68-1.51(m,2H) ;MS(ESI(+))m/e 486(M+H)$^+$.

[0604] 实施例 838

(3S)-N-(4-{[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基] 氧基 } 苯基)-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺如实施例 1A 中所述制备标题化合物,用 (S)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基氧基) 苯基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2,2- 二甲基丙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz,DMSO-d_6) δ ppm9.98(s,1H),7.55-7.48(m,2H),7.24(d,J＝9.1Hz,1H),6.96-6.90(m,2H),6.83(d,J＝9.1Hz,1H),4.59-4.50(m,1H),3.94-3.80(m,2H),3.74(dd,J＝10.3,7.9Hz,1H),3.65-3.52(m,2H),3.32-3.18(m,4H),2.40(s,3H),2.34-2.08(m,2H),1.97-1.83(m,2H),1.58-1.43(m,2H),1.20(s,9H);MS(ESI(+))m/e 466(M+H)$^+$.

[0605] 实施例 839

(3S)-N-(4-{[1-(环己基羰基)哌啶-4-基]氧基}苯基)-1-(6-甲基哒嗪-3-基)吡咯烷-3-甲酰胺

如实施例 1A 中所述制备标题化合物,用 (S)-1-(6-甲基哒嗪-3-基)-N-(4-(哌啶-4-基氧基)苯基)吡咯烷-3-甲酰胺代替叔丁基 4-(4-氨基苯氧基)哌啶-1-甲酸酯和用环己烷羧酸代替 1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

^{1}H NMR(400MHz,DMSO-d_6) δ ppm 9.98(s,1H),7.55-7.48(m,2H),7.24(d,J＝9.1Hz,1H),6.97-6.90(m,2H),6.83(d,J＝9.2Hz,1H),4.52(dq,J＝7.8,3.9Hz,1H),3.89-3.66(m,3H),3.68-3.49(m,2H),3.45-3.13(m,3H),2.61-2.55(m,1H),2.40(s,3H),2.36-2.11(m,2H),2.04-1.80(m,2H),1.74-1.08(m,13H);MS(ESI(+))m/e 492(M+H)$^+$.

[0606] 实施例 840

N-{4-[8-(2-甲基丙酰基)-8-氮杂双环[3.2.1]辛-3-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺实施例 840A

叔丁基 3-(4-硝基苯基)-8-氮杂双环[3.2.1]辛-2-烯-8-甲酸酯

如实施例 148A 中所述制备标题化合物,用 2,2-二甲基-1-(3-(4,4,5,5-四甲基-1,3,2-二氧杂环戊硼烷-2-基)-8-氮杂双环[3.2.1]辛-3-烯-8-基)丙-1-酮代替 1-异丁基-4-(4,4,5,5-四甲基-1,3,2-二氧杂环戊硼烷-2-基)-1H-吡唑和用 1-溴-4-硝基苯代替 4-溴苯胺。

[0607] 实施例 840B

叔丁基 3-(4-氨基苯基)-8-氮杂双环[3.2.1]辛烷-8-甲酸酯

如实施例 1B 中所述制备标题化合物,用叔丁基 3-(4-硝基苯基)-8-氮杂双环[3.2.1]辛-2-烯-8-甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基)氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯。

[0608] 实施例 840C

叔丁基 3-(4-(1-((苄基氧基)羰基)氮杂环丁烷-3-甲酰胺基)苯基)-8-氮杂双环[3.2.1]辛烷-8-甲酸酯

如实施例 1A 中所述制备标题化合物,用叔丁基 3-(4-氨基苯基)-8-氮杂双环[3.2.1]辛烷-8-甲酸酯代替叔丁基 4-(4-氨基苯氧基)哌啶-1-甲酸酯和用 1-((苄基氧基)羰基)氮杂环丁烷-3-甲酸代替 1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

[0609] 实施例 840D

叔丁基 3-(4-(氮杂环丁烷-3-甲酰胺基)苯基)-8-氮杂双环[3.2.1]辛烷-8-甲酸酯

如实施例 1B 中所述制备标题化合物,用叔丁基 3-(4-(1-((苄基氧基)羰基)氮杂环丁烷-3-甲酰胺基)苯基)-8-氮杂双环[3.2.1]辛烷-8-甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基)氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯。

[0610] 实施例 840F

叔丁基 3-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-8- 氮杂双环 [3.2.1] 辛烷 -8- 甲酸酯如实施例 147A 中所述制备标题化合物，用叔丁基 3-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基)-8- 氮杂双环 [3.2.1] 辛烷 -8- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0611] 实施例 840G

叔丁基 3-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-8- 氮杂双环 [3.2.1] 辛烷 -8- 甲酸酯

如实施例 147B 中所述制备标题化合物，用叔丁基 3-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-8- 氮杂双环 [3.2.1] 辛烷 -8- 甲酸酯代替 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0612] 实施例 840H

N-(4-(8- 氮杂双环 [3.2.1] 辛烷 -3- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物，用叔丁基 3-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-8- 氮杂双环 [3.2.1] 辛烷 -8- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0613] 实施例 840I

N-{4-[8-(2- 甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺如实施例 1A 中所述制备标题化合物，用 N-(4-(8- 氮杂双环 [3.2.1] 辛烷 -3- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用异丁酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.03(s,1H),8.56(dd,J = 4.5,1.3Hz,1H),7.52(dd,J = 7.4,3.4H2,2H),7.37(dd,J = 9.0,4.5Hz,1H),7.18(dd,J = 17.7,8.6Hz,2H),6.82(dd, J = 9.0,1.3Hz,1H),4.51(ddd, J = 15.0,5.1,4.4Hz,1H),4.43-4.29(m,1H),4.18(dt, J = 14.0,8.1Hz,4H),3.72(ddd, J = 8.4,5.9,2.5Hz,1H),2.77(dt.J = 13.4,6.7Hz,1H), 2.48-2.14(m,3H),2.04-1.37(m,7H),1.15-0.94(m,6H) ;MS(ESI(+))m/e 434(M+H)$^+$.

[0614] 实施例 841

1-(哒嗪 -3- 基)-N-{4-[8-(4,4,4- 三氟丁酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(4-(8- 氮杂双环 [3.2.1] 辛烷 -3- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 4,4,4- 三氟丁酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.03(d, J = 3.6Hz,1H),8.56(dd, J = 4.5,1.1Hz, 1H),7.53(dd, J = 8.6,2.7Hz,2H),7.37(dt, J = 14.0,7.0Hz,1H),7.21(dd, J = 23.0, 8.6Hz,2H),6.80(dd, J = 19.3,8.9Hz,1H),4.61-4.47(m,1H),4.32(dd, J = 16.5,8.6Hz, 1H),4.23{t,J = 8.3Hz,2H),4.14(t,J = 7.0Hz,2H),3.82-3.62(m,1H),3.22-3.04(m,1H), 3.04-2.90(m,1H),2.78-2.50(m,6H),2.41-2.12(m,1H),2.05-1.38(m,8H) ;MS(ESI(+))m/e 488(M+H)$^+$.

[0615] 实施例 842

N-[4-(8- 苯甲酰基 -8- 氮杂双环 [3.2.1] 辛 -3- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(8- 氮杂双环 [3.2.1] 辛烷 -3- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.04(d, J = 2.4Hz,1H),8.56(dt, J = 9.1,4.5Hz, 1H),7.63-7.42(m,7H),7.37(dt, J = 14.0,7.0Hz,1H),7.29(d, J = 8.5Hz,1H),7.23(d, J = 8.5Hz,1H),6.91-6.70(m,1H),4.69(d, J = 6.1Hz,1H),4.24(t, J = 8.3Hz,2H), 4.19-4.11(m,2H),4.01(d, J = 14.9Hz,1H),3.85-3.61(m,1H),2.47-2.22(m,1H), 2.02-1.53(m,7H),MS(ESI(+))m/e 468(M+H)$^+$.

[0616] 实施例 843

N-{4-[8-(2- 氟苯甲酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(8- 氮杂双环 [3.2.1] 辛烷 -3- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.04(s,1H),8.56(dd, J = 4.5,1.3Hz,1H), 7.59-7.44(m,4H),7.46-7.16(m,5H),6.82(dd, J = 9.0,1.4Hz,1H),4.73-4.65(m,1H), 4.24(t, J = 8.3Hz,2H),4.14(dd, J = 8.0,5.9Hz,2H),3.81-3.67(m,2H),2.10(s,1H), 2.05-1.35(m,8H) ;MS(ESI(+))m/e 486(M+H)$^+$.

[0617] 实施例 844

N-{4-[8-(2,2- 二甲基丙酰基)-8- 氮杂双环 [3.2.1] 辛 -3- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(8- 氮杂双环 [3.2.1] 辛烷 -3- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2,2- 二甲基丙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.02(s,1H),8.56(dd, J = 4.5,1.3Hz,1H), 7.56-7.49(m,2H),7.38(dd, J = 9.0,4.5Hz,1H),7.24-7.14(m,2H),6.82(dd, J = 9.0, 1.4Hz,1H),4.66-4.51(m,2H),4.23(t, J = 8.3Hz,2H),4.14(dd, J = 8.1,5.9Hz,2H), 3.72(tt, J = 8.5,5.9Hz,1H),2.43-2.07(m,3H),1.92-1.39(m,8H),1.23-1.17(m,9H) ; MS(ESI(+))m/e 448(M+H)$^+$.

[0618] 实施例 845

N-(4-{8-[(1- 甲基环丙基) 羰基]-8- 氮杂双环 [3.2.1] 辛 -3- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(8- 氮杂双环 [3.2.1] 辛烷 -3- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1- 甲基环丙基乙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm10.03(s,1H),8.56(dd, J = 4.5,1.3Hz,1H),

7.56-7.49(m,2H),7.38(dd,J = 8.9,4.5Hz,1H),7.26-7.15(m,2H),6.82(dd,J = 8.9,1.4Hz,1H),4.62-4.38(m,2H),4.23(t,J = 8.3Hz,2H),4.14(dd,d = 8.1,5.9Hz,2H),3.72(ttJ = 8.5,5.9Hz,1H),2.37-2.21(m,1H),1.93-1.45(m,8H),1.28(d,J = 5.7Hz,3H),1.02-0.72(m,2H),0.51(dd,J = 6.2,2.1Hz,2H) ;MS(ESI(+))m/e 446(M+H)$^+$.

[0619] 实施例 846

N-{4-[1-(2- 甲氧基乙基)-3-(2- 甲基丙基)-1H- 吡唑 -5- 基] 苯基}-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 805 中所述制备标题化合物,用 4- 甲基戊 -1- 炔代替实施例 805A 中的乙炔基环丙烷和用 (2- 甲氧基乙基) 肼代替 805B 中的甲基肼。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 10.21(s,1H),8.56(dd,J = 4.4,1.2Hz,1H),7.78-7.58(m,4H),7.24(d,J = 8.5Hz,1H),6.42(s,1H),4.45-4.25(m,3H),4.18(t,J = 5.5Hz,2H),3.87-3.73(m,1H),3.69(t,J = 5.5Hz,2H),3.46-3.30(m,4H),3.22(s,3H),2.01-1.84(m,1H),0.95(d,J = 6.6Hz,6H) ;MS(ESI(+))m/e 435(M+H)$^+$.

[0620] 实施例 853

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基} 氨基) 苯基]-4- 氟哌啶 -1- 甲酸酯

如实施例 809C 中所述制备标题化合物,用苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基} 氨基) 苯基]-4- 羟基哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-((苄基氧基) 羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-4- 羟基哌啶 -1- 甲酸酯。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 10.18-10.11(m,1H),7.67-7.57(m,2H),7.53(d,J = 9.3Hz,1H),7.47-7.23(m,7H),6.96(d,J = 9.3Hz,1H),5.14-5.08(m,2H),4.26(t,J = 8.4Hz,2H),4.17(dd,J = 8.3,5.8Hz,2H),4.09-3.98(m,2H),3.80-3.60(m,2H),3.30-3.20(m,2H),2.2-1.8(m,3H) ;MS(ESI(+))m/e 524(M+H)$^+$.

[0621] 实施例 854

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基} 氨基) 苯基]-4- 羟基哌啶 -1- 甲酸酯实施例 854A

苄基 4-(4- 氨基苯基)-4- 羟基哌啶 -1- 甲酸酯

如实施例 809A 中所述制备标题化合物,用苄基 4- 氧代哌啶 -1- 甲酸酯代替叔丁基 4- 氧代哌啶 -1- 甲酸酯。

[0622] 实施例 854B

苄基 4-[4-({[1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基} 氨基) 苯基]-4- 羟基哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用苄基 4-(4- 氨基苯基)-4- 羟基哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 10.06(s,1H),7.59-7.49(m,3H),7.41-7.28(m,7H),6.96(d,J = 9.3Hz,1H),5.09(s,2H),5.04(s,1H),4.26(t,J = 8.4Hz,2H),4.16(dd,J = 8.3,5.8Hz,2H),3.97-3.86(m,2H),3.73(tt,J = 8.5,5.8Hz,1H),3.3-3.0(m,2H),1.91-1.70(m,2H),1.63-1.54(m,2H) ;MS(ESI(+))m/e 522.0(M+H)$^+$.

[0623] 实施例 857

N-{4-[4- 氟 -1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 857A

N-(4-(4- 氟哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用叔丁基 4- 氟 -4-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基] 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0624] 实施例 857B

N-{4-[4- 氟 -1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(4- 氟哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(300MHz, DMSO-d_6) δ ppm 10.06(s,1H),7.59-7.49(m,3H),7.41-7.28(m,7H),6.96(d, J = 9.3Hz,1H),5.09(s,2H),5.04(s,1H),4.26(t, J = 8.4Hz,2H),4.16(dd, J = 8.3,5.8Hz,2H),3.97-3.86(m,2H),3.73(tt, J = 8.5,5.8Hz,1H),3.3-3.0(m,2H),1.91-1.70(m,2H),1.63-1.54(m,2H) ;MS(ESI(+))m/e 478(M+H)$^+$.

[0625] 实施例 863

N-[4-(1- 苯甲酰基 -4- 氟哌啶 -4- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(4- 氟哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.20-10.03(m,1H),8.57(d, J = 4.5Hz,1H),7.68-7.59(m,2H),7.60-7.30(m,8H),6.87-6.80(m,1H),4.78-4.09(m,5H),4.10-3.44(m,3H),3.14-3.01(m,1H),2.25-1.51(m,4H) ;MS(ESI(+))m/e 460(M+H)$^+$.

[0626] 实施例 864

N-{4-[1-(2,2- 二甲基丙酰基)-4- 氟哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(4-(4- 氟哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2,2- 二甲基丙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.20-10.02(m,1H),8.56(dd, J = 4.5,1.3Hz,1H),7.67-7.58(m,2H),7.47-7.30(m,3H),6.83(dd, J = 8.9,1.4Hz,1H),4.48-4.10(m,6H),3.80-3.69(m,1H),3.23-2.96(m,2H),2.07-1.60(m,4H),1.23(s,9H) ;MS(ESI(+))m/e 440(M+H)$^+$.

[0627] 实施例 865

N-{4-[3- 叔丁基 -1-(2- 甲氧基乙基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮

杂环丁烷 -3- 甲酰胺

如实施例 805 中所述制备标题化合物，用 3,3- 二甲基丁 -1- 炔代替实施例 805A 中的乙炔基环丙烷和用 (2- 甲氧基乙基) 肼代替实施例 805B 中的甲基肼。

^{1}H NMR(400MHz,DMSO-d_6) δ ppm 10.14(s,1H),8.57(dd,J = 4.5,1.3Hz,1H),7.70(d,J = 8.7Hz,2H),7.64(d,J = 8.7Hz,2H),7.39(dd,J = 8.9,4.5Hz,1H),6.84(d,J = 8.9Hz,1H),6.40(s,1H),4.31(t,J = 6.0Hz,2H),4.25(t,J = 8.3Hz,2H),4.17(dd,J = 8.0,6.0Hz,2H),3.83(t,J = 6.0Hz,2H),3.75(tt,J = 8.7,6.1Hz,1H),3.25(s,3H),1.37(s,9H) ;MS(ESI(+))m/e 435(M+H)$^+$.

[0628] 实施例 866

N-[4-(1- 丁基 -3- 叔丁基 -1H- 吡唑 -5- 基) 苯基]-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 805 中所述制备标题化合物，用 3,3- 二甲基丁 -1- 炔代替实施例 805A 中的乙炔基环丙烷和用丁基肼代替 805B 中的甲基肼。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.14(s,1H),8.57(dd, J = 4.5,1.3Hz,1H),7.69(d,J = 8.7Hz,2H),7.63(d,J = 8.8Hz,2H),7.39(dd,J = 8.9,4.5Hz,1H),6.84(dd,J = 8.9,1.3Hz,1H),6.38(s,1H),4.25(t, J = 8.3Hz,2H),4.21-4.09(m,4H),3.81-3.70(m,1H),1.92-1.77(m,2H),1.46-1.37(m,2H),1.36(s,9H),0.94(t,J = 7.3Hz,3H) ;MS(ESI(+))m/e 433(M+H)$^+$.

[0629] 实施例 867

N-{4-[3- 叔丁基 -1-(四氢 -2H- 吡喃 -4- 基甲基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 805 中所述制备标题化合物，用 3,3- 二甲基丁 -1- 炔代替实施例 805A 中的乙炔基环丙烷和用 (四氢 -2H- 吡喃 -4- 基甲基) 肼代替实施例 805B 中的甲基肼。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.14(s,1H),8.57(dd, J = 4.5,1.3Hz,1H),7.70(d,J = 8.7Hz,2H),7.63(d, J = 8.8Hz,2H),7.39(dd, J = 8.9,4.5Hz,1H),6.83(dd, J = 8.9,1.4Hz,1H),6.41(s,1H),4.25(t, J = 8.3Hz,2H),4.16(dd, J = 8.1,5.9Hz,2H),4.03(d, J = 7.0Hz,2H),3.85(dd, J = 11.3,3.0Hz,2H),3.80-3.71(m,1H),3.32-3.22(m,2H),2.39-2.25(m,1H),1.55(dd, J = 12.8,1.9Hz,2H),1.37(s,9H),1.42-1.30(m,2H) ;MS(ESI(+))m/e 475(M+H)$^+$.

[0630] 实施例 868

N-{2- 氟 -4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 868A

叔丁基 4-(4-(1-(5,6- 二氯哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺基)-3- 氟苯基) 哌啶 -1- 甲酸酯

如实施例 618 中所述制备标题化合物，用叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基)-3- 氟苯基) 哌啶 -1- 甲酸酯代替 (R)-5-(1- 异丁基 -1H- 吡唑 -4- 基)-N-(吡咯烷 -3- 基) 噻吩 -2- 甲酰胺。

[0631] 实施例 868B

叔丁基 4-(3- 氟 -4-(1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 147B 中所述制备标题化合物，用叔丁基 4-(4-(1-(5,6- 二氯哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺基)-3- 氟苯基) 哌啶 -1- 甲酸酯代替 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯。

[0632] 实施例 868C

N-(2- 氟 -4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物，用叔丁基 4-(3- 氟 -4-(1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0633] 实施例 868D

N-{2- 氟 -4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(2- 氟 -4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.39(s,1H),8.66(d, J = 6.3Hz,1H),8.52(d, J = 3.0Hz,1H),7.66-7.37(m,4H),7.35-7.27(m,3H),6.68(dd, J = 6.3,3.2Hz,1H),4.71-4.62(m,1H),4.37-3.92(m,4H),3.94-2.70(m,5H),1.88-12(m,4H) ;MS(ESI(+))m/e 478(M+H)$^+$.

[0634] 实施例 869

N-[4-(1- 苯甲酰基哌啶 -4- 基)-2- 氟苯基]-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(2- 氟 -4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz,DMSO-d_6) δ ppm 10.27(s,1H),8.61(dd,J = 6.0,0.9Hz,1H),8.51(dd,J = 3.0,0.9Hz,1H),7.57(dd,J = 12.9,2.0Hz,1H),7.51-7.38(m,5H),7.34(t,J = 8.4Hz,1H),7.28(dd, J = 8.4,2.0Hz,1H),6.55(dd, J = 6.0,3.0Hz,1H),4.71-4.51(m,1H),4.22(t, J = 8.4Hz,2H),4.12(dd, J = 8.2,5.7Hz,2H),4.04-3.45(m,2H),3.22-2.76(m,3H),2.08-1.33(m,4H) ;MS(ESI(+))m/e 460(M+H)$^+$.

[0635] 实施例 870

N-{4-[1-(2,2- 二甲基丙酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(2- 氟 -4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2,2- 二甲基丙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(500MHz,DMSO-d_6) δ ppm 10.28(s,1H),8.61(dd,J = 6.0,0.9Hz,1H),8.51(d,J = 3.4Hz,1H),7.68-7.24(m,3H),6.57(dd, J = 6.1,3.0Hz,1H),4.5(d,2H),4.30-4.13(m,

4H),3.90-2.78(m,4H),1.79-1.71(m,2H),1.72-1.44(m,2H),1.21(s,9H) ;MS(ESI(+))m/e 440(M+H)$^+$.

[0636] 实施例 871

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-2- 氟苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(2- 氟 -4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 3,3,- 二甲基丁酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(500MHz.DMSO-d_6) δ ppm 10.28(s,1H),8.62(d, J = 6.1Hz,1H),8.51(d, J = 3.4Hz,1H),7.60-7.23(m,3H),6.57(dd, J = 6.1,3.0Hz,1H),4.65-4.58(m,1H),4.30-4.00(m,5H),3.85-2.83(m,3H),2.60-2.50(m,1H),2.30(d, J = 14.0Hz,1H),2.21(d, J = 14.0Hz,1H),1.79-1.40(m,4H),1.00(s,9H) ;MS(ESI(+))m/e 454(M+H)$^+$.

[0637] 实施例 872

N-{2- 氟 -4-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(2- 氟 -4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 4,4,4- 三氟丁酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(500MHz, DMSO-d_6) δ ppm 10.3(s,1H),8.70-8.50(m,2H),7.90-7.20(m,3H),6.55-6.65(m,1H),4.6(, d,1H),4.30-3.90(m,5H),3.80-2.90(m,3H),2.80-2.50(m,5H),1.80-1.40(m,4H) ;MS(ESI(+))m/e 480(M+H)$^+$.

[0638] 实施例 873

N-(4-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 148A 中所述制备标题化合物,用 N-(4- 溴苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替 4- 溴苯胺和用叔丁基 4- 甲基 -4-((4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑 -1- 基) 甲基) 哌啶 -1- 甲酸酯代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑,随后为如实施例 1D 中所述进行 TFA 脱保护以产生作为 TFA 盐的标题化合物。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.24(s,1H),8.57(d, J = 4.0Hz,1H),8.52(s,1H),8.40(s,1H),8.11(s,1H),7.87(s,1H),7.80(dd, J = 9.3,4.3Hz,1H),7.63(d, J = 8.6Hz,2H),7.55(d, J = 8.5Hz,2H),7.45(d, J = 9.3Hz,1H),4.47(t, J = 9.1Hz,2H),4.43-4.34(m,2H),4.08(s,2H),3.81(ddd, J = 14.5,8.7,6.0Hz,1H),3.27-3.13(m,2H),3.13-2.97(m,2H),1.73-1.58(m,2H),1.57-1.42(m,2H),0.98(s,3H) ;MS(ESI(+))m/e 432(M+H)$^+$.

[0639] 实施例 874

N-{4-[1- 甲基 -3-(三氟甲基)-1H- 吡唑 -5- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 805 中所述制备标题化合物,用 3,3,3- 三氟丙 -1- 炔代替实施例 805A 中的

乙炔基环丙烷。

^{1}H NMR(500MHz, DMSO-d_6) δ ppm 10.47(s,1H),8.57(d, J = 3.8Hz,1H),7.80(d, J = 8.4Hz,2H),7.57(d, J = 8.4Hz,2H),7.56-7.49(m,1H),7.06(d, J = 8.6Hz,1H),6.87(s,1H),4.34(t, J = 8.4Hz,2H),4.29-4.22(m,2H),3.92(s,3H),3.86-3.78(m,1H) ;MS(ESI(+))m/e 403(M+H)$^+$.

[0640] 实施例 875

1-(6- 氯哒嗪 -3- 基)-N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺实施例 875A

4-(1- 新戊基 -1H- 吡唑 -4- 基) 苯胺

如实施例 148A 中所述进行制备标题化合物,用 1- 新戊基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑。

[0641] 实施例 875B

1-(6- 氯哒嗪 -3- 基)-N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 } 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 4-(1- 新戊基 -1H- 吡唑 -4- 基) 苯胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.10(s,1H),8.04(s,1H),7.82(s,1H),7.61(d, J = 8.7Hz,2H),7.56-7.50(m,3H),6.98(d,J = 9.3Hz,1H),4.27(t,J = 8.5Hz,2H),4.19(dd,J = 8.3,5.9Hz,2H),3.90(s,2H),3.74(tt,J = 8.6,5.9Hz,1H),0.92(s,9H) ;MS(ESI(+))m/e 425(M+H)$^+$.

[0642] 实施例 876

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 876A

叔丁基 4-(4-(1-(6- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 1C 中所述制备标题化合物,用 5- 溴 -2- 甲基吡啶代替 3- 溴吡啶和用叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0643] 实施例 876B

1-(6- 甲基吡啶 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用叔丁基 4-(4-(1-(6- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0644] 实施例 876C

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(6- 甲基吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 1-(6- 甲基吡啶 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 9.99(s,1H),7.73(d, J = 2.8Hz,1H),7.53(d, J = 8.5Hz,2H),7.48-7.39(m,5H),7.22(d,J = 8.6Hz,2H),7.04(d,J = 8.3Hz,1H),6.80(dd,J = 8.3,2.9Hz,1H),4.62(s,1H),4.05(t,J = 7.7Hz,2H),3.90(t,J = 6.7Hz,2H),3.69(ddd, J = 14.5,8.1,6.3Hz,2H),3.13(s,1H),2.99-2.69(m,2H),2.34(s,3H),1.89-1.47(m,4H), MS(ESI(+))m/e 455(M+H)$^+$.

[0645] 实施例 877

N-(4-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 877A

叔丁基 1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酸酯

如实施例 1C 中所述制备标题化合物，用叔丁基氮杂环丁烷 -3- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0646] 实施例 877B

1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酸

如实施例 1D 中所述制备标题化合物，用叔丁基 1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0647] 实施例 877C

N-(4- 溴苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 4- 溴苯胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0648] 实施例 877D

N-(4-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺

标题化合物如实施例 148A 中所述，用 N-(4- 溴苯基)-1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替 4- 溴苯胺和用叔丁基 4- 甲基 -4-((4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑 -1- 基) 甲基) 哌啶 -1- 甲酸酯代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑，随后为如实施例 1D 中所述进行 TFA 脱保护以产生作为 TFA 盐的标题化合物。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.21(s,1H),8.58(s,1H),8.45(s,1H),8.15(d, J = 5.3Hz,1H),8.10(s,1H),8.08(d, J = 2.6Hz,1H),7.86(s,1H),7.77(dd, J = 8.6,5.4Hz, 1H),7.62(d,J = 8.7Hz,2H),7.58-7.51(m,3H),4.24(t,J = 8.3Hz,2H),4.15(dd,J = 7.9, 6.0Hz,2H),4.08(s,2H),3.79(dq, J = 8.6,5.9Hz,1H),3.28-3.12(m,2H),3.12-2.95(m, 2H),1.65(ddd, J = 13.4,9.3,3.8Hz,2H),1.56-1.40(m,2H),0.97(s,3H) ;MS(ESI(+))m/e 431(M+H)$^+$.

[0649] 实施例 878

N-{4-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

向 1-(6- 氯哒嗪 -3- 基)-N-(4-(1- 新戊基 -1H- 吡唑 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺 (0.076g,0.179mmol) 加入甲基氯化锌 (II)(2.0M 于 THF 中)(0.179ml,0.358mmol) 和 5mg 的钯催化剂。将反应混合物加热至 60C 并产生稠的沉淀物。加入 N- 甲基吡咯烷 (0.2ml) 并将混合物加热至 85℃ 2 小时。将混合物用二氯甲烷稀释并通过正相色谱纯化以产生标题化合物。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.11(s,1H),8.04(s,1H),7.82(s,1H),7.61(d, J = 8.7Hz,2H),7.53(d, J = 8.7Hz,2H),7.43(d, J = 9.2Hz,1H),6.99(d, J = 9.1Hz,1H), 4.27(t, J = 8.5Hz,2H),4.19(dd, J = 8.2,6.1Hz,2H),3.90(s,2H),3.75(ddd, J = 17.0, 8.5,6.0Hz,1H),2.45(s,3H),0.92(s.9H) ;MS(ESI(+))m/e405(M+H)$^+$.

[0650] 实施例 879

N-{3- 氟 -4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 879A

叔丁基 4-(4- 氨基 -2- 氟苯基)-5,6- 二氢吡啶 -1(2H)- 甲酸酯

标题化合物如实施例 148A 中所述进行制备,用 4- 溴 -3- 氟苯胺代替 4- 溴苯胺和用叔丁基 4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-5,6- 二氢吡啶 -1(2H)- 甲酸酯代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑。

[0651] 实施例 879B

叔丁基 4-(4- 氨基 -2- 氟苯基) 哌啶 -1- 甲酸酯

如实施例 1B 中所述制备标题化合物,用叔丁基 4-(4- 氨基 -2- 氟苯基)-5,6- 二氢吡啶 -1(2H)- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0652] 实施例 879C

叔丁基 4-(2- 氟 -4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用叔丁基 4-(4- 氨基 -2- 氟苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0653] 实施例 879D

N-(3- 氟 -4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用叔丁基 4-(2- 氟 -4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0654] 实施例 879E

N-{3- 氟 -4-[1-(3- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(3- 氟 -4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 3- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz,DMSO-d_6) δ ppm 9.86(s,1H),8.56(dd,J = 4.5,1.1Hz,1H),7.79(t,J = 8.3Hz,1H),7.56-7.45(m,1H),7.38(dd,J = 9.0,4.5Hz,1H),7.25(ddd,J = 20.2,14.3,8.7Hz,4H),7.10(d,J = 8.2Hz,1H),6.83(dd,J = 8.9,1.0Hz,1H),4.60(s,1H),4.19(dt,J = 14.0,8.2Hz,4H),3.99-3.74(m,1H),3.59(s,1H),3.07(d,J = 59.7Hz,1H),2.85(dd,J = 39.3,27.7Hz,2H),2.08-1.43(m,4H) ;MS(ESI(+))m/e 478.3(M+H)$^+$.

[0655] 表 21.

以下实施例基本上如实施例 879 中所述制备，代替实施例 879E 中的合适的羧酸。

实施例		名称	MS
880		N-{3-氟-4-[1-(2-甲基丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 426 (M+H)$^+$
881		N-{3-氟-4-[1-(3,3,3-三氟丙酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 466 (M+H)$^+$
882		N-{4-[1-(3,3-二甲基丁酰基)哌啶-4-基]-3-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 454 (M+H)$^+$
883		N-{3-氟-4-[1-(4,4,4-三氟丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 480 (M+H)$^+$
884		N-[4-(1-苯甲酰基哌啶-4-基)-3-氟苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 460 (M+H)$^+$
885		N-{3-氟-4-[1-(2-氟苯甲酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 478 (M+H)$^+$
886		N-{4-[1-(2,2-二甲基丙酰基)哌啶-4-基]-3-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 440 (M+H)$^+$
887		N-{3-氟-4-[1-(3-甲基丁酰基)哌啶-4-基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 440 (M+H)$^+$
888		N-{4-[1-(环丙基乙酰基)哌啶-4-基]-3-氟苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 (M+H)$^+$

[0656] 实施例 889

N-{4-[1-(2- 氟苯甲酰基)-4- 羟基哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 889A

苄基 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-4- 羟基哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物，用苄基 4-(4- 氨基苯基)-4- 羟基哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0657] 实施例 889B

N-(4-(4- 羟基哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1B 中所述制备标题化合物，用苄基 4-(4-(1-(6- 氯哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-4- 羟基哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0658] 实施例 889C

N-{4-[1-(2- 氟苯甲酰基)-4- 羟基哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(4-(4- 羟基哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.08(s,1H),8.56(dd, J = 4.5,1.3Hz,1H), 7.61-7.54(m,2H),7.55-7.33(m,5H),7.35-7.22(m,2H),6.83(dd, J = 8.9,1.3Hz,1H), 5.16(s,1H),4.50-4.42(m,1H),4.24(1, J = 8.3Hz,2H),4.15(dd, J = 8.1,5.9Hz.2H), 3.79-3.68(m,1H),3.52-3.41(m,1H),3.27-3.13(m,2H),2.07-1.65(m,3H),1.66-1.40(m, 1H) ;MS(ESI(+))m/e 476.1(M+H)$^+$.

[0659] 实施例 890

N-{4-[1-(2,2- 二甲基丙酰基)-4- 羟基哌啶 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(4-(4- 羟基哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2,2- 二甲基丙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.06(s,1H),8.56(dd, J = 4.5,1.3Hz,1H), 7.59-7.53(m,2H),7.46-7.33(m,3H),6.83(dd, J = 8.9,1.3Hz,1H),5.06(s,1H), 4.30-4.08(m,6H),3.79-3.68(m,1H),3.25-3.13(m,2H),1.83-1.68(m,2H),1.66-1.58(m, 2H),1.22(s,9H) ;MS(ESI(+))m/e438.2(M+H)$^+$.

[0660] 实施例 891

1-(6- 甲基哒嗪 -3- 基)-N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺

实施例 891A

叔丁基 1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸酯

如实施例 1C 中所述制备标题化合物，用 3- 氯 -6- 甲基哒嗪代替 3- 溴吡啶和用叔丁基氮杂环丁烷 -3- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0661] 实施例 891B

1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸

如实施例 1D 中所述制备标题化合物，用叔丁基 1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0662] 实施例 891C

N-(4- 溴苯基)-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 4- 溴苯胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0663] 实施例 891D

1-(6- 甲基哒嗪 -3- 基)-N-(4-{1-[(4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基]-1H- 吡唑 -4- 基 } 苯基) 氮杂环丁烷 -3- 甲酰胺

标题化合物如实施例 148A 中所述进行制备，用 N-(4- 溴苯基)-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替 4- 溴苯胺和用 1-((4- 甲基四氢 -2H- 吡喃 -4- 基) 甲基)-4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.08(s,1H),8.06(s,1H),7.82(s,1H),7.61(d, J = 8.7Hz,2H),7.52(d, J = 8.6Hz,2H),7.29(d, J = 9.1Hz,1H),6.79(d, J = 9.0Hz,1H),4.20(t, J = 8.2Hz,2H),4.12(dd, J = 7.8,6.2Hz,2H),4.02(s,2H),3.78-3.64(m,3H),3.52(ddd, J = 11.8,9.3,2.9Hz,2H),2.44(s.3H),1.51(ddd, J = 13.3,9.1,4.1Hz,2H),1.30-1.19(m,2H),0.97(s,3H) ;MS(ESI(+))m/e 447(M+H)$^+$.

[0664] 实施例 892

(3S)-N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

实施例 892A

(S)- 叔丁基 4-(4-(1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 1C 中所述制备标题化合物，用 3- 溴 -6- 甲基哒嗪代替 3- 溴吡啶和用 (S)- 叔丁基 4-(4-(吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0665] 实施例 892B

(S)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 吡咯烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物，用 (S)- 叔丁基 4-(4-(1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0666] 实施例 892C

(3S)-N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(6- 甲基哒嗪 -3- 基) 吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 (S)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MH7, DMSO-d_6) δ ppm10.25-9.59(m,1H),7.63-7.39(m,4H),7.38-7.11(m,5H),6.84(dd,.J = 10.8,7.3Hz,1H),4.79-4.47(m,1H),3.85-3.39(m,6H),3.25-3.07(m,

1H),3.00-2.68(m,2H),2.42(s,3H),2.37-2.09(m,2H),1.97-1.37(m,4H) ;MS(ESI(+))m/e 488.3(M+H)$^+$.

[0667] (S)-叔丁基 4-(4-(吡咯烷 -3- 甲酰胺基)苯基)哌啶 -1- 甲酸酯

实施例 893

(3S)-N-[4-(1- 苯甲酰基哌啶 -4- 基)苯基]-1-(6- 甲基哒嗪 -3- 基)吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (S)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基)苯基)吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基)哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.25-9.84(m,1H),7.62-7.51(m,2H),7.50-7.36(m,5H),7.31-7.12(m,3H),6.91-6.76(m,1H),4.77-4.30(m,1H),3.98-3.37(m,7H),3.02-2.62(m,2H),2.42(s,3H),2.38-2.01(m,2H),1.97-1.43(m,4H) ;MS(ESI(+))m/e 470.2(M+H)$^+$.

[0668] 实施例 894

(3S)-N-{4-[1-(2,2- 二甲基丙酰基)哌啶 -4- 基]苯基}-1-(6- 甲基哒嗪 -3- 基)吡咯烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (S)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基)苯基)吡咯烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基)哌啶 -1- 甲酸酯和用 2,2- 二甲基丙酸代替 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.04(s,1H),7.56-7.50(m,2H),7.23(d, J = 9.1Hz,1H),7.21-7.14(m,2H),6.83(d, J = 9.1Hz,1H),4.45-4.36(m,2H),3.74(dd, J = 10.3,7.9Hz,1H),3.64-3.52(m,2H),3.50-3.39(m,1H),3.35-3.25(m,1H),2.93-2.66(m,3H),2.40(s,3H),2.37-2.11(m,2H),1.82-1.74(m,2H),1.53-1.35(m,2H),1.22(s,9H) ;MS(ESI(+))m/e 450.3(M+H)$^+$.

[0669] 实施例 895

N-{4-[(1- 苯甲酰基哌啶 -4- 基)甲基]苯基}-1-(哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺

实施例 895A

4-(吡啶 -4- 基甲基)苯胺

如实施例 1B 中所述制备标题化合物,用 4-(4- 硝基苄基)吡啶代替叔丁基 4-(4-(1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酰胺基)苯氧基)哌啶 -1- 甲酸酯。

[0670] 实施例 348B

2,2,2- 三氟 -N-(4-(吡啶 -4- 基甲基)苯基)乙酰胺

将 4-(吡啶 -4- 基甲基)苯胺 (21.6g,117mmol) 和三乙胺 (19.61ml,141mmol) 在二氯甲烷 (586ml) 中的溶液冷却至 0℃。经另外的漏斗在 20 分钟的时间段内逐滴添加三氟乙酸酐 (19.87ml,141mmol)。将混合物在 0℃下搅拌 1 小时,并随后在室温下搅拌 2 小时。将反应混合物随后真空浓缩并将产生的残余物通过常规相柱色谱纯化以产生标题化合物。

[0671] 实施例 895C

2,2,2- 三氟 -N-(4-(哌啶 -4- 基甲基)苯基)乙酰胺

将 2,2,2- 三氟 -N-(4-(吡啶 -4- 基甲基) 苯基) 乙酰胺 (28.5g,102mmol) 和乙酸 (205ml) 加入在 500mL 不锈钢耐压瓶中的氧化铂 (Ⅳ)(3.42g,15.06mmol) 中,并将混合物在 40psi 下搅拌 16 小时。将混合物经尼龙膜过滤并真空浓缩 ;并将产生的残余物溶入甲醇 (100mL) 并倒入二乙醚 (600mL) 中。将沉淀物过滤,用醚洗涤并用硫酸钠干燥以产生标题化合物。

[0672] 实施例 895D

叔丁基 4-(4- 氨基苯甲基) 哌啶 -1- 甲酸酯

将 2,2,2- 三氟 -N-(4-(哌啶 -4- 基甲基) 苯基) 乙酰胺 (26.4g,92mmol) 在二氯甲烷 (369ml) 中的溶液冷却至 0℃并缓慢加入三乙胺 (19.28ml,138mmol)。向所获的溶液中在 10 分钟内经添加漏斗加入在二氯甲烷 (75ml) 中的二叔丁基二碳酸酯 (22.14g,101mmol)。将 0℃混合物搅拌 2 小时并缓慢加温过夜。将反应混合物再次冷却至 0℃,用 1N 含水氢氧化钠 (100ml) 处理,加温至室温并搅拌 1 小时。分离双层,将有机物用水和盐水洗涤,用硫酸镁干燥,过滤并真空浓缩。将残余物通过正相色谱纯化以产生标题化合物。

[0673] 实施例 895E

叔丁基 4-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苄基) 哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用叔丁基 4-(4- 氨基苄基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0674] 实施例 895F

N-(4-(哌啶 -4- 基甲基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用叔丁基 4-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苄基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0675] 实施例 895G

如实施例 1A 中所述制备标题化合物,用 N-(4-(哌啶 -4- 基甲基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.03(s,1H),8.56(dd, J = 4.5,1.3Hz,1H),7.52(d, J = 8.5Hz,2H),7.47-7.28(m,6H),7.11(d, J = 8.5Hz,2H),6.83(dd, J = 9.0.1.3Hz,1H),4.58-4.34(m,1H),4.23(t, J = 8,3Hz,2H),4.14(dd, J = 8.1,6.0Hz,2H),3.72(tt, J = 8.6,6.0Hz,1H),3.66-3.47(m,1H),3.08-2.83(m,1H),2.83-2.59(m,1H),1.87-1.69(m,1H),1.69-1.57(m,1H),1,57-1.41(m,1H).1,31-0.90(m,2H) ;MS(ESI(+))m/e 456(M+H)$^+$.

[0676] 表 22.

以下实施例基本上如实施例 895 中所述制备,代替实施例 895G 中的合适的羧酸。一些产物通过快速色谱纯化而其他通过反向 HPLC 纯化。因此,一些实施例分离为三氟乙酸盐。

实施例	名称	MS
896	N-(4-{[1-(2-氯苯甲酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 474 $(M+H)^+$
897	N-(4-{[1-(2,2-二甲基丙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
898	N-(4-{[1-(3,3-二甲基丁酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 $(M+H)^+$
899	N-(4-{[1-(2-乙基丁酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 $(M+H)^+$
900	1-(哒嗪-3-基)-N-(4-{[1-(4,4,4-三氟丁酰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 $(M+H)^+$
901	N-(4-{[1-(2-甲基丙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
902	N-[4-[(1-乙酰基哌啶-4-基)甲基]苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 394 $(M+H)^+$
903	N-[4-({1-[(2S)-2-甲基丁酰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
904	N-[4-({1-[(1-甲基环丙基)羰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)	(ESI(+))

		氮杂环丁烷-3-甲酰胺	m/e 434 (M+H)+
927		1-(哒嗪-3-基)-N-(4-{[1-(1,3-噻唑-5-基羰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 463 (M+H)+
928		N-(4-{[1-(环戊基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 448 (M+H)+
929		N-(4-{[1-(1H-吡唑-4-基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 446 (M+H)+
930		N-(4-{[1-(2,2-二甲基丁酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
931		N-[4-({1-[(2-甲基环丙基)羰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 434 (M+H)+
932		N-[4-({1-[(甲基硫基)乙酰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 440 (M+H)+
933		N-[4-({1-[(1S,4R)-双环[2.2.1]庚-2-基乙酰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 488 (M+H)+
934		N-(4-{[1-(2-甲基戊酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
935		N-(4-{[1-(4-甲基戊酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
936		N-[4-({1-[3-(甲基硫基)丙酰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 454 (M+H)+
937		1-(哒嗪-3-基)-N-(4-{[1-(1,3-噻唑-4-基羰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 463 (M+H)+
938		N-(4-{[1-(1H-吡唑-5-基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 446 (M+H)+
939		N-[4-({1-[(6-甲基吡啶-3-基)羰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 471 (M+H)+
940		N-[4-({1-[(3-甲基噻吩-2-基)羰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 476 (M+H)+
941		N-(4-{[1-(戊-4-炔酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 432 (M+H)+
942		1-(哒嗪-3-基)-N-(4-{[1-(噻吩-3-基羰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 (M+H)+
943		N-(4-{[1-(甲氧基乙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e XXX (M+H)+
944		1-(哒嗪-3-基)-N-(4-{[1-(四氢呋喃-2-基羰基)哌啶-4-基]甲基}苯基)	(ESI(+))

		氮杂环丁烷-3-甲酰胺	m/e 424 $(M+H)^+$
945		N-[4-({1-[(2-甲氧基乙氧基)乙酰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 468 $(M+H)^+$
946		N-(4-{[1-(乙氧基乙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 438 $(M+H)^+$
947		1-(哒嗪-3-基)-N-(4-{[1-(噻吩-2-基羰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 $(M+H)^+$
948		N-{4-[(1-己酰基哌啶-4-基)甲基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 $(M+H)^+$
949		N-[4-({1-[(1-甲基-1H-吡咯-2-基)羰基]哌啶-4-基}甲基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 459 $(M+H)^+$
950		N-(4-{[1-(丁-3-烯酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 420 $(M+H)^+$
951		1-(哒嗪-3-基)-N-(4-{[1-(1,3-噻唑-2-基羰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 463 $(M+H)^+$
952		N-(4-{[1-(呋喃-2-基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 446 $(M+H)^+$
953		N-(4-{[1-(1,2-吡-5-基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 447 $(M+H)^+$
954		1-(哒嗪-3-基)-N-(4-{[1-(吡啶-2-基羰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 457 $(M+H)^+$
955		N-(4-{[1-(呋喃-3-基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 446 $(M+H)^+$
956		N-(4-{[1-(环丙基乙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 434 $(M+H)^+$
957		N-(4-{[1-(2-甲基丁酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
958		N-{4-[(1-丙酰基哌啶-4-基)甲基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 408 $(M+H)^+$
959		N-{4-[(1-丁酰基哌啶-4-基)甲基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 422 $(M+H)^+$
960		N-(4-{[1-(环丁基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 434 $(M+H)^+$
961		N-{4-[(1-戊酰基哌啶-4-基)甲基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 $(M+H)^+$
962		N-(4-{[1-(环戊基乙酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂	(ESI(+))

		环丁烷-3-甲酰胺	m/e 462 (M+H)+
963		N-(4-{[1-(2-甲基苯甲酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 470 (M+H)+
964		N-(4-{[1-(3-甲基戊酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 450 (M+H)+
965		N-(4-{[1-(环己基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 (M+H)+
966		N-(4-{[1-(3-甲基丁酰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 436 (M+H)+
967		N-(4-{[1-(环丙基羰基)哌啶-4-基]甲基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 420(M+H)+
968		1-(哒嗪-3-基)-N-(4-{[1-(3,3,3-三氟丙酰基)哌啶-4-基]甲基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 462 (M+H)+

[0677] 实施例 905

N-[4-(1-{[4- 甲基 -1-(氧杂环丁烷 -3- 基) 哌啶 -4- 基] 甲基 }-1H- 吡唑 -4- 基) 苯基]-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 905A

叔丁基 4- 甲基 -4-((4-(4-(1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-1H- 吡唑 -1- 基) 甲基) 哌啶 -1- 甲酸酯

标题化合物如实施例 148A 中所述进行制备，用 N-(4- 溴苯基)-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替 4- 溴苯胺和用叔丁基 4- 甲基 -4-((4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑 -1- 基) 甲基) 哌啶 -1- 甲酸酯代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑。

[0678] 实施例 905B

N-(4-(1-((4- 甲基哌啶 -4- 基) 甲基)-1H- 吡唑 -4- 基) 苯基)-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物，用叔丁基 4- 甲基 -4-((4-(4-(1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-1H- 吡唑 -1- 基) 甲基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0679] 实施例 905C

N-[4-(1-{[4- 甲基 -1-(氧杂环丁烷 -3- 基) 哌啶 -4- 基] 甲基 }-1H- 吡唑 -4- 基) 苯基]-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

将 N-(4-(1-((4- 甲基哌啶 -4- 基) 甲基)-1H- 吡唑 -4- 基) 苯基)-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺溶于甲醇 (3ml) 并用氧杂环丁烷 -3- 酮 (0.022ml，0.338mmol) 和氰基硼氢化钠 (0.021g，0.338mmol) 处理并搅拌过夜。将混合物浓缩，通过正相色谱纯化，用醚研磨并浓缩以产生标题化合物。

^{1}H NMR(400MHz，DMSO-d_6) δ ppm 10.09(s，1H)，8.05(s，1H)，7.82(s，1H)，7.64-7.58(m，2H)，7.56-7.49(m，2H)，7.29(d，J = 9.1Hz，1H)，6.80(d，J = 9.0Hz，1H)，4.51(t，J =

6.4Hz,2H),4.40(t,J＝5.8Hz,2H),4.20(t,J＝8.3Hz,2H),4.12(dd,J＝7.9,6.1Hz,2H),3.98(s,2H),3.73(tt,J ＝ 8.5,6.1Hz,1H),3.48-3.39(m,1H),2.44(s,3H),2.42-2.33(m,2H),2.16-1.99(m,2H),1.58-1.46(m,2H),1.30(d,J ＝ 12.6Hz,2H),0.89(s,3H);MS(ESI(+))m/e502(M+H)$^+$.

[0680] 实施例 906

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(4- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 906A

叔丁基 4-(4-(1-(4- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 1C 中所述制备标题化合物,用 3- 氯 -4- 甲基哒嗪代替 3- 溴吡啶和用叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0681] 实施例 906B

1-(4- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用叔丁基 4-(4-(1-(4- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0682] 实施例 906C

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(4- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 1-(4- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.03(s,1H),8.49(d, J ＝ 4.6Hz,1H),7.58-7.52(m,2H),7.53-7.37(m,5H),7.25-7.17(m,3H),4.81-4.37(m,1H),4.39-4.25(m,4H),4.26-3.38(m,2H),3.24-2.58(m,3H),2.19(s,3H),2.10-1.11(m,4H) ;MS(ESI(+))m/e 456.2(M+H)$^+$

[0683] 实施例 907

5-[1-(2- 氟苯甲酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 呋喃 -2- 甲酰胺

实施例 907A

5-(1-(叔丁氧基羰基)-1,2,3,6- 四氢吡啶 -4- 基) 呋喃 -2- 甲酸

标题化合物如实施例 148A 中所述进行制备,用 5- 溴呋喃 -2- 甲酸代替 4- 溴苯胺和用叔丁基 4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-5,6- 二氢吡啶 -1(2H)- 甲酸酯代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑。

[0684] 实施例 907B

5-(1-(叔丁氧基羰基) 哌啶 -4- 基) 呋喃 -2- 甲酸

如实施例 1B 中所述制备标题化合物,用 5-(1-(叔丁氧基羰基)-1,2,3,6- 四氢吡

啶 -4- 基) 呋喃 -2- 甲酸代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0685] 实施例 907C

(S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 胺

如实施例 1C 中所述制备标题化合物,用 3,6- 二氯哒嗪代替 3- 溴吡啶和用 (S)- 叔丁基吡咯烷 -3- 基氨基甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯,随后为如实施例 1D 中所述进行 TFA 脱保护。

[0686] 实施例 907D

(S)- 叔丁基 4-(5-((1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基) 氨基甲酰基) 呋喃 -2- 基) 哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用 (S)-1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 5-(1-(叔丁氧基羰基) 哌啶 -4- 基) 呋喃 -2- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0687] 实施例 907E

(S)- 叔丁基 4-(5-((1-(哒嗪 -3- 基) 吡咯烷 -3- 基) 氨基甲酰基) 呋喃 -2- 基) 哌啶 -1- 甲酸酯

如实施例 1B 中所述制备标题化合物,用 (S)- 叔丁基 4-(5-((1-(6- 氯哒嗪 -3- 基) 吡咯烷 -3- 基) 氨基甲酰基) 呋喃 -2- 基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0688] 实施例 907F

(S)-5-(哌啶 -4- 基)-N-(1-(哒嗪 -3- 基) 吡咯烷 -3- 基) 呋喃 -2- 甲酰胺

如实施例 1D 中所述制备标题化合物,用 (S)- 叔丁基 4-(5-((1-(哒嗪 -3- 基) 吡咯烷 -3- 基) 氨基甲酰基) 呋喃 -2- 基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0689] 实施例 907G

5-[1-(2- 氟苯甲酰基) 哌啶 -4- 基]-N-[(3S)-1-(哒嗪 -3- 基) 吡咯烷 -3- 基] 呋喃 -2- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (S)-5-(哌啶 -4- 基)-N-(1-(哒嗪 -3- 基) 吡咯烷 -3- 基) 呋喃 -2- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm8.48(dd, J = 4.4,0.9Hz,1H),8.40(d, J = 7.0Hz, 1H),7.55-7.46(m,1H),7.41(t, J = 6.9Hz,1H),7.37-7.24(m,3H),7.06(d, J = 3.4Hz, 1H),6.86(dd, J = 9.1,0.8Hz,1H),6.31(d, J = 3.4Hz,1H),4.67-4.47(m,2H),3.76(dd, J = 10.8,6.9Hz,1H),3.70-3.59(m,1H),3.59-3.48(m,1H),3.48-3.39(m,2H),3.19(t, J = 12.1Hz,1H),3.08-2.89(m,2H),2.33-2.19(m,1H),2.13-2.02(m,2H),1.99-1.88(m,1H), 1.67-1.41(m,2H) ;MS(ESI(+))m/e 464(M+H)$^+$.

[0690] 实施例 908

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(3- 甲基哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 908A

叔丁基 4-(4-(1-(3- 甲基哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯

如实施例 1C 中所述制备标题化合物，用 4- 氯 -3- 甲基哒嗪代替 3- 溴吡啶和用叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0691] 实施例 908B

1-(3- 甲基哒嗪 -4- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物，用叔丁基 4-(4-(1-(3- 甲基哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0692] 实施例 908C

N-[4-(1- 苯甲酰基哌啶 -4- 基) 苯基]-1-(3- 甲基哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 1-(3- 甲基哒嗪 -4- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.05(s,1H),8.55(d, J = 5.8Hz,1H),7.57-7.51(m,2H),7.49-7.33(m,5H),7.26-7.19(m,2H),6.45(d, J = 5.8Hz,1H),4.62(s,1H),4.31(t, J = 8.4Hz,2H),4.24(dd, J = 20.4,14.1Hz,3H),3.66(ddd, J = 14.6,8.5,6.1Hz,2H),2.76(t, J = 11.9Hz,2H),2.52(s,3H),2.13-1.45(m,5H) ;MS(ESI(+))m/e 456.3(M+H)$^+$.

[0693] 实施例 909

N-{4-[1-(2- 氟苯甲酰基) 哌啶 -4- 基] 苯基 }-1-(3- 甲基哒嗪 -4- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 1-(3- 甲基哒嗪 -4- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.08(s,1H),8.55(d, J = 5.8Hz,1H),7.76-7.24(m,8H),6.45(d, J = 5.8Hz,1H),4.50-4.45(m,1H),4.32(t, J = 8.3Hz,2H),4.23(d, J = 13.9Hz,2H),3.73-3.62(m,1H),3.50-3.41(m,1H),3.26-3.07(m,2H),2.94-2.56(m,3H),2.45-1.03(m,5H), ;MS(ESI(+))m/e 474.2(M+H)$^+$.

[0694] 实施例 910

N-(4-{1-[(2- 氨基吡啶 -3- 基) 羰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物，用 N-(4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2- 氨基烟酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.04(s,1H),8.56(dd, J = 4.5,1.1Hz,1H),8.00(dd, J = 4.9,1.8Hz,1H),7.54(d, J = 8.5Hz,2H),7.46-7.32(m,2H),7.21(d, J = 8.5Hz,2H),

6.83(dd, J = 9.0,1.2Hz,1H),6.59(dd, J = 7.3,4.9Hz,1H),5.92(s,2H),4.24(t, J = 8.3Hz,2H),4.14(dd,J = 8.0,6.0Hz,2H),4.09-3.84(m,2H),3.73(tt,J = 8.5,6.0Hz,1H),2.99(bs,2H),2.74(tt, J = 11.7,3.2Hz,1H),1.76(d, J = 11.8Hz,2H),1.70-1.52(m,2H) ;MS(ESI(+))m/e 458(M+H)$^+$.

[0695] 实施例 911

1- 甲基 -5-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基) 苯基]-1H- 吡唑 -3- 甲酸

将乙基 1- 甲基 -5-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-1H- 吡唑 -3- 甲酸酯 (368mg,0.905mmol) 溶于四氢呋喃 (3.38mL) 和甲醇 (3.38mL) 随后加入 1N 含水氢氧化锂 (1.35mL,1.350mmol)。将混合物在 60℃下加热 2 小时。将混合物浓缩至干燥,悬浮于水中并用 1N 含水 HCl 处理至 pH 2。将溶液用乙酸乙酯萃取,并将有机层用硫酸钠干燥,过滤并浓缩以产生静置时凝固的无色浆状物。将固体用醚研磨并通过过滤收集以产生标题化合物。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 12.67(s,1H),10.32(bs,1H),8.60-8.55(m,1H),7.77(d, J = 8.4Hz,2H),7.54(d, J = 8.4Hz,2H),7.42(dd, J = 9.0,4.5Hz,1H),6.89(d, J = 8.9Hz,1H),6.80(s,1H),4.34-4.13(m,4H),3.91(s,3H),3.83-3.74(m,1H) ;MS(ESI(+)) m/e 379(M+H)$^+$.

[0696] 实施例 912

乙基 1- 甲基 -5-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基) 氨基) 苯基]-1H- 吡唑 -3- 甲酸酯

实施例 912A

乙基 4-(4- 硝基苯基)-2,4- 二氧代丁酸酯

将 1-(4- 硝基苯基) 乙酮 (2g,12.11mmol) 溶于四氢呋喃 (20mL) 中并冷却至 0℃。逐滴加入乙醇钠 (21% 于乙醇中)(7.85g,24.22mmol) 并将所获的溶液在 0℃下搅拌 15 分钟。逐滴加入草酸二乙酯 (Diethyl oxylate)(1.947g,13.32mmol) 并移除冰浴。将混合物在室温下搅拌 3 小时并用 1N 含水 HCl(125mL) 稀释。将所获的悬浮液搅拌 30 分钟并通过过滤收集以产生标题化合物。

[0697] 实施例 912B

乙基 1- 甲基 -5-(4- 硝基苯基)-1H- 吡唑 -3- 甲酸酯

将乙基 4-(4- 硝基苯基)-2,4- 二氧代丁酸酯 (500mg,1.885mmol) 溶于六氟异丙醇 (4ml) 并逐滴加入甲基肼 (87mg,1.885mmol)。将反应化合物在室温搅拌 3 小时,浓缩至干燥,用醚研磨 ;并过滤以产生标题化合物。

[0698] 实施例 912C

乙基 5-(4- 氨基苯基)-1- 甲基 -1H- 吡唑 -3- 甲酸酯

如实施例 1B 中所述制备标题化合物,用乙基 1- 甲基 -5-(4- 硝基苯基)-1H- 吡唑 -3- 甲酸酯代替叔丁基 4-(4-(1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0699] 实施例 912D

乙基 1- 甲基 -5-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基) 氨基) 苯

基]-1H-吡唑-3-甲酸酯

如实施例1A中所述制备标题化合物，用乙基5-(4-氨基苯基)-1-甲基-1H-吡唑-3-甲酸酯代替叔丁基4-(4-氨基苯氧基)哌啶-1-甲酸酯和用1-(哒嗪-3-基)氮杂环丁烷-3-甲酸代替1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.31(s,1H),8.57(dd, J = 4.5,1.3Hz,1H),7.77(d, J = 8.7Hz,2H),7.54(d, J = 8.6Hz,2H),7.39(dd, J = 8.9,4.5Hz,1H),6.84(s,1H),6.84(dd, J = 9.0,1.4Hz,1H),4.32-4.22(m,4H),4.18(dd, J = 8.1,5.8Hz,2H),3.92(s,3H),3.84-3.72(m,1H),1.30(t, J = 7.1Hz,3H);MS(ESI(+))m/e 407(M+H)$^+$.

[0700] 实施例913

乙基1-苯基-5-[4-({1-(哒嗪-3-基)氮杂环丁烷-3-基]羰基)氨基)苯基]-1H-吡唑-3-甲酸酯标题化合物如实施例912中所述进行制备，用苯肼代替实施例912B中的甲基肼。

^{1}H NMR(500MHz, DMSO-d_6) δ ppm 10.24(s,1H),8.56(dd, J = 4.5,1.3Hz,1H),7.60(d, J = 8.7Hz,2H),7.51-7.41(m,3H),7.38(dd, J = 9.0,4.5Hz,1H),7.34-7.30(m,2H),7.20(d, J = 8.7Hz,2H),7.08(s,1H).6.82(dd, J = 9.0,1.3Hz,1H),4.33(q, J = 7.1Hz,2H),4.24(1, J = 8.4Hz,2H),4.14(dd, J = 8.0,6.0Hz,2H),3.77-3.69(m,1H),1.32(t, J = 7.1Hz,3H);MS(ESI(+))m/e 469(M+H)$^+$.

[0701] 实施例914

N-{6-[1-(2-氟苯甲酰基)哌啶-4-基]吡啶-3-基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺

实施例914A

叔丁基4-(5-(1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺基)吡啶-2-基)哌啶-1-甲酸酯

如实施例1A中所述制备标题化合物，用叔丁基4-(5-氨基吡啶-2-基)哌啶-1-甲酸酯代替叔丁基4-(4-氨基苯氧基)哌啶-1-甲酸酯和用1-(哒嗪-3-基)氮杂环丁烷-3-甲酸代替1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

[0702] 实施例914B

N-(6-(哌啶-4-基)吡啶-3-基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺

如实施例1D中所述制备标题化合物，用叔丁基4-(5-(1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺基)吡啶-2-基)哌啶-1-甲酸酯代替叔丁基4-(4-(1-(吡啶-3-基)氮杂环丁烷-3-甲酰胺基)苯氧基)哌啶-1-甲酸酯。

[0703] 实施例914C

N-{6-[1-(2-氟苯甲酰基)哌啶-4-基]吡啶-3-基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺

如实施例1A中所述制备标题化合物，用N-(6-(哌啶-4-基)吡啶-3-基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺代替叔丁基4-(4-氨基苯氧基)哌啶-1-甲酸酯和用2-氟苯甲酸代替1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.27(s,1H),8.67(d, J = 2.5Hz,1H),8.57(dd, J = 4.5,1.2Hz,1H),8.01(dd, J = 8.5,2.5Hz,1H),7.56-7.46(m,1H),7.46-7.35(m,2H),

7.35-7.23(m,3H),6.83(dd,J = 9.0,1.2Hz,1H),4.64(d,J = 13.0Hz,1H),4.26(t,J = 8.4Hz,2H),4.16(dd,J = 8.0,6.0Hz,2H),3.76(tt,J = 8.5,5.9Hz,1H),3.47(d,J = 12.6Hz,1H),3.19(t,J = 12.3Hz,1H),3.01-2.85(m,2H),1.94(d,J = 13.0Hz,1H),1.79(d,J = 12.1Hz,1H).1.73-1.53(m,2H);MS(ESI(+))m/e 461(M+H)$^+$.

[0704] 实施例 915

N-(4-{[(3R)-1-(3- 甲基丁酰基)吡咯烷 -3- 基]氧基)苯基)-1-(6- 甲基哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺

实施例 915A

(R)- 叔丁基 3-(4-(1-(6- 甲基哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺基)苯氧基)吡咯烷 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用 (R)- 叔丁基 3-(4- 氨基苯氧基)吡咯烷 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基)哌啶 -1- 甲酸酯和用 1-(6- 甲基哒嗪 -3- 基)氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

[0705] 实施例 915B

(R)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(吡咯烷 -3- 基氧基)苯基)氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用 (R)- 叔丁基 3-(4-(1-(6- 甲基哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺基)苯氧基)吡咯烷 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基)氮杂环丁烷 -3- 甲酰胺基)苯氧基)哌啶 -1- 甲酸酯。

[0706] 实施例 915C

N-(4-{[(3R)-1-(3- 甲基丁酰基)吡咯烷 -3- 基]氧基)苯基)-1-(6- 甲基哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (R)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(吡咯烷 -3- 基氧基)苯基)氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基)哌啶 -1- 甲酸酯和用 3- 甲基丁酸代替 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz,DMSO-d_6,T = 90 ℃)δ ppm 9.63(s,1H),7.49(d,J = 8.9Hz,2H),7.21(d,J = 9.0Hz,1H),6.88(d,J = 8.7Hz,2H),6.71(d,J = 9.0Hz,1H),5.03-4.85(m,1H),4.16(dt,J = 14.0,8.0Hz,4H),3.69(tt,J = 8.5,6.1Hz,1H),3.62-3.34(m,3H),2.43(s,3H),2.23-1.98(m,6H),0.91(d,J = 6.2Hz,6H);MS(ESI(+))m/e 438(M+H)$^+$.

[0707] 实施例 916

N-(4-{[(3R)-1-(2- 甲基丙酰基)吡咯烷 -3- 基]氧基)苯基)-1-(6- 甲基哒嗪 -3- 基)氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (R)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(吡咯烷 -3- 基氧基)苯基)氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基)哌啶 -1- 甲酸酯和用异丁酸代替 1-(苄基氧基羰基)氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz,DMSO-d_6,T = 90 ℃)δ ppm 9.63(s,1H),7.50(d,J = 9.0Hz,2H),7.21(d,J = 9.0Hz,1H),6.88(d,J = 8.9Hz,2H),6.71(d,J = 9.0Hz,1H),5.01-4.86(m,1H),4.23-4.10(m,4H),3.74-3.64(m,1H),3.64-3.40(m,4H),2.72-2.58(m,1H),2.43(s,3H),2.26-1.98(m,2H),1.03(dd,J = 9.7,4.0Hz,6H);MS(ESI(+))m/e 424(M+H)$^+$.

[0708] 实施例 917

N-(4-{[(3R)-1-(2,4- 二氟苯甲酰基) 吡咯烷 -3- 基] 氧基) 苯基)-1-(6- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (R)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(吡咯烷 -3- 基氧基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2,4- 二氟苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6, T = 90 ℃) δ ppm 9.63(bs,1H),7.53-7.44(m,3H),7.25-7.18(m,2H),7.14-7.03(m,1H),6.95-6.80(m,2H),6.71(d, J = 8.9Hz,1H),5.05-4.92(m,1H),4.19(t, J = 8.2Hz,2H),4.13(t, J = 7.0Hz,2H),3.68(tdd, J = 10.3,5.0,1.7Hz,1H),3.82-3.22(m,4H),2.43(s,3H),2.32-2.05(m,2H) ;MS(ESI(+))m/e 494(M+H)$^+$.

[0709] 实施例 918

1-(6- 甲基哒嗪 -3- 基)-N-(4-{[(3R)-1-(1,3- 噻唑 -4- 基羰基) 吡咯烷 -3- 基] 氧基) 苯基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 (R)-1-(6- 甲基哒嗪 -3- 基)-N-(4-(吡咯烷 -3- 基氧基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用噻唑 -4- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6, T = 90 ℃) δ ppm 9.63(s,1H),9.09(d, J = 1.6Hz,1H),8.19(d, J = 2.0Hz,1H),7.49(d, J = 8.7Hz,2H),7.21(d, J = 9.0Hz,1H),6.89(d, J = 8.6Hz,2H),6.71(d, J = 9.0Hz,1H),5.00(dt, J = 4.5,2.2Hz,1H),4.16(dt, J = 14.0,8.0Hz,4H),4.09-3.57(m,4H),3.69(tt, J = 8.4,6.1Hz,1H),2.43(s,3H),2.20(dd, J = 33.6,24.3Hz,2H) ;MS(ESI(+))m/e 465.2(M+H)$^+$.

[0710] 实施例 919

1-(哒嗪 -3- 基)-N-{6-[1-(4,4,4- 三氟丁酰基) 哌啶 -4- 基] 吡啶 -3- 基 } 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(6-(哌啶 -4- 基) 吡啶 -3- 基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 4,4,4- 三氟丁酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.27(s,1H),8.67(d, J = 2.6Hz,1H),8.57(dd, J = 4.5,1.3Hz,1H),8.00(dd, J = 8.5,2.6Hz,1H),7.40(dd, J = 9.0,4.5Hz,1H),7.26(d, J = 8.5Hz,1H),6.86(dd, J = 9.0,1.3Hz,1H),4.50(d, J = 13.0Hz,1H),4.26(t, J = 8.4Hz,2H),4.17(dd, J = 8.2,5.9Hz,2H),3.97(d, J = 13.6Hz,1H),3.76(tt, J = 8.6,5.9Hz,1H),3.11(dd, J = 18.5,7.6Hz,1H),2.90(tt, J = 11.7,3.6Hz,1H),2.76-2.59(m,2H),2.59-2.43(m,2H),1.91-1.77(m,2H),1.66(qd, J = 12.6,4.0Hz,1H),1.51(qd, J = 12.7,4.1Hz,1H) ;MS(ESI(+))m/e 463(M+H)$^+$.

[0711] 实施例 920

N-{6-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 吡啶 -3- 基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 N-(6-(哌啶 -4- 基) 吡啶 -3- 基)-1-(哒

嗪-3-基）氮杂环丁烷-3-甲酰胺代替叔丁基4-(4-氨基苯氧基）哌啶-1-甲酸酯和用3,3-二甲基丁酸代替1-(苄基氧基羰基）氮杂环丁烷-3-甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.26(s,1H),8.66(d, J = 2.5Hz,1H),8.57(dd, J = 4.5,1.1Hz,1H),8.00(dd, J = 8.5,2.6Hz,1H),7.38(dd, J = 9.0,4.5Hz,1H),7.25(d, J = 8.5Hz,1H),6.83(dd, J = 9.0,1.2Hz,1H),4.58(d, J = 12.9Hz,1H),4.26(t, J = 8.4Hz,2H),4.16(dd,J = 8.0,6.0Hz,2H),4.07(d,J = 13.4Hz,1H),3.76(tt,J = 8.5,5.9Hz,1H),3.10(t,J = 12.1Hz,1H),2.88(tt,J = 11.7,3.6Hz,1H),2.59(t,J = 11.8Hz,1H),2.29(d,J = 14.0Hz,1H),2.22(d, J = 14.0Hz,1H),1.84(t, J = 10.8Hz,2H),1.60(qd, J = 12.7,3.8Hz,1H),1.48(qd,J = 12.7,4.0Hz,1H),1.00(s,9H) ;MS(ESI(+))m/e 437(M+H)$^+$.

[0712] 实施例921

(3S)-N-[4-(1-苯甲酰基哌啶-4-基）苯基]-1-(4-甲基哒嗪-3-基）吡咯烷-3-甲酰胺

实施例921A

(S)-叔丁基4-(4-(1-(4-甲基哒嗪-3-基）吡咯烷-3-甲酰胺基）苯基）哌啶-1-甲酸酯

如实施例1C中所述制备标题化合物,用3-氯-4-甲基哒嗪代替3-溴吡啶和用(S)-叔丁基4-(4-(吡咯烷-3-甲酰胺基）苯基）哌啶-1-甲酸酯代替叔丁基4-(4-(氮杂环丁烷-3-甲酰胺基）苯氧基）哌啶-1-甲酸酯。

[0713] 实施例921B

(S)-1-(4-甲基哒嗪-3-基)-N-(4-(哌啶-4-基）苯基）吡咯烷-3-甲酰胺

如实施例1D中所述制备标题化合物,用(S)-叔丁基4-(4-(1-(4-甲基哒嗪-3-基）吡咯烷-3-甲酰胺基）苯基）哌啶-1-甲酸酯代替叔丁基4-(4-(1-(吡啶-3-基）氮杂环丁烷-3-甲酰胺基）苯氧基）哌啶-1-甲酸酯。

[0714] 实施例921C

(3S)-N-[4-(1-苯甲酰基哌啶-4-基）苯基]-1-(4-甲基哒嗪-3-基）吡咯烷-3-甲酰胺

如实施例1A中所述制备标题化合物,用(S)-1-(4-甲基哒嗪-3-基)-N-(4-(哌啶-4-基）苯基）吡咯烷-3-甲酰胺代替叔丁基4-(4-氨基苯氧基）哌啶-1-甲酸酯和用苯甲酸代替1-(苄基氧基羰基）氮杂环丁烷-3-甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.03(s,1H),8.46(d, J = 4.6Hz,1H),7.58-7.52(m,2H),7.50-7.37(m,5H),7.28-7.15(m,3H),4.71-4.55(m,1H),3.89-3.38(m,5H),3.28-2.58(m,4H),2.34(s,3H),2.32-1.98(m,2H),2.00-1.49(m,4H) ;MS(ESI(+))m/e 470.2(M+H)$^+$.

[0715] 实施例922

(3S)-N-{4-[1-(2,2-二甲基丙酰基）哌啶-4-基]苯基)-1-(4-甲基哒嗪-3-基）吡咯烷-3-甲酰胺

如实施例1A中所述制备标题化合物,用(S)-1-(4-甲基哒嗪-3-基)-N-(4-(哌啶-4-基）苯基）吡咯烷-3-甲酰胺代替叔丁基4-(4-氨基苯氧基）哌啶-1-甲酸酯和用2,2-二甲基丙酸代替1-(苄基氧基羰基）氮杂环丁烷-3-甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.02(s,1H),8.46(d, J = 4.6Hz,1H),7.57-7.51(m,2H),7.22-7.13(m,3H),4.45-4.36(m,2H),3.85-3.72(m,2H),3.68(dd, J = 7.9,5.7Hz,2H),3.21(p, J = 7.7Hz,1H),2.93-2.66(m,3H),2.34(s,3H),2.31-2.05(m,2H),1.82-1.74(m,2H),1.53-1.34(m,2H),1,22(s,9H) ;MS(ESI(+))m/e 450.3(M+H)$^+$.

[0716] 实施例 923

N-{4-[1- 苯基 -3-(三氟甲基)-1H- 吡唑 -5- 基] 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 805 中所述制备标题化合物,用 3,3,3- 三氟丙 -1- 炔代替实施例 805A 中的乙炔基环丙烷和用苯肼代替实施例 805B 中的甲基肼。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.26(s,1H),8.56(dd, J = 4.5,1.3Hz,1H),7.61(d, J = 8.7Hz,2H),7.50-7.44(m,3H),7.41-7.31(m,3H),7.23(d, J = 8.7Hz,2H),7.14(s,1H),6.83(dd,J = 8.9,1.4Hz,1H),4.24(t,J = 8.3Hz,2H),4.14(dd,J = 8.1,5.8Hz,2H),3.74(tt,J = 8.5,5.8Hz,1H) ;MS(ESI(+))m/e 465.1(M+H)$^+$.

[0717] 实施例 924

N-{6-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 吡啶 -3- 基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 924A

N-(6- 氯吡啶 -3- 基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 6- 氯吡啶 -3- 胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

[0718] 实施例 924B

N-{6-[1-(2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 吡啶 -3- 基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

标题化合物如实施例 148A 中所述进行制备,用 N-(6- 氯吡啶 -3- 基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替 4- 溴苯胺和用 1- 新戊基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.31(s,1H),8.69(d, J = 2.6Hz,1H),8.57(dd, J = 4.5,1.3Hz,1H),8.18(s,1H),8.06(dd, J = 8.6,2.6Hz,1H),7.95(d, J = 0.4Hz,1H),7.63(dd,J = 8.6,0.4Hz,1H),7.39(dd,J = 8.9,4.5Hz,1H),6.84(dd,J = 9.0,1.4Hz,1H),4.27(t, J = 8.4Hz,2H),4.18(dd, J = 8.2,5.9Hz,2H),3.94(s,2H),3.78(tt, J = 8.6,5.9Hz,1H),0.93(s,9H) ;MS(ESI(+))m/e 392(M+H)$^+$,

[0719] 实施例 925

叔丁基 4-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基 } 氨基)-1H- 吡唑 -1- 基] 哌啶 -1- 甲酸酯

如实施例 1A 中所述制备标题化合物,用叔丁基 4-(4- 氨基 -1H- 吡唑 -1- 基) 哌啶 -1- 甲酸酯代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.15(s,1H),8.56(dd, J = 4.5,1.3Hz,1H),7.98-7.90(m,1H),7.47(d, J = 0.5Hz,1H),7.38(dd, J = 9.0,4.5Hz,1H),6.82(dd, J = 9.0,1.4Hz,1H),4.31(tt, J = 11.3,3.9Hz,1H),4.22(t, J = 8.3Hz,2H),4.12(dd, J = 8.1,6.0Hz,2H),4.02(d, J = 12.3Hz,2H),3.67(tt, J = 8.6,6.0Hz,1H),2.88(bs,2H),1.95(dd,J = 12.4,2.4Hz,2H),1.74(qd,J = 12.4,4.4Hz,2H),1.41(s,9H) ;MS(ESI(+))m/e 428(M+H)$^+$.

[0720] 实施例 926

N-(6-{1-[(4- 甲基哌啶 -4- 基) 甲基]-1H- 吡唑 -4- 基) 吡啶 -3- 基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺标题化合物如实施例 148A 中所述进行制备,用 N-(6- 氯吡啶 -3- 基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替 4- 溴苯胺和用叔丁基 4- 甲基 -4-((4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑 -1- 基) 甲基) 哌啶 -1- 甲酸酯代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑,随后为如实施例 1D 中所述进行 TFA 脱保护,以产生作为 TFA 盐的标题化合物。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.63(s,1H),8.79(d, J = 2.5Hz,1H),8.67-8.54(m,2H),8.52-8.39(m,1H),8.31(s,1H),8.13(dd, J = 8.7,2.5Hz,1H),8.05(s,1H),7.84(dd, J = 9.4,4.4Hz,1H),7.76(d, J = 8.7Hz,1H),7.51(dd, J = 9.4,0.9Hz,1H),4.51(t, J = 9.3Hz,2H),4.44(dd, J = 9.5,5.9Hz,2H),4.14(s,2H),3.87(tt, J = 8.8,5.9Hz,1H),3.29-3.14(m,2H),3.14-2.96(m,2H),1.74-1.58(m,2H),1.56-1.42(m,2H),0.98(s,3H) ;MS(ESI(+))m/e 433(M+H)$^+$.

[0721] 实施例 969

N-{4-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基] 苯基}-1-(4- 甲基哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1A 中所述制备标题化合物,用 1-(4- 甲基哒嗪 -3- 基)-N-(4-(哌啶 -4- 基) 苯基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 3,3- 二甲基丁酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.02(s,1H),8.49(d, J = 4.6Hz,1H),7.57-7.51(m,2H),7.22-7.14(m,3H),4.65-4.57(m,1H),4.39-4.24(m,4H),4.12-4.03(m,1H),3.68(p, J = 7.4Hz,1H),3.07(t, J = 12.0Hz,1H),2.77-2.64(m,1H),2.34-2.26(m,1H),2.25-2.16(m,4H),2.12-1.56(m,2H),1.58-1.07(m,3H),1.09-0.87(m,9H) ;MS(ESI(+))m/e 450.3(M+H)$^+$.

[0722] 实施例 970

N-{1-[1-(3,3- 二甲基丁酰基) 哌啶 -4- 基]-1H- 吡唑 -4- 基}-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 970A

N-(1-(哌啶 -4- 基)-1H- 吡唑 -4- 基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用叔丁基 4-[4-({[1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 基] 羰基} 氨基)-1H- 吡唑 -1- 基] 哌啶 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯。

[0723] 实施例 970B

N-{1-[1-(3,3-二甲基丁酰基)哌啶-4-基]-1H-吡唑-4-基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺

如实施例1A中所述制备标题化合物,用N-(1-(哌啶-4-基)-1H-吡唑-4-基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺代替叔丁基4-(4-氨基苯氧基)哌啶-1-甲酸酯和用3,3-二甲基丁酸代替1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

^{1}H NMR(500MHz, DMSO-d_6) δ ppm10.16(s,1H),8.56(dd, J = 4.5,1.1Hz,1H),7.95(s,1H),7.46(s,1H),7.38(dd, J = 9.0,4.5Hz,1H),6.83(dd, J = 9.0,1.2Hz,1H),4.53(d, J = 13.3Hz,1H),4.38(tt,J = 11.3,4.0Hz,1H),4.23(t,J = 8.3Hz,2H),4.12(dd,J = 8.0,6.1Hz,2H),4.07(d, J = 13.6Hz,1H),3.67(tt, J = 8.5,6.0Hz,1H),3.15(t, J = 12.1Hz,1H),2.66(t,J = 11.9Hz,1H),2.30(d,J = 14.1Hz,1H),2.23(d,J = 14.1Hz,1H),1.98(t,J = 10.7Hz,2H),1.80(qd, J = 12.3,4.1Hz,1H),1.68(qd, J = 12.3,4.2Hz,1H),1.00(s,9H);MS(ESI(+))m/e 426$(M+H)^+$.

[0724] 实施例971

N-{1-[1-(2-氟苯甲酰基)哌啶-4-基]-1H-吡唑-4-基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺

如实施例1A中所述制备标题化合物,用N-(1-(哌啶-4-基)-1H-吡唑-4-基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺代替叔丁基4-(4-氨基苯氧基)哌啶-1-甲酸酯和用2-氟苯甲酸代替1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm10.15(s,1H),8.56(dd, J = 4.5,1.3Hz,1H),7.98(s,1H),7.54-7.42(m,3H),7.38(dd,J = 9.0,4.5Hz,1H),7.34-7.26(m,2H),6.82(dd,J = 9.0,1.3Hz,1H),4.59(d, J = 13.3Hz,1H),4.45(tt, J = 11.2,3.9Hz,1H),4.23(t, J = 8.3Hz,2H),4.12(dd, J = 8.0,6.0Hz,2H),3.67(tt, J = 8.5,6.0Hz,1H),3.47(d, J = 13.3Hz,1H),3.22(t, J = 12.2Hz,1H),2.98(td, J = 13.0,2.7Hz,1H),2.09(d, J = 11.2Hz,1H),2.00-1.91(m,1H),1.90-1.74(m,2H);MS(ESI(+))m/e 450$(M+H)^+$.

[0725] 实施例972

N-[4-(苯基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺

实施例972A

甲基4-(1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺基)苯甲酸酯

如实施例1A中所述制备标题化合物,用甲基4-氨基苯甲酸酯代替叔丁基4-(4-氨基苯氧基)哌啶-1-甲酸酯和用1-(哒嗪-3-基)氮杂环丁烷-3-甲酸代替1-(苄基氧基羰基)氮杂环丁烷-3-甲酸。

[0726] 实施例972B

4-(1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺基)苯甲酸

程序按照如实施例911中所述进行,用甲基4-(1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺基)苯甲酸酯代替乙基1-甲基-5-(4-(1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺基)苯基)-1H-吡唑-3-甲酸酯。

[0727] 实施例972C

N-[4-(苯基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺

如实施例1A中所述制备标题化合物,用苯胺代替叔丁基4-(4-氨基苯氧基)哌

啶 -1- 甲酸酯和用 4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯甲酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸。

^{1}H NMR(400MHz, DMSO-d_6/D_2O) δ ppm 8.53(dd, J = 4.4,1.3Hz,1H),7.98-7.92(m,2H),7.77-7.65(m,5H),7.38-7.24(m,3H),7.15-7.07(m,1H),4,49(t, J = 9.0Hz,2H),4.46-4.38(m,2H),4.00-3.81(m,1H) ;MS(ESI(+))m/e 374(M+H)$^+$.

[0728] 表 23.

以下实施例基本上如实施例 972 中所述制备,代替实施例 972C 中的合适的胺。一些产物通过快速色谱纯化而其他通过反向 HPLC 纯化。因此,一些实施例分离为三氟乙酸盐。

实施例		名称	MS
973		N-{4-[(2,2-二甲基丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 368 (M+H)$^+$
974		N-{4-[(3-甲氧基-2,2-二甲基丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 398 (M+H)$^+$
975		N-{4-[(2-环丙基乙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-	(ESI(+))

		3-甲酰胺	m/e XXX (M+H)+
976		N-(4-{[2-(2-乙基哌啶-1-基)乙基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 366 (M+H)+
977		N-{4-[(环丁基甲基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 366 (M+H)+
978		N-{4-[(2S)-丁烷-2-基氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 354 (M+H)+
979		N-[4-(丁基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 354 (M+H)+
980		N-{4-[(2,2-二甲基四氢-2H-吡喃-4-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 410 (M+H)+
981		N-(4-{[(1S)-1-环丙基乙基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 366 (M+H)+
982		N-[4-({2-[甲基(苯基)氨基]乙基}氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 430 (M+H)+
983		N-{4-[1,1'-双(环丙基)-1-基氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 378 (M+H)+
984		1-(哒嗪-3-基)-N-[4-(喹喏-3-基氨基甲酰基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 366 (M+H)+
985		N-(4-{[(1R)-1-环丙基乙基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 366 (M+H)+
986		N-{4-[(1-甲基哌啶-4-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 395 (M+H)+
987		N-{4-[(2R)-丁烷-2-基氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 354 (M+H)+
988		N-[4-(1-氮杂双环[2.2.2]辛-3-基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 407 (M+H)+
989		1-(哒嗪-3-基)-N-[4-[(四氢呋喃-3-基甲基)氨基甲酰基]苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 382 (M+H)+
990		N-{4-[(氧杂环丁烷-3-基甲基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 368 (M+H)+
991		N-{4-[(2-甲基环丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 352 (M+H)+
992		N-[4-(环丁基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 352 (M+H)+
993		N-{4-[(1-甲基环丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-	(ESI(+))

		3-甲酰胺	m/e 352 (M+H)+
994		N-{4-[(2-甲氧基-2-甲基丙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 384 (M+H)+
995		N-{4-[(环丙基甲基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 352 (M+H)+
996		1-(哒嗪-3-基)-N-(4-{[(2R)-四氢呋喃-2-基甲基]氨基甲酰基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 382 (M+H)+
997		1-(哒嗪-3-基)-N-{4-[(3,3,3-三氟丙基)氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 394 (M+H)+
998		N-{4-[(1-甲基哌啶-3-基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 395 (M+H)+
999		N-(4-{[(3-甲基氧杂环丁烷-3-基)甲基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 382 (M+H)+
1000		1-(哒嗪-3-基)-N-(4-{[(2S)-四氢呋喃-2-基甲基]氨基甲酰基}苯基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 382 (M+H)+
1001		1-(哒嗪-3-基)-N-{4-[(四氢-2H-吡喃-4-基甲基)氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 396 (M+H)+
1002		1-(哒嗪-3-基)-N-[4-(四氢-2H-吡喃-4-基氨基甲酰基)苯基]氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 382 (M+H)+
1003		N-(4-{[(1-甲基哌啶-3-基)甲基]氨基甲酰基}苯基)-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 409 (M+H)+
1004		N-[4-(环丙基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 338 (M+H)+
1005		N-[4-(环戊基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 366 (M+H)+
1006		N-[4-(苄基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 388 (M+H)+
1007		N-{4-[(3-氟苯基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 392 (M+H)+
1008		N-[4-(丙基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 340 (M+H)+
1009		N-{4-[(4-氟苯基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 392 (M+H)+
1010		N-{4-[(2-氟苯基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 392 (M+H)+
1011		N-{4-[(1-甲基环丁基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-	(ESI(+))

		3-甲酰胺	m/e 366 (M+H)+
1012		N-[4-(丙-2-烯-1-基氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 338 (M+H)+
1020		1-(哒嗪-3-基)-N-{4-[(3S)-四氢呋喃-3-基氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 368 (M+H)+
1021		N-[4-({4-[2-(二甲基氨基)乙基]苯基}氨基甲酰基)苯基]-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 445 (M+H)+
1022		1-(哒嗪-3-基)-N-{4-[(3R)-四氢呋喃-3-基氨基甲酰基]苯基}氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 368 (M+H)+
1023		N-{4-[(2-甲氧基乙基)氨基甲酰基]苯基}-1-(哒嗪-3-基)氮杂环丁烷-3-甲酰胺	(ESI(+)) m/e 356 (M+H)+

[0729] 实施例 1024

N-{4-[1-(3- 氨基 -2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 1024A

叔丁基 (2,2- 二甲基 -3-(4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑 -1- 基) 丙基) 氨基甲酸酯

将叔丁基 (3- 羟基 -2,2- 二甲基丙基) 氨基甲酸酯 (1.000g,4.92mmol)、4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑 (1.145g,5.90mmol) 和 2-(三丁基亚膦基) 乙腈 (2-(tributylphosphoranylidene)acetonitrile)(1.425g,5.90mmol) 的溶液在甲苯 (20ml) 中在 90℃下一同搅拌过夜。将反应混合物浓缩并通过正相色谱纯化以产生标题化合物。

[0730] 实施例 1024B

叔丁基 (2,2- 二甲基 -3-(4-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-1H- 吡唑 -1- 基) 丙基) 氨基甲酸酯

标题化合物如实施例 148A 中所述进行制备,用 N-(4- 溴苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替 4- 溴苯胺和用叔丁基 (2,2- 二甲基 -3-(4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑 -1- 基) 丙基) 氨基甲酸酯代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑。

[0731] 实施例 1024C

N-{4-[1-(3- 氨基 -2,2- 二甲基丙基)-1H- 吡唑 -4- 基] 苯基 }-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用叔丁基 (2,2- 二甲基 -3-(4-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-1H- 吡唑 -1- 基) 丙基) 氨基甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯,以产生作为 TFA 盐的标题化合物。

^{1}H NMR(500MHz, DMSO-d_6) δ ppm 10.26(s,1H),8.57(dd, J = 4.4,1.1Hz,1H),8.12(s,1H),7.95(bs,3H),7.92(s,1H),7.74(dd, J = 9.3,4.4Hz,1H),7.64(d, J = 8.7Hz,2H),7.55(d, J = 8.6Hz,2H),7.36(d, J = 9.2Hz,1H),4.44(t, J = 9.1Hz,2H),4.37(dd, J =

9.2,5.9Hz,2H),4.10(s,2H),3.81(tt,J = 8.8,5.9Hz,1H),2.83-2.70(m,2H),0.96(s,6H);MS(ESI(+))m/e 406(M+H)$^+$.

[0732] 实施例 1025

N-(4-{1-[2,2- 二甲基 -3-(哌嗪 -1- 基) 丙基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

实施例 1025A

叔丁基 4-(2,2- 二甲基 -3-(4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑 -1- 基) 丙基) 哌啶 -1- 甲酸酯

如实施例 1024A 中所述制备标题化合物,用叔丁基 4-(3- 羟基 -2,2- 二甲基丙基) 哌啶 -1- 甲酸酯代替叔丁基 (3- 羟基 -2,2- 二甲基丙基) 氨基甲酸酯。

[0733] 实施例 1025B

叔丁基 4-(2,2- 二甲基 -3-(4-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-1H- 吡唑 -1- 基) 丙基) 哌嗪 -1- 甲酸酯

标题化合物如实施例 148A 中所述进行制备,用 N-(4- 溴苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替 4- 溴苯胺和用叔丁基 4-(2,2- 二甲基 -3-(4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑 -1- 基) 丙基) 哌啶 -1- 甲酸酯代替 1- 异丁基 -4-(4,4,5,5- 四甲基 -1,3,2- 二氧杂环戊硼烷 -2- 基)-1H- 吡唑。

[0734] 实施例 1025C

N-(4-{1-[2,2- 二甲基 -3-(哌嗪 -1- 基) 丙基]-1H- 吡唑 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺

如实施例 1D 中所述制备标题化合物,用叔丁基 4-(2,2- 二甲基 -3-(4-(4-(1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯基)-1H- 吡唑 -1- 基) 丙基) 哌嗪 -1- 甲酸酯代替叔丁基 4-(4-(1-(吡啶 -3- 基) 氮杂环丁烷 -3- 甲酰胺基) 苯氧基) 哌啶 -1- 甲酸酯,以产生作为 TFA 盐的标题化合物。

^{1}H NMR(500MHz, DMSO-d_6) δ ppm 10.25(s,1H),8.81(s,2H),8.57(dd, J = 4.3,1.0Hz,1H),8.07(s,1H),7.86(s,1H),7.80(dd, J = 9.3,4.4Hz,1H),7.62(d, J = 8.7Hz,2H),7.54(d,J = 8.6Hz,2H),7.45(d,J = 8.9Hz,1H),4.47(t,J = 9.2Hz,2H),4.40(dd,J = 9.3,5.9Hz,2H),4.03(s,2H),3.87-3.74(m,1H),3.19(s,4H),2.92(s,4H),2.45(s,2H),0.89(s,6H);MS(ESI(+))m/e 475(M+H)$^+$.

[0735] 实施例 1026

N-(4-{1-[2- 甲基 -2-(哌嗪 -1- 基) 丙酰基] 哌啶 -4- 基 } 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺如实施例 1A 中所述制备标题化合物,用 N-(4-(哌啶 -4- 基) 苯基)-1-(哒嗪 -3- 基) 氮杂环丁烷 -3- 甲酰胺代替叔丁基 4-(4- 氨基苯氧基) 哌啶 -1- 甲酸酯和用 2-(4-(叔丁氧基羰基) 哌嗪 -1- 基)-2- 甲基丙酸代替 1-(苄基氧基羰基) 氮杂环丁烷 -3- 甲酸,随后为如实施例 1D 中所述进行 TFA 脱保护,以产生作为 TFA 盐的标题化合物。

^{1}H NMR(400MHz, DMSO-d_6) δ ppm 10.17(s,1H),8.67(s,2H),8.56(d, J = 4.3Hz,1H),7.77(dd, J = 9.3,4.4Hz,1H),7.55(d, J = 8.4Hz,2H),7.42(d, J = 9.3Hz,1H),7.21(d, J = 8.5Hz,2H),5.27(s,1H),4.59(s,1H),4.45(t,J = 9.1Hz,2H),4.37(dd,J = 9.2,5.9Hz,

2H),3.91-3.71(m,1H),3.11(s,5H),2.81-2.53(m,6H),1.80(d, J = 12.0Hz,2H),1.45(td, J = 12.3,9.1Hz,2H),1.21(s,6H) ;MS(ESI(+))m/e 492(M+H)$^+$。

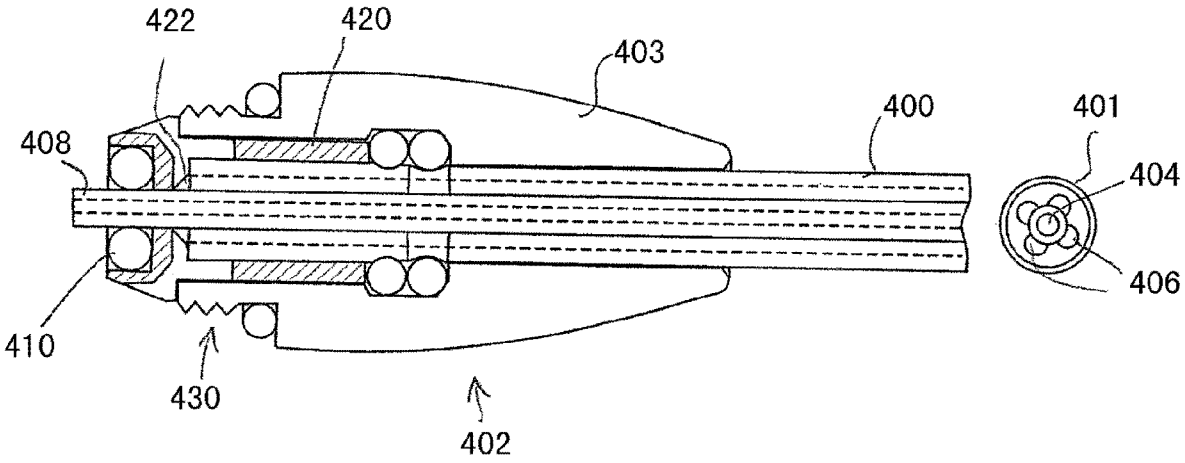


图 4