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(54) Title: METHODS OF USING COMBINATIONS OF MEK AND JAK-2 INHIBITORS

(57) Abstract: A method of treating a disease in a mammal, comprising administering to the mammal a therapeutically effective amount of a MEK compound of Formula I(M), or a pharmaceutical composition comprising a therapeutically effective amount of a MEK compound of Formula I(M) and a pharmaceutically acceptable carrier, in combination with a therapeutically effective amount of a JAK-2 compound of Formula I(J), or a pharmaceutical composition comprising a therapeutically effective amount of a JAK-2 compound of Formula I(J) and a pharmaceutically acceptable carrier, wherein the MEK compound of Formula I(M) and JAK-2 compound of Formula I(J) are as defined in the specification.

METHODS OF USING COMBINATIONS OF MEK AND JAK-2 INHIBITORS

BACKGROUND OF THE INVENTION

Cross Reference to Related Applications

[0001] This application claims the benefit of copending United States Provisional Application No. 60/921,878, filed on April 3, 2007, which is incorporated herein by reference in its entirety.

Field of the Invention

[0002] This invention relates to methods of using certain inhibitors of MEK in combination with certain inhibitors of JAK-2 for the treatment of diseases in mammals, especially humans.

State of the Art

[0003] Improvements in the specificity of agents used to treat cancer is of considerable interest because of the therapeutic benefits which would be realized if the side effects associated with the administration of these agents could be reduced. Traditionally, dramatic improvements in the treatment of cancer are associated with identification of therapeutic agents acting through novel mechanisms.

[0004] Protein kinases are enzymes that catalyze the phosphorylation of proteins, in particular, hydroxy groups on tyrosine, serine and threonine residues of proteins. The consequences of this seemingly simple activity are staggering; cell differentiation and proliferation; i.e., virtually all aspects of cell life in one-way or another depend on protein kinase activity. Furthermore, abnormal protein kinase activity has been related to a host of disorders, ranging from relatively non-life threatening diseases such as psoriasis to extremely virulent diseases such as glioblastoma (brain cancer).

[0005] Tyrosine kinases can be categorized as receptor type or non-receptor type. Receptor-type tyrosine kinases have an extracellular, a transmembrane, and an intracellular portion, while non-receptor type tyrosine kinases are wholly intracellular. They are comprised of a large number of transmembrane receptors with diverse biological activity. In fact, about 20 different subfamilies of receptor-type tyrosine kinases have been identified. One tyrosine kinase subfamily, designated the HER subfamily, is

comprised of EGFR (HER1), HER2, HER3, and HER4. Ligands of this subfamily of receptors identified so far include epithelial growth factor, TGF-alpha, amphiregulin, HB-EGF, betacellulin and heregulin. Another subfamily of these receptor-type tyrosine kinases is the insulin subfamily, which includes INS-R, IGF-IR, and IR-R. The PDGF subfamily includes the PDGF-alpha and beta receptors, CSFIR, c-kit and FLK-II. In addition, there is the FLK family, which is comprised of the kinase insert domain receptor (KDR), fetal liver kinase-1 (FLK-1), fetal liver kinase-4 (FLK-4) and the fms-like tyrosine kinase-1 (flt-1).

[0006] The non-receptor type of tyrosine kinases is also comprised of numerous subfamilies, including Src, Frk, Btk, Csk, Abl, Zap70, Fes/Fps, Fak, Jak, Ack, and LIMK. Each of these subfamilies is further sub-divided into varying receptors. For example, the Src subfamily is one of the largest and includes Src, Yes, Fyn, Lyn, Lck, Blk, Hck, Fgr, and Yrk. The Src subfamily of enzymes has been linked to oncogenesis. For a more detailed discussion of the non-receptor type of tyrosine kinases, see Bolen, *Oncogene*, **8**:2025-2031 (1993), which is hereby incorporated by reference.

[0007] Since protein kinases and their ligands play critical roles in various cellular activities, deregulation of protein kinase enzymatic activity can lead to altered cellular properties, such as uncontrolled cell growth associated with cancer. In addition to oncological indications, altered kinase signaling is implicated in numerous other pathological diseases. These include, but are not limited to: immunological disorders, cardiovascular diseases, inflammatory diseases, and degenerative diseases. Therefore, both receptor and non-receptor protein kinases are attractive targets for small molecule drug discovery.

[0008] One particularly attractive goal for therapeutic use of kinase modulation relates to oncological indications. For example, modulation of protein kinase activity for the treatment of cancer has been demonstrated successfully with the FDA approval of Gleevec® (imatinib mesylate, produced by Novartis Pharmaceutical Corporation of East Hanover, NJ) for the treatment of Chronic Myeloid Leukemia (CML) and gastrointestinal stroma cancers. Gleevec is a selective Abl kinase inhibitor.

[0009] Modulation (particularly inhibition) of cell proliferation and angiogenesis, two cellular processes needed for tumor growth and survival, is an attractive goal for development of small-molecule drugs. Anti-angiogenic therapy represents a potentially important approach for the treatment of solid tumors and other diseases associated with

dysregulated vascularization, including ischemic coronary artery disease, diabetic retinopathy, psoriasis and rheumatoid arthritis. Cell antiproliferative agents are also desirable to slow or stop the growth of tumors.

[0010] Another target for small-molecule modulation, with respect to antiangiogenic and antiproliferative activity is MEK. Inhibition of MEK1 (MAPK/ERK Kinase) is a promising strategy to control the growth of tumors that are dependent on aberrant ERK/MAPK pathway signaling. The MEK-ERK signal transduction cascade is a conserved pathway which regulates cell growth, proliferation, differentiation, and apoptosis in response to growth factors, cytokines, and hormones. This pathway operates downstream of Ras which is often upregulated or mutated in human tumors. It has been demonstrated that MEK is an effector of Ras function. The ERK/MAPK pathway is upregulated in 30% of all tumors and oncogenic activating mutations in K-Ras and B-Raf have been identified in 22% and 18% of all cancers respectively (Allen et al., 2003; Bamford S, 2004; Davies et al., 2002; Malumbres and Barbacid, 2003). A large portion of human cancers, including 66% (B-Raf) of malignant melanomas, 60% (K-Ras) and 4% (B-Raf) of pancreatic cancers, 50% of colorectal cancers (colon, in particular, K-Ras: 30%, B-Raf: 15%), 20% (K-Ras) of lung cancers, 27% (B-Raf) papillary and anaplastic thyroid cancer, and 10-20% (B-Raf) of endometriod ovarian cancers, harbor activating Ras and Raf mutations. It has been shown that inhibition of the ERK pathway, and in particular inhibition of MEK kinase activity, results in anti-metastatic and anti-angiogenic effects largely due to a reduction of cell-cell contact and motility as well as downregulation of vascular endothelial growth factor (VEGF) expression. Furthermore, expression of dominant negative MEK, or ERK reduced the transforming ability of mutant Ras as seen in cell culture and in primary and metastatic growth of human tumor xenografts *in vivo*. Therefore, the MEK-ERK signal transduction pathway is an appropriate pathway to target for therapeutic intervention.

[0011] Binding of growth factors and cytokines to their cell surface receptors results in activation of intracellular signaling pathways which control cell proliferation, survival and differentiation. Key components of these pathways are protein kinases, which phosphorylate tyrosine, serine or threonine residues and thereby modulate the activity of substrate proteins. Two major signaling pathways which emanate from growth factor and cytokine receptors are the Ras/raf/MEK/Erk and the JAK/STAT pathways. Activation of the small GTPase Ras, leads to activation of a cascade of serine / threonine kinases which

initiates with Raf and, via activation of MEK, results in stimulation of ERK activity and phosphorylation of numerous substrates that control cellular proliferation and differentiation. Activation of members of the JAK family of cytoplasmic tyrosine kinases results in phosphorylation of members of the STAT family of inducible transcription factors. Phosphorylation of a key regulatory tyrosine residue in STAT proteins by JAKs results in their dimerization, translocation to the nucleus and binding to specific DNA sequences in the promoters and enhancers of regulated genes. The DNA-bound STATs serve to promote the transcription of these genes, many of which are involved in the control of cellular growth.

[0012] The Ras/Raf/MEK/ERK and JAK/STAT pathways intersect at the levels of the STAT proteins. The STATs are substrates for ERK kinases and are phosphorylated by ERKs in their C-terminal transcriptional activation domain. Phosphorylation at this site is required for efficient transcriptional activation by STAT proteins.

[0013] Constitutive STAT activation is a feature of a wide variety of human tumors. In particular, activation of STAT5 is observed in leukemias, including CML, AML and ALL, whereas activation of STAT3 is a common feature of solid tumors including prostate carcinoma, non-small cell lung carcinoma and head and neck tumors. Reduction of STAT3 or STAT5 levels results in a reduction in tumor cell growth and in some case induction of tumor cell apoptosis in preclinical models. It is therefore desirable to develop strategies for pharmacologically inhibiting STAT activity in tumor cells as a method for treating cancers.

SUMMARY OF THE INVENTION

[0014] In one aspect, the methods of the invention involve simultaneous inhibition of both tyrosine and serine phosphorylation of STATs which is intended to maximally inhibit STAT activity thereby providing maximal opportunity to achieve therapeutic benefit in patients whose tumors have activated STATs.

[0015] The following only summarizes certain aspects of the invention and is not intended to be limiting in nature. These aspects and other aspects and embodiments are described more fully below. All references cited in this specification are hereby incorporated by reference in their entirety. In the event of a discrepancy between the express disclosure of this specification and the references incorporated by reference, the express disclosure of this specification shall control.

[0016] This invention provides methods that inhibit, regulate and/or modulate the signal transduction of kinases, particularly MEK and JAK-2.

[0017] In one aspect, the invention relates to a method of treating a disease, such as cancer, comprising administering to a mammal, including humans, a therapeutically effective amount of a MEK inhibitor of Formula I(M) or Formula I(N) as defined below, or a pharmaceutical composition comprising a therapeutically effective amount of the MEK compound of Formula I(M) or Formula I(N) and a pharmaceutically acceptable carrier, in combination with a therapeutically effective amount of a JAK-2 inhibitor, as defined below, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a therapeutically effective amount of the JAK-2 inhibitor and a pharmaceutically acceptable carrier, wherein the mammal is in need of the treatment.

[0018] In another aspect, the invention relates to a method of treating a disease, such as cancer, comprising administering to a mammal, including humans, a therapeutically effective amount of a JAK-2 compound of Formula I(J), as defined below, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a therapeutically effective amount of the JAK-2 compound of Formula I(J) and a pharmaceutically acceptable carrier, in combination with a MEK inhibitor, as defined below, or a pharmaceutical composition comprising a therapeutically effective amount of the MEK inhibitor and a pharmaceutically acceptable carrier, wherein the mammal is in need of the treatment.

[0019] In another aspect, the invention relates to a method of treating a disease, such as cancer, comprising administering to a mammal, including humans, a therapeutically effective amount of a JAK-2 compound of Formula I(J), as defined below, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a therapeutically effective amount of the JAK-2 compound and a pharmaceutically acceptable carrier, in combination with a MEK compound of Formula I(M) or Formula I(N) as defined below, or a pharmaceutical composition comprising a therapeutically effective amount of the MEK compound of Formula I(M) or Formula I(N) and a pharmaceutically acceptable carrier, wherein the mammal is in need of the treatment.

[0020] There are many different aspects of the compounds, pharmaceutical compositions thereof, and methods of use thereof, as described hereinbelow, and each aspect is non-limiting in regard to the scope of the invention. The transitional term "comprising" as used herein, which is synonymous with "including," "containing," or "characterized by,"

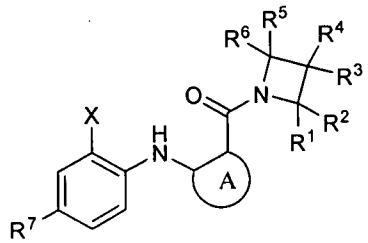
is inclusive or open-ended and does not exclude additional, unrecited elements or method steps.

DETAILED DESCRIPTION OF THE INVENTION

"MEK COMPOUNDS"

[0021] The MEK compounds regulate and/or modulate the signal transduction of MEK and are azetidin-1-yl(2-(2-fluorophenylamino)cyclic)methanones derivatives. The MEK compounds described below are non-limiting examples of "MEK inhibitors" defined hereinabove. These MEK compounds are described in a separate section from the JAK-2 compounds. All of the substituents for the MEK compounds described below are defined separately from the JAK-2 compounds so that every substituent in the MEK compounds that also appears in the JAK-2 compounds has a separate and distinct definition for each of these two compounds. For instance, R^1 for the JAK-2 compounds has a separate and distinct definition from R^1 for the MEK compounds.

[0022] In one aspect, the MEK compound is of Formula I(N):



I(N)

or a pharmaceutically acceptable salt thereof, wherein A, X, R^1, R^2, R^3, R^4, R^5, R^6, and R^7 are as defined in Group A, Group B, Group C, or Group D.

Group A:

[0023] A is arylene optionally substituted with one, two, three or four groups selected from R^{10}, R^{12}, R^{14}, and R^{16}, wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen, alkyl, alkenyl, alkynyl, halo, haloalkoxy, hydroxy, alkoxy, amino, alkylamino, dialkylamino, haloalkyl, $-NHS(O)_2R^8$, -CN, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$ and $-NR^8C(O)R^{8'}$;

X is alkyl, halo, haloalkyl, or haloalkoxy;

R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$,

$-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached form C(O) or C(=NOH);

m is 0, 1, or 2;

R^7 is hydrogen, halo or alkyl;

R^8, $R^{8'}$ and $R^{8''}$ are independently selected from hydrogen, hydroxy, optionally substituted alkoxy, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two three, four, or five groups independently selected from alkyl, halo, hydroxy, hydroxyalkyl, optionally substituted alkoxy, alkoxyalkyl, haloalkyl, carboxy, alkoxycarbonyl, alkenyloxycarbonyl, optionally substituted cycloalkyl, optionally substituted cycloalkyloxycarbonyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted aryloxycarbonyl, optionally substituted arylalkyl, optionally substituted arylalkyloxy, optionally substituted arylalkyloxycarbonyl, nitro, cyano, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, $-S(O)_nR^{31}$ (wherein n is 0, 1, or 2 and R^{31} is optionally substituted alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-NR^{34}SO_2R^{34a}$ (wherein R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl), $-SO_2NR^{35}R^{35a}$ (wherein R^{35} is hydrogen or alkyl and R^{35a} is

alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl), $-NR^{32}C(O)R^{32a}$ (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl), $-NR^{30}R^{30'}$ (wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), and $-C(O)NR^{33}R^{33a}$ (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl);

R^9 is alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally susbstituted with one, two, three, four, or five groups selected from halo, hydroxy, alkyl, haloalkyl, haloalkoxy, amino, alkylamino, and dialkylamino;

R^{25} and R^{25b} are independently hydrogen, alkyl, alkenyl, optionally sbustituted cycloalkyl, or optionally substituted aryl; and

R^{25a} is hydrogen, alkyl, or alkenyl;

Group B:

A is heteroarylene optionally substituted with one, two, three, or four groups selected from R^{10}, R^{12}, R^{14}, R^{16} and R^{19}, wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen, alkyl, alkenyl, alkynyl, halo, haloalkoxy, hydroxy, alkoxy, cyano, amino, alkylamino, dialkylamino, haloalkyl, alkylsulfonylamino, alkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, alkenyloxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, or alkylcarbonylamino; wherein R^{19} is hydrogen, alkyl, or alkenyl; and wherein each alkyl and alkenyl, either alone or as part of another group within R^{10}, R^{12}, R^{14}, R^{16}, and R^{19} is independently optionally substituted with halo, hydroxy, or alkoxy;

X is alkyl, halo, haloalkyl, or haloalkoxy;

R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently

selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached form C(O) or C(=NOH);

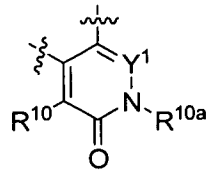
m is 1 or 2;

R^7 is hydrogen, halo or alkyl; and

R^8, $R^{8'}$ and $R^{8''}$ are independently selected from hydrogen, hydroxy, optionally substituted alkoxy, alkyl, haloalkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl, wherein the alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two three, four, or five groups independently selected from alkyl, halo, hydroxy, hydroxyalkyl, optionally substituted alkoxy, alkoxyalkyl, haloalkyl, carboxy, carboxy ester, nitro, cyano, $-S(O)_nR^{31}$ (wherein n is 0, 1, or 2 and R^{31} is optionally substituted alkyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-NR^{36}S(O)_2R^{36a}$ (wherein R^{36} is hydrogen, alkyl, or alkenyl and R^{36a} is alkyl, alkenyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-S(O)_2NR^{37}R^{37a}$ (wherein R^{37} is hydrogen, alkyl, or alkenyl and R^{37a} is alkyl, alkenyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted aryloxy, optionally substituted arylalkyloxy, optionally substituted heteroaryl, $-NHC(O)R^{32}$ (wherein R^{32} is alkyl, alkenyl, alkoxy, or cycloalkyl) and $-NR^{30}R^{30'}$ (wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), and $-C(O)NHR^{33}$ (wherein R^{33} is alkyl, alkenyl, alkynyl, or cycloalkyl);

Group C:

A is



(a)

wherein R^{10} is hydrogen, alkyl, alkenyl, alkynyl, halo, haloalkoxy, hydroxy, alkoxy, amino, alkylamino, dialkylamino, haloalkyl, $-NHS(O)_2R^8$, -CN, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$ and $-NR^8C(O)R^{8'}$;

R^{10a} is hydrogen, alkyl, or alkenyl;

Y^1 is =CH- or =N-;

X is alkyl, halo, haloalkyl, or haloalkoxy;

R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached form C(O) or C(=NOH);

m is 1 or 2;

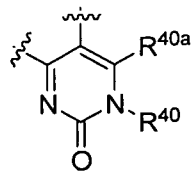
R^7 is hydrogen, halo or alkyl; and

R^8, $R^{8'}$ and $R_{8''}$ are independently selected from hydrogen, hydroxy, optionally substituted alkoxy, alkyl, haloalkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl, wherein the alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl,

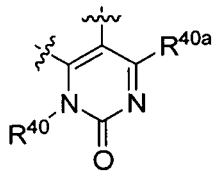
and heterocycloalkyl are independently optionally substituted with one, two three, four, or five groups independently selected from alkyl, halo, hydroxy, hydroxyalkyl, optionally substituted alkoxy, alkoxyalkyl, haloalkyl, carboxy, carboxy ester, nitro, cyano, $-S(O)_nR^{31}$ (wherein n is 0, 1, or 2 and R^{31} is optionally substituted alkyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-NR^{36}S(O)_2R^{36a}$ (wherein R^{36} is hydrogen, alkyl, or alkenyl and R^{36a} is alkyl, alkenyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-S(O)_2NR^{37}R^{37a}$ (wherein R^{37} is hydrogen, alkyl, or alkenyl and R^{37a} is alkyl, alkenyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted aryloxy, optionally substituted arylalkyloxy, optionally substituted heteroaryl, $-NHC(O)R^{32}$ (wherein R^{32} is alkyl, alkenyl, alkoxy, or cycloalkyl) and $-NR^{30}R^{30'}$ (wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), and $-C(O)NHR^{33}$ (wherein R^{33} is alkyl, alkenyl, alkynyl, or cycloalkyl); or

Group D:

A is



(b) or



(c)

R^{40} and R^{40a} are independently hydrogen or alkyl;

X is alkyl, halo, haloalkyl, or haloalkoxy;

R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$,

$-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached form C(O) or C(=NOH);

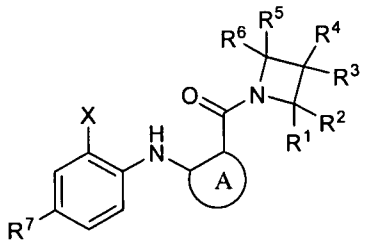
m is 1 or 2;

R^7 is hydrogen, halo or alkyl; and

R^8, $R^{8'}$ and $R_{8''}$ are independently selected from hydrogen, hydroxy, optionally substituted alkoxy, alkyl, haloalkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl, wherein the alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two three, four, or five groups independently selected from alkyl, halo, hydroxy, hydroxyalkyl, optionally substituted alkoxy, alkoxyalkyl, haloalkyl, carboxy, carboxy ester, nitro, cyano, $-S(O)_nR^{31}$ (wherein n is 0, 1, or 2 and R^{31} is optionally substituted alkyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-NR^{36}S(O)_2R^{36a}$ (wherein R^{36} is hydrogen, alkyl, or alkenyl and R^{36a} is alkyl, alkenyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-S(O)_2NR^{37}R^{37a}$ (wherein R^{37} is hydrogen, alkyl, or alkenyl and R^{37a} is alkyl, alkenyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl,

optionally substituted arylalkyl, optionally substituted aryloxy, optionally substituted arylalkyloxy, optionally substituted heteroaryl, -NHC(O)R^{32} (wherein R^{32} is alkyl, alkenyl, alkoxy, or cycloalkyl) and -$NR^{30}R^{30'}$ (wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), and -C(O)NHR^{33} (wherein R^{33} is alkyl, alkenyl, alkynyl, or cycloalkyl).

[0024] In another aspect, the MEK compound is of Formula I(M):



I(M)

or a pharmaceutically acceptable salt thereof, wherein A, X, R^1, R^2, R^3, R^4, R^5, R^6, and R^7 are as defined in Group A, Group B, Group C, or Group D:

wherein A, X, R^1, R^2, R^3, R^4, R^5, R^6, and R^7 are as defined in Group A, Group B, Group C, or Group D:

Group A

A is phenylene optionally substituted with one or two groups selected from R^{10}, R^{12}, R^{14}, and R^{16} wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen or halo;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen, halo, hydroxy, alkoxy, or amino;

R^4 is hydrogen, -$NR^8R^{8'}$, -C(O)$NR^8R^{8'}$, -$NR^8C(O)OR^{8'}$, -$NR^8C(O)R^{8'}$, -$CH_2N(R^{25})(NR^{25a}R^{25b})$, -$CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, -$CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, -$CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, -$CH_2NR^{25}C(=NH)(R^{25})$, -$CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, cycloalkyl, heterocycloalkyl, or heteroaryl; wherein the alkyl is optionally substituted with one, two, or three groups independently selected from -OR^8, halo, nitro, -$S(O)_mR^9$, optionally substituted heterocycloalkyl, -$NR^8R^{8'}$, -$NR^8C(O)R^{8'}$, -$NR^8S(O)_2R^9$, -$NR^8C(O)OR^{8'}$, and aryl; wherein the cycloalkyl is optionally substituted with one or two groups selected from -OR^8 and -$NR^8R^{8'}$; wherein the heterocycloalkyl is optionally substituted with one or two groups independently

selected from alkyl and -C(O)OR^8; and wherein the heteroaryl is optionally substituted with -NR^{8}R$^{8'}$; or

R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH);

m is 0;

R^7 is halo;

R^8 and R$^{8'}$ are independently selected from hydrogen, hydroxy, alkyl, alkenyl, alkynyl, aryl, heterocycloalkyl, heteroaryl, and cycloalkyl;

wherein the R^8 and R$^{8'}$ alkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, -NR^{30}R$^{30'}$ (wherein R^{30} and R$^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), optionally substituted heteroaryl, optionally substituted cycloalkyl), optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, -C(O)NR^{33}R^{33a} (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), optionally substituted aryloxy, -S(O)$_n$R^{31} (wherein n is 0 and R^{31} is alkyl), carboxy, alkoxycarbonyl, and -NR^{32}C(O)R^{32a} (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl); or wherein the alkyl is optionally substituted with one, two, three, four, or five halo;

wherein the R^8 and R$^{8'}$ heteroaryl are independently optionally substituted with one or two groups indendently selected from amino and alkyl;

wherein the R^8 and R$^{8'}$ heterocycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from alkyl, alkoxycarbonyl, optionally substituted arylalkyl, hydroxy, alkoxy, and hydroxyalkyl;

wherein the R^8 and R$^{8'}$ aryl are independently optionally substituted with one or two groups indendently selected from hydroxy, alkoxy, halo, -NR^{32}C(O)R^{32a} (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl), and -NR^{34}SO$_2$R^{34a} (wherein R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl); and

wherein the R^8 and R$^{8'}$ cycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, hydroxyalkyl, alkoxy, carboxy, -C(O)NR^{33}R^{33a} (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), and optionally substituted cycloalkyl; and

R^9 is alkyl or aryl;

Group B

A is thien-3,4-diyl, benzo[*d*]isoxazol-5,6-diyl, 1*H*-indazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), benzo[*d*]oxazol-5,6-diyl, 1*H*-benzo[d]imidazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), 1*H*-benzo[*d*][1,2,3]triazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), imidazo[1,2-*a*]pyridin-6,7-diyl, cinnolin-6,7-diyl, quinolin-6,7-diyl, pyridin-3,4-diyl, 1-oxido-pyridin-3,4-diyl, [1,2,4]triazolo[4,3-a]pyridin-6,7-diyl, or 2,3-dihydroimidazo[1,2-a]pyridin-6,7-diyl; wherein A is optionally substituted with one, two, or three groups independently selected from R^{10}, R^{12}, R^{14}, R^{16} and R^{19} wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen, alkyl, halo, or amino; and R^{19} is hydrogen or alkyl;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

R^4 is $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ and wherein the heteroaryl is optionaly substituted with alkyl;

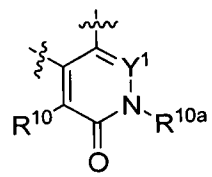
R^7 is halo;

R^8 is hydrogen or alkyl; and

$R^{8'}$ is hydrogen, alkyl, or cycloalkyl; wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl;

Group C

A is



(a)

R^{10} is hydrogen or halo;

R^{10a} is hydrogen or alkyl;

Y^1 is =CH- or =N-;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

R^4 is $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ and wherein the heteroaryl is optionaly substituted with alkyl;

R^7 is halo;

R^8 is hydrogen or alkyl; and

$R^{8'}$ is hydrogen, alkyl, or cycloalkyl; wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl.

[0025] The MEK compounds can also be used as a pharmaceutical composition which comprises a compound of Formula I(M), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, excipient, or diluent.

DETAILED DESCRIPTION OF THE INVENTION

Abbreviations and Definitions

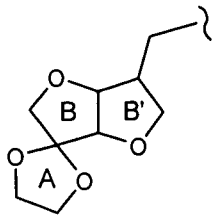
[0026] The following abbreviations and terms have the indicated meanings throughout:

Abbreviation	Meaning
Ac	Acetyl
Br	Broad
°C	degrees Celsius
CBZ	CarboBenZoxy = benzyloxycarbonyl
D	Doublet
Dd	doublet of doublet
Dt	doublet of triplet
DAST	(diethylamino)sulfur trifluoride
DCM	Dichloromethane
DIPEA	*N,N*-diisopropylethylamine
DMAP	4-dimethylaminopyridine
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
DPPA	Diphenylphosphoryl azide
EDCI	1-(3-dimethylaminopropyl)-3-ethylcarbodiimide
EI	Electron Impact ionization
Et	Ethyl
G	gram(s)
GC	gas chromatography
h or hr	hour(s)
HBTU	2-(1*H*-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate
HOAc	acetic acid
HOBt	Hydroxybenzotriazole
HPLC	high pressure liquid chromatography

L	liter(s)
LDA	lithium diiospropylamide
LHMDS	lithium hexamethyldisilazide
M	molar or molarity
M	Multiplet
MCPBA	meta-chloroperbenzoic acid
Me	Methyl
Mg	milligram(s)
MHz	megahertz (frequency)
Min	minute(s)
mL	milliliter(s)
mM	Millimolar
Mmol	millimole(s)
Mol	mole(s)
MS	mass spectral analysis
N	normal or normality
nM	Nanomolar
NMM	*N*-methylmorpholine
NMR	nuclear magnetic resonance spectroscopy
PyBOP	benzotriazole-1-yl-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate
Q	Quartet
RT	room temperature
S	Singlet
s-	Secondary
t-	Tertiary
T or tr	Triplet
THF	Tetrahydrofuran
μL	microliter(s)
μM	micromole(s) or micromolar

[0027] The symbol "-" means a single bond, "=" means a double bond, "≡" means a triple bond, and "---" means a single bond and optionally a double bond. When chemical structures are depicted or described, unless explicitly stated otherwise, all carbons are assumed to have hydrogen substitution to conform to a valence of four.

[0028] "Spiro", "Spirocyclyl" or "spiro ring" refers to a ring originating from a particular annular carbon of another ring. For example, as depicted below, a ring atom of a saturated bridged ring system (rings B and B'), but not a bridgehead atom, can be a shared atom between the saturated bridged ring system and a spirocyclyl (ring A) attached thereto.



[0029] "Yield" for each of the reactions described herein is expressed as a percentage of the theoretical yield.

[0030] "Patient" for the purposes of the present invention includes humans and other animals, particularly mammals, and other organisms. Thus the methods are applicable to both human therapy and veterinary applications. In a specific embodiment the patient is a mammal, and in a more specific embodiment the patient is human.

[0031] "Kinase-dependent diseases or conditions" refer to pathologic conditions that depend on the activity of one or more protein kinases. Kinases either directly or indirectly participate in the signal transduction pathways of a variety of cellular activities including proliferation, adhesion, migration, differentiation and invasion. Diseases associated with kinase activities include tumor growth, the pathologic neovascularization that supports solid tumor growth, and associated with other diseases wherein excessive local vascularization is involved such as ocular diseases (diabetic retinopathy, age-related macular degeneration, and the like) and inflammation (psoriasis, rheumatoid arthritis, and the like).

[0032] While not wishing to be bound to theory, phosphatases can also play a role in "kinase-dependent diseases or conditions" as cognates of kinases; that is, kinases phosphorylate and phosphatases dephosphorylate, for example protein substrates. Therefore compounds of the invention, while modulating kinase activity as described herein, may also modulate, either directly or indirectly, phosphatase activity. This additional modulation, if present, may be synergistic (or not) to activity of compounds of the invention toward a related or otherwise interdependent kinase or kinase family. In any case, as stated previously, the compounds of the invention are useful for treating diseases characterized in part by abnormal levels of cell proliferation (*i.e.* tumor growth), programmed cell death (apoptosis), cell migration and invasion and angiogenesis associated with tumor growth.

[0033] "Therapeutically effective amount" is an amount of a compound of the invention, that when administered to a patient, ameliorates a symptom of the disease. The amount of a compound of the invention which constitutes a "therapeutically effective

amount" will vary depending on the compound, the disease state and its severity, the age of the patient to be treated, and the like. The therapeutically effective amount can be determined routinely by one of ordinary skill in the art having regard to their knowledge and to this disclosure.

[0034] "Cancer" refers to cellular-proliferative disease states, including but not limited to: Cardiac: sarcoma (angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma), myxoma, rhabdomyoma, fibroma, lipoma and teratoma; Lung: bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hanlartoma, inesothelioma; Gastrointestinal: esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma), stomach (carcinoma, lymphoma, leiomyosarcoma), pancreas (ductal adenocarcinoma, insulinorna, glucagonoma, gastrinoma, carcinoid tumors, vipoma), small bowel (adenocarcinorna, lymphoma, carcinoid tumors, Karposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma), large bowel (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); Genitourinary tract: kidney (adenocarcinoma, Wilm's tumor [nephroblastoma], lymphoma, leukemia), bladder and urethra (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma), prostate (adenocarcinoma, sarcoma), testis (seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); Liver: hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma; Bone: osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor chordoma, osteochronfroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors; Nervous system: skull (osteoma, hemangioma, granuloma, xanthoma, osteitis defornians), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma [pinealoma], glioblastorna multiform, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord neurofibroma, meningioma, glioma, sarcoma); Gynecological: uterus (endometrial carcinoma), cervix (cervical carcinoma, pre-tumor cervical dysplasia), ovaries (ovarian

carcinoma [serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma], granulosa-thecal cell tumors, Sertoli-Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma (embryonal rhabdomyosarcoma], fallopian tubes (carcinoma); Hematologic: blood (myeloid leukemia [acute and chronic], acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma [malignant lymphoma]; Skin: malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Karposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis; and Adrenal Glands: neuroblastoma. Thus, the term "cancerous cell" as provided herein, includes a cell afflicted by any one of the above-identified conditions.

[0035] A "pharmaceutically acceptable salt" of a compound means a salt that is pharmaceutically acceptable and that possesses the desired pharmacological activity of the parent compound. It is understood that the pharmaceutically acceptable salts are non-toxic. Additional information on suitable pharmaceutically acceptable salts can be found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, PA, 1985, which is incorporated herein by reference or S. M. Berge, et al., "Pharmaceutical Salts," J. Pharm. Sci., 1977;66:1-19 both of which are incorporated herein by reference.

[0036] Examples of pharmaceutically acceptable acid addition salts include those formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like; as well as organic acids such as acetic acid, trifluoroacetic acid, propionic acid, hexanoic acid, cyclopentanepropionic acid, glycolic acid, pyruvic acid, lactic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, 3-(4-hydroxybenzoyl)benzoic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, 1,2-ethanedisulfonic acid, 2-hydroxyethanesulfonic acid, benzenesulfonic acid, 4-chlorobenzenesulfonic acid, 2-naphthalenesulfonic acid, 4-toluenesulfonic acid, camphorsulfonic acid, glucoheptonic acid, 4,4'-methylenebis-(3-hydroxy-2-ene-1-carboxylic acid), 3-phenylpropionic acid, trimethylacetic acid, tertiary butylacetic acid,

lauryl sulfuric acid, gluconic acid, glutamic acid, hydroxynaphthoic acid, salicylic acid, stearic acid, muconic acid, p-toluenesulfonic acid, and salicylic acid and the like.

[0037] Examples of a pharmaceutically acceptable base addition salts include those formed when an acidic proton present in the parent compound is replaced by a metal ion, such as sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Preferable salts are the ammonium, potassium, sodium, calcium, and magnesium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include, but are not limited to, salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins. Examples of organic bases include isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, ethanolamine, 2-dimethylaminoethanol, 2-diethylaminoethanol, dicyclohexylamine, lysine, arginine, histidine, caffeine, procaine, hydrabamine, choline, betaine, ethylenediamine, glucosamine, methylglucamine, theobromine, purines, piperazine, piperidine, N-ethylpiperidine, tromethamine, *N*-methylglucamine, polyamine resins, and the like. Exemplary organic bases are isopropylamine, diethylamine, ethanolamine, trimethylamine, dicyclohexylamine, choline, and caffeine.

[0038] "Prodrug" refers to compounds that are transformed (typically rapidly) *in vivo* to yield the parent compound of the above formulae, for example, by hydrolysis in blood. Common examples include, but are not limited to, ester and amide forms of a compound having an active form bearing a carboxylic acid moiety. Examples of pharmaceutically acceptable esters of the compounds of this invention include, but are not limited to, alkyl esters (for example with between about one and about six carbons) the alkyl group is a straight or branched chain. Acceptable esters also include cycloalkyl esters and arylalkyl esters such as, but not limited to benzyl. Examples of pharmaceutically acceptable amides of the compounds of this invention include, but are not limited to, primary amides, and secondary and tertiary alkyl amides (for example with between about one and about six carbons). Amides and esters of the compounds of the present invention may be prepared according to conventional methods. A thorough discussion of prodrugs is provided in T. Higuchi and V. Stella, "Pro-drugs as Novel Delivery Systems," Vol 14 of the A.C.S. Symposium Series, and in Bioreversible Carriers in Drug Design, ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987, both of which are incorporated herein by reference for all purposes.

[0039] "Metabolite" refers to the break-down or end product of a compound or its salt produced by metabolism or biotransformation in the animal or human body; for example, biotransformation to a more polar molecule such as by oxidation, reduction, or hydrolysis, or to a conjugate (see Goodman and Gilman, "The Pharmacological Basis of Therapeutics" 8.sup.th Ed., Pergamon Press, Gilman et al. (eds), 1990 for a discussion of biotransformation). As used herein, the metabolite of a compound of the invention or its salt may be the biologically active form of the compound in the body. In one example, a prodrug may be used such that the biologically active form, a metabolite, is released *in vivo*. In another example, a biologically active metabolite is discovered serendipitously, that is, no prodrug design *per se* was undertaken. An assay for activity of a metabolite of a compound of the present invention is known to one of skill in the art in light of the present disclosure.

[0040] "Treating" or "treatment" of a disease, disorder, or syndrome, as used herein, includes (i) preventing the disease, disorder, or syndrome from occurring in a human, i.e. causing the clinical symptoms of the disease, disorder, or syndrome not to develop in an animal that may be exposed to or predisposed to the disease, disorder, or syndrome but does not yet experience or display symptoms of the disease, disorder, or syndrome; (ii) inhibiting the disease, disorder, or syndrome, *i.e.*, arresting its development; and (iii) relieving the disease, disorder, or syndrome, *i.e.*, causing regression of the disease, disorder, or syndrome. As is known in the art, adjustments for systemic versus localized delivery, age, body weight, general health, sex, diet, time of administration, drug interaction and the severity of the condition may be necessary, and will be ascertainable with routine experimentation by one of ordinary skill in the art.

[0041] "Mammal" is intended to mean any various warm-blooded vertebrate animals of the class Mammalia, including humans, dogs, cats, and the like, characterized by a covering of hair on the skin and, in the female, milk-producing mammary glands for nourishing the young.

[0042] "MEK inhibitors" are intended to include all MEK inhibitors including the MEK compounds of Formulae I(M) and I(N) defined hereinbelow. MEK inhibitors, including the MEK compounds, include pharmaceutically acceptable salts or solvates throughout this application whether it is explicitly stated or not.

[0043] "JAK-2 inhibitors" are intended to include all JAK-2 inhibitors including the JAK-2 compounds of Formula I(J) defined hereinbelow. JAK-2 inhibitors, including the

JAK-2 compounds, include pharmaceutically acceptable salts or solvates throughout this application whether it is explicitly stated or not.

"MEK Compounds"

[0044] In one embodiment of the MEK compound, R^7 is halo and all other substituents are as defined in the above for the compound of Formula I(M) or Formula I(N) for Group A, Group B, Group C, or Group D. In a more specific embodiment, R^7 is iodo or bromo. In an even more specific embodiment, R^7 is iodo. Yet even more specifically, the MEK compound is that wherein R^7 is iodo or bromo and all other substituents are as defined in the compound of Formula I(M) or Formula I(N) for Group A.

[0045] In another embodiment of the MEK compound, X is halo and all other substituents are as defined in the compound of Formula I(M) or Formula I(N) for Group A, Group B, Group C, or Group D. In a more specific embodiment, X is fluoro or chloro. In an even more specific embodiment, X is fluoro. Yet even more specifically, the MEK compound is that wherein X is fluoro or chloro and all other substituents are as defined in the compound of Formula I(M) or Formula I(N) for Group A.

[0046] In another embodiment of the MEK compound, R^7 and X are halo and all other substituents are as defined in the compound of Formula I(M) or Formula I(N) for Group A, Group B, Group C, or Group D. More specifcally, R^7 is iodo and X is fluoro. Even more specifically, the MEK compound is that wherein R^7 is iodo and X is fluoro and all other substituents are as defined in the compound of Formula I(M) or Formula I(N) for Group A.

[0047] In another embodiment of the MEK compound, R^1, R^2, R^5, and R^6 are hydrogen and all other substituents are as defined in the compound of Formula I(M) or Formula I(N) for Group A, Group B, Group C, or Group D. More specifically, R^1, R^2, R^5, and R^6 are hydrogen and all other substituents are as defined in the compound of Formula I(M) or Formula I(N) for Group A.

[0048] In another embodiment of the MEK compound, the substituents of Formula I are as defined in Group A in the compound of Formula I(M) or Formula I(N).

[0049] In another embodiment of the MEK compound (A1), X and R^7 are halo and all other substituents are as defined in Group A in the compound of Formula I(M) or Formula I(N).

[0050] In another embodiment of the MEK compound (A2), the substituents for the compound of Formula I(M) or Formula I(N) are as defined in Group A, wherein R^{10} and R^{12} are independently hydrogen or halo. In a more specific embodiment, R^{10} and R^{12} are independently hydrogen or fluoro. More specifically, R^{10} is 3-fluoro and R^{12} is hydrogen. In another more specific embodiment, R^{10} and R^{12} are fluoro, more specifically, 3-fluoro and 4-fluoro, 4-fluoro and 5-fluoro, or 4-fluoro and 6-fluoro.

[0051] In another embodiment of the MEK compound (A3), the compound is that wherein R^1, R^2, R^5 and R^6 are hydrogen and all other substituents are as defined in the compound of Formula I(M) or Formula I(N) for Group A.

[0052] In another embodiment of the MEK compound (A4), the compound of Formula I(M) or Formula I(N) is as defined in Group A, wherein X, R^7, and A are as defined in the compound of Formula I(M) or Formula I(N); and

one of R^1, R^2, R^3, R^4, R^5, and R^6 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; and the others of R^1, R^2, R^3, R^4, R^5, and R^6 are as defined in the compound of Formula I(M) or Formula I(N); or

one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached forms C(O) or C(=NOH); and the others of R^1, R^2, R^3, R^4, R^5, and R^6 are as defined in the compound of Formula I(M) or Formula I(N).

[0053] In another embodiment of the MEK compound (A5), the compound of Formula I(M) or Formula I(N) is selected from Group A, wherein X, R^7, and A are as defined in the compound of Formula I(M) or Formula I(N); and

R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; and R^4 is as defined in the compound of Formula I(M) or Formula I(N); or

R^3 and R^4, together with the carbon to which they are attached, form -C(O) or -C(=NOH); and

R^1, R^2, R^5 and R^6 are as defined in the the compound of Formula I(M) or Formula I(N).

[0054] A more specific embodiment of embodiment A5 is that wherein R^1, R^2, R^5 and R^6 are hydrogen.

[0055] In another embodiment of the MEK compound (A6), the compound of Formula I(M) or Formula I(N) is selected from Group A, wherein X, R^7, and A are as defined in the compound of Formula I(M) or Formula I(N); and

R^3 and R^4 are independently halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl,

and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or

R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH);

R^1, R^2, R^5 and R^6 are are as defined in the compound of Formula I(M) or Formula I(N).

[0056] A more specific embodiment of embodiment A6 is that wherein R^1, R^2, R^5 and R^6 are hydrogen.

[0057] In another embodiment of the MEK compound (A7), the compound of Formula I(M) or Formula I(N) is selected from Group A, wherein X and R^7 are halo; A is phenylene optionally substituted with R^{10} and R^{12}, wherein R^{10} and R^{12} are independently hydrogen or halo; R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen and R^4 is $-NR^8R^{8'}$ (wherein R^8 is hydrogen, hydroxy, alkyl, alkoxy, aryl, cycloalkyl, heteroaryl, or heterocycloalkyl and $R^{8'}$ is hydroxy, alkoxy, aryl, cycloalkyl, heteroaryl, or heterocycloalkyl), $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, alkenyl, and alkynyl; wherein the alkenyl and alkynyl are optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or

R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH);

m, $R^{8''}$, and R^9 are as defined in the compound of Formula I(M) or Formula I(N) or Formula I(N) for a compound of Group A; and unless otherwise specified in this embodiment, R^8 and $R^{8'}$ are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group A.

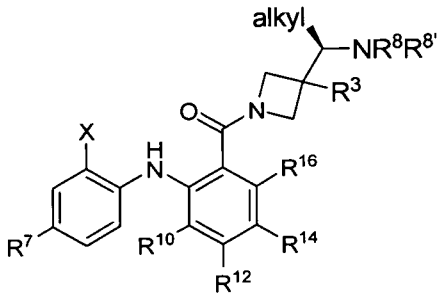
[0058] In another embodiment of the MEK compound (A8), the compound of Formula I(M) or Formula I(N) is selected from Group A, wherein R^3 is hydrogen, halo, hydroxy,

alkoxy, or amino. More specifically, R^3 is hydrogen, fluoro, hydroxy, methoxy, or amino. Even more specifically, R^3 is hydrogen or hydroxy. Yet even more specifically, R^3 is hydroxy.

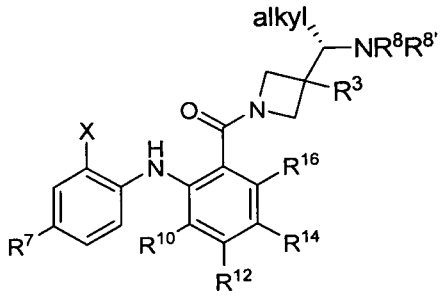
[0059] In a more specific embodiment of embodiment of A8, X and R^7 are halo; A is phenylene optionally substituted with R^{10} and R^{12}, wherein R^{10} and R^{12} are independently hydrogen or halo; R^1, R^2, R^5 and R^6 are hydrogen; and R^4 is as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group A.

[0060] Another specific embodiment of the MEK compound (A9) is that wherein the compound of Formula I(M) or Formula I(N) is selected from Group A, wherein R^1, R^2, R^5 and R^6 are hydrogen; R^3 is hydrogen, halo, hydroxy, alkoxy, or amino; and R^4 is heterocycloalkyl, heteroaryl, or alkyl substituted with $-NR^8R^{8'}$, wherein R^8 and $R^{8'}$ and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group A.

[0061] Another specific embodiment of embodiment A9 is that wherein R^4 is alkyl substituted with $-NR^8R^{8'}$, wherein R^8 and $R^{8'}$ and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group A. Specifically, the compound is of Formula I(a) or I(b):



I(a);



I(b)

wherein R^3 is as defined in A9; X, R^7, R^8, $R^{8'}$, R^{10}, R^{12}, R^{14}, and R^{16} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group A.

[0062] Another specific embodiment of embodiment A9 is that wherein R^4 is heterocycloalkyl.

[0063] In another specific embodiment of embodiment A9, the compound is that wherein X and R^7 are halo; A is phenylene optionally substituted with R^{10} and R^{12}, wherein R^{10} and R^{12} are independently hydrogen or halo; R^3 is hydroxy; and R^4 is alkyl substituted with $-NR^8R^{8'}$ or R^4 is heterocycloalkyl optionally substituted with one, two, or three groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl,

optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; and wherein m, R^3, R^8, $R^{8'}$, $R^{8''}$, and R^9 are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group A.

[0064] In another embodiment of the MEK compound (A10), the compound of Formula I(M) or Formula I(N) is selected from Group A, wherein

R^4 is

a) hydrogen;

b) $-CH_2N(R^{25})(NR^{25a}R^{25b})$;

c) $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$;

d) $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$;

e) $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$;

f) $-CH_2NR^{25}C(=NH)(R^{25})$;

g) $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$;

h) alkyl;

i) alkyl substituted with one or two $-OR^8$, wherein R^8 is hydrogen, aryl, or alkyl, wherein the alkyl is substituted with one or two hydroxy;

j) alkyl substituted with one, two, or three halo;

k) alkyl substituted with nitro;

l) alkyl substituted with $-S(O)_mR^9$ (wherein m is 0 and R^9 is aryl);

m) alkyl substituted with optionally substituted heterocycloalkyl;

n) alkenyl;

o) $-NR^8R^{8'}$ (wherein R^8 and $R^{8'}$ are independently hydrogen; alkyl; alkenyl; alkyl substituted with one or two hydroxy; alkyl substituted with one or two $-NR^{30}R^{30'}$, wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; alkyl substituted with optionally substituted heteroaryl; or alkyl substituted with optionally substituted cycloalkyl);

p) $-C(O)NR^8R^{8'}$ (wherein R^8 is hydrogen, alkyl, or alkenyl; and $R^{8'}$ is hydrogen; hydroxy; alkyl; alkenyl; alkyl substituted with one or two hydroxy; alkyl substituted with optionally substituted heterocycloalkyl; alkyl substituted with $-NR^{30}R^{30'}$, wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; or optionally substituted alkoxy);

q) $-NR^8C(O)OR^{8'}$ (wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl);

r) alkyl substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen, alkyl, alkenyl, alkynyl, or alkyl substituted with one or two hydroxy; and $R^{8'}$ is hydrogen; hydroxy; alkoxy; alkyl; alkenyl; alkynyl; optionally substituted alkoxy; alkyl substituted with one or two hydroxy; alkyl substituted with one or two alkoxy; alkyl substituted with $-NR^{30}R^{30'}$, wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; alkyl substituted with one or two hydroxy and one or two $-NR^{30}R^{30'}$, wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; alkyl substituted with one, two, three, four, or five halo; alkyl substituted with optionally substituted cycloalkyl; alkyl substituted with optionally substituted aryl; alkyl substituted with one or two hydroxy and one optionally substituted aryl; alkyl substituted with optionally substituted heterocycloalkyl; alkyl substituted with optionally substituted heteroaryl; heteroaryl; aryl; aryl substituted with one or two hydroxy; aryl substituted with one or two alkoxy; aryl substituted with one or two halo; aryl substituted with one or two $-NR^{32}C(O)R^{32a}$, wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl; aryl substituted with $-NR^{34}SO_2R^{34a}$, wherein R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl; cycloalkyl; cycloalkyl substituted with one or two hydroxy; cycloalkyl substituted with one or two hydroxy and one or two hydroxyalkyl; cycloalkyl substituted with one or two alkoxy; cycloalkyl substituted with carboxy; cycloalkyl substituted with $-C(O)NR^{33}R^{33a}$, wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl; alkyl substituted with $-C(O)NR^{33}R^{33a}$, wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl; cycloalkyl substituted with optionally substituted cycloalkyl; heterocycloalkyl; heterocycloalkyl substituted with alkyl; heterocycloalkyl substituted with alkoxycarbonyl; heterocycloalkyl substituted with optionally substituted arylalkyl; heterocycloalkyl substituted with one or two hydroxy; heterocycloalkyl substituted with one or two alkoxy; heterocycloalkyl substituted with one or two hydroxyalkyl; heterocycloalkyl substituted with one or two hydroxy, one or two alkoxy, and one or two hydroxyalkyl; alkyl substituted with optionally substituted aryloxy; alkyl substituted with $-S(O)_nR^{31}$, wherein n is 0 and R^{31} is alkyl; alkyl substituted with carboxy; alkyl substituted with alkoxycarbonyl; or alkyl substituted with $-NR^{32}C(O)R^{32a}$, wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl);

s) $-NR^8C(O)R^{8'}$ (wherein R^8 is hydrogen, alkyl, or alkenyl; and $R^{8'}$ is hydrogen; alkyl; alkyl substituted with one or two hydroxy; alkyl substituted with optionally substituted heterocycloalkyl; alkyl substituted with $-NR^{30}R^{30'}$, wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, hydroxyalkyl, or alkenyl);

t) cycloalkyl;

u) cycloalkyl substituted with $-NR^8R^{8'}$, wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl;

v) heterocycloalkyl;

w) heterocycloalkyl substituted with $-NR^8R^{8'}$, wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl;

x) heterocycloalkyl substituted with one or two alkyl;

y) heterocylcloalkyl substituted with $-C(O)OR^8$, wherein R^8 is alkyl or alkenyl;

z) alkyl substituted with $-NR^8C(O)R^{8'}$ (wherein R^8 is hydrogen, alkyl, or alkenyl and $R^{8'}$ is alkyl; alkenyl; or alkyl substituted with alkoxy, aryl, and one, two, or three halo);

aa) heteroaryl;

bb) heteroaryl substituted with $-NR^8R^{8'}$, wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl; alkyl substituted with optionally substituted heteroaryl;

cc) alkyl substituted with $-NR^8S(O)_2R^9$, wherein R^8 is hydrogen, alkyl, or alkenyl and R^9 is alkyl or alkenyl;

dd) alkyl substituted with $-NR^8C(O)OR^{8'}$, wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl;

ee) alkyl substituted with one aryl and one $-NR^8R^{8'}$, wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl; or

ff) alkyl substituted with one or two $-OR^8$ (wherein R^8 is hydrogen) and one or two $-NR^8R^{8'}$ wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl.

[0065] Even more specifically, R^4 is hydrogen, $-CH_2N(H)(NHCH_3)$, $-CH_2NHC(=NH)(NH_2)$, $-CH_2NHC(=NH)(NHNO_2)$, $-CH_2NHC(=NH)(NHCN)$, $-CH_2NHC(=NH)$(phenyl), $-CH_2NHC(NH_2)=CH(NO_2)$, methyl, ethyl, hydroxymethyl, 2,3-dihydroxypropyl, 3-hydroxy-2-methyl-prop-2-yl, *N*-(1-methoxy-prop-2-yl)-aminomethyl, *N*-(ethoxypropyl)-aminomethyl, *N*-(ethoxyethyl)-aminomethyl, *N*-(2,2-dimethoxyethyl)-aminomethyl, *N*-(methoxyethyl)-aminomethyl, *N*-(isopropxyethyl)-aminomethyl, trifluoromethyl, 1-nitro-ethyl, 1-methyl-1-nitro-ethyl, 1-nitro-propyl, 3-

methyl-1-nitro-butyl, phenylthiomethyl, allyl, ethenyl, 2-methylthio-ethylaminomethyl, 3-methylthio-propylaminomethyl, *N*-(*tert*-butoxycarbonylaminopropyl)-aminomethyl, *N*-(1-carboxyethyl)-aminomethyl, *N*-(1*R*-carboxyethyl)-aminomethyl, *N*-(1*S*-carboxyethyl)-aminomethyl, *N*-(1-methoxycarbonylethyl)-aminomethyl, $-NH_2$, $-NH(CH_2)_3CH_3$, $-NHCH_3$, $-NH(CH_2CH_3)$, $-NHCH_2CH(CH_3)_2$, $-NHCH_2CH_2OH$, $-NHCH_2CH_2CH_2NH_2$, $-N(CH_3)CH_2CH_2$(heteroaryl), $-NHCH_2$(cycloalkyl), $-C(O)NH_2$, $-C(O)NHOH$, $-C(O)NH(OCH_2CH(OH)CH_2OH)$, $-C(O)NH(CH_2)_3CH_3$, $-C(O)NHCH_2CH{=}CH_2$, $-C(O)NHCH_2CH_3$, $-C(O)NHCH_2CH_2OH$, $-C(O)NHCH_2CH(OH)CH_2OH$, $-C(O)NHCH_2CH_2CH(OH)CH_2OH$, $-C(O)NHCH_2CH_2$(piperidin-1-yl), $-C(O)NH$(phenyl), $-C(O)NHCH_2CH_2N(CH_2CH_3)_2$, $-NHC(O)OC(CH_3)_3$, $-NHC(O)OCH_3$, azetidinylmethyl, pyrrolidinylmethyl, 3-hydroxy-pyrrolidinylmethyl, 2-(methoxymethyl)-pyrrolidinylmethyl, 2*S*-(methoxymethyl)-pyrrolidinylmethyl, 2*R*-(methoxymethyl)-pyrrolidinylmethyl, morpholinylmethyl, hydroxypiperidinylmethyl, 4-alkyl-piperazinylmethyl, 4-alkyl-homopiperazinylmethyl, 4-(heterocycloalkyl)-piperidinylmethyl, 4-(dialkylaminoalkyl)-piperazinylmethyl, *N*-hydroxyaminomethyl, *N*-methoxyaminomethyl, *N*-ethoxyaminomethyl, *N*-ethylaminomethyl, 1-(*N*-ethyl-amino)-ethyl, *N,N*-diethylaminomethyl, *N,N*-dimethylaminomethyl, aminomethyl, 1-amino-ethyl, 1*R*-amino-ethyl, 1*S*-amino-ethyl, 1_(methylamino)-ethyl, 1-(*N,N*-dimethylamino)-ethyl, 1-amino-1-methyl-ethyl, 1-aminopropyl, 1*S*-aminopropyl, 1*R*-aminopropyl, *N*-(n-propyl)-aminomethyl, *N*-(isopropyl)-aminomethyl, 2-(*N*-isopropylamino)-ethyl, 3-(*N*-isopropylamino)-2-methyl-prop-2-yl, 1-(*N*-ethyl-amino)-propyl, 1-(*N,N*-diethyl-amino)-propyl, 1-aminobutyl, 1-amino-isobutyl, *N*-(2-aminoethyl)-aminomethyl, *N*-(n-butyl)-aminomethyl, *N*-isobutylaminomethyl, *tert*-butylaminomethyl, 1-(*tert*-butylamino)-ethyl, *sec*-butylaminomethyl, *N*-(2-methyl-but-3-yl)-aminomethyl, *N*-(3,3-dimethyl-butyl)-aminomethyl, *N*-(3-methylbut-3-yl)-aminomethyl, *N*-(2-methylbutyl)-aminomethyl, *N*-(pent-3-yl)-aminomethyl, n-pentylaminomethyl, isopentylaminomethyl, *sec*-pentylaminomethyl, neopentylaminomethyl, *N*-(2,2,4-trimethyl-pent-4-yl)-aminomethyl, *N*-(2-ethyl-butyl)-aminomethyl, *N*-allyl-aminomethyl, 3-methyl-but-1-yn-3-ylaminomethyl, *N*-(2,3-dihydroxypropyloxy)-aminomethyl, *N*-cyclopropylaminomethyl, *N*-cyclobutylaminomethyl, *N*-cyclopentylaminomethyl, *N*-cyclopenten-4-ylaminomethyl, *N*-(1(*R,S*)-hydroxy-cyclopent-2-yl)-aminomethyl, *N*-(1*S*-hydroxy-cyclopent-2-yl)-aminomethyl, *N*-(1*R*-hydroxy-cyclopent-2-yl)-aminomethyl, *N*-(1(*R,S*)-hydroxy-

1-methyl-cyclopent-2-yl)-aminomethyl, *N*-(1*S*-hydroxy-1-methyl-cyclopent-2-yl)-aminomethyl, *N*-(1*R*-hydroxy-1-methyl-cyclopent-2-yl)-aminomethyl, *N*-(3,4-dihydroxy-cyclopentyl)-aminomethyl, *N*-(1-hydroxymethyl-cyclopent-1-yl)-aminomethyl, *N*-(2,3-dihydroxy-4-hydroxymethyl-cyclopentyl)-aminomethyl, *N*-(1(*R,S*)-methoxy-cyclopent-2-yl)-aminomethyl, *N*-(1*S*-methoxy-cyclopent-2-yl)-aminomethyl, *N*-(1*R*-methoxy-cyclopent-2-yl)-aminomethyl, *N*-(1-carboxy-cyclopentyl)-aminomethyl, *N*-cyclohexylaminomethyl, *N*-(1(*R,S*)-hydroxy-cyclohex-2-yl)-aminomethyl, *N*-(*cis*-4-hydroxy-cyclohexyl)-aminomethyl, *N*-(*trans*-4-hydroxy-cyclohexyl)-aminomethyl, 1-[*N*-(*cis*-4-hydroxy-cyclohexyl)-amino]-ethyl, 1-[*N*-(*trans*-4-hydroxy-cyclohexyl)-amino]-ethyl, *N*-(1(*R*)-hydroxy-cyclohex-2-yl)-aminomethyl, *N*-(1(*S*)-hydroxy-cyclohex-2-yl)-aminomethyl, *N*-(1-hydroxymethyl-cyclohexyl)-aminomethyl, *N*-(2-cyclohexyl-cyclohexyl)-aminomethyl, *N*-{(2*R*,3*S*,4*R*,6*R*)-2-(hydroxymethyl)-3,4-dihydroxy-6-methoxy-tetrahydro-2*H*-pyran-5-yl}-aminomethyl, *N*-(cycloheptyl)-aminomethyl, *N*-(cyclooctyl)-aminomethyl, [(1r,3r,5*R*,7*R*)-tricyclo[3.3.1.1~3,7~]dec-2-ylamino]methyl, *N*-[1-(cyclopropylaminocarbonyl)-cyclopentyl]-aminomethyl, $-CH_2NHC(CH_3)_2C(O)NH$(cyclohexyl), $-CH_2NHC(CH_3)_2C(O)NH(CH_2CH_3)$, *N*-(1-benzyloxy-cyclopent-2-yl)-aminomethyl, *N*-(cyclopropylmethyl)-aminomethyl, *N*-(cyclohexylmethyl)-aminomethyl, *N*-(1-cyclohexylethyl)-aminomethyl, *N*-(imidazolyl)-aminomethyl, *N*-(1,3,5-triazinyl)-aminomethyl, *N*-(5-hydroxy-pyrazol-3-yl)-aminomethyl, *N*-(5-methyl-pyrazol-3-yl)-aminomethyl, *N*-(benzimidazolyl)-aminomethyl, *N*-(pyrimidin-2-yl)-aminomethyl, *N*-(pyridin-2-yl)-aminomethyl, *N*-(pyridin-3-yl)-aminomethyl, *N*-(pyridin-4-yl)-aminomethyl, *N*-indan-1-yl-aminomethyl, *N*-indan-2-yl-aminomethyl, phenylaminomethyl, *N*-(2-hydroxyphenyl)-aminomethyl, *N*-(3-hydroxyphenyl)-aminomethyl, *N*-(4-hydroxyphenyl)-aminomethyl, *N*-(2-methoxyphenyl)-aminomethyl, *N*-(3-methoxyphenyl)-aminomethyl, *N*-(4-methoxyphenyl)-aminomethyl, *N*-(2-fluorophenyl)-aminomethyl, *N*-(3-fluorophenyl)-aminomethyl, *N*-(4-fluorophenyl)-aminomethyl, *N*-(2-chlorophenyl)-aminomethyl, *N*-(3-chlorophenyl)-aminomethyl, *N*-(4-chlorophenyl)-aminomethyl, *N*-(3-methylcarbonylamino-phenyl)-aminomethyl, *N*-(4-methylcarbonylamino-phenyl)-aminomethyl, *N*-(2-aminophenyl)-aminomethyl, *N*-(3-aminophenyl)-aminomethyl, *N*-(4-aminophenyl)-aminomethyl, *N*-(2-methylsulfonylaminophenyl)-aminomethyl, *N*-(3-methylsulfonylaminophenyl)-aminomethyl, *N*-(4-methylsulfonylaminophenyl)-aminomethyl, *N*-(2-fluoro-4-hydroxy-phenyl)-aminomethyl, *N*-(3-fluoro-4-hydroxy-

phenyl)-aminomethyl, *N*-(benzyl)-aminomethyl, *N*-(2-hydroxyphenylmethyl)-aminomethyl, *N*-(3-hydroxyphenylmethyl)-aminomethyl, *N*-(4-hydroxyphenylmethyl)-aminomethyl, *N*-(2-(*N*-methylpiperazin-1-yl)-phenylmethyl)-aminomethyl, *N*-(4-alkyl-phenethyl)-aminomethyl, *N*-(1-hydroxy-3-phenyl-prop-2-yl)-aminomethyl, *N*-(pyrrolidin-2-ylmethyl)-aminomethyl, *N*-(*N*-alkyl-pyrrolidinylmethyl)-aminomethyl, *N*-(*N*-alkyl-pyrrolidinylethyl)-aminomethyl, *N*-(pyrrolidinylpropyl)-aminomethyl, *N*-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-aminomethyl, *N*-(tetrahydrofuranylmethyl)-aminomethyl, *N*-(tetrahydro-2*H*-pyran-4-ylmethyl)-aminomethyl, *N*-(tetrahydro-2*H*-pyranylethyl)-aminomethyl, *N*-(piperidin-4-ylmethyl)-aminomethyl, *N*-(*N*-methylpiperidin-4-ylmethyl)-aminomethyl, *N*-(*N*-*tert*-butoxycarbonylpiperidin-4-ylmethyl)-aminomethyl, *N*-(*N*-methylimidazol-4-ylmethyl)-aminomethyl, *N*-(*N*-methylimidazol-5-ylmethyl)-aminomethyl, *N*-[2-(imidazol-4-yl)-ethyl]-aminomethyl, *N*-[3-(imidazolyl)-propyl]-aminomethyl, *N*-(pyridin-3-ylethyl)-aminomethyl, *N*-(pyridin-4-ylethyl)-aminomethyl, *N*-(thien-2-ylethyl)-aminomethyl, *N*-(furan-2-ylethyl)-aminomethyl, *N*-(5-methyl-1,3,4-oxadiazol-2-ylmethyl)-aminomethyl, *N*-(2-indolin-3-ylethyl)-aminomethyl, 2-(*N,N*-dimethylamino)-ethylaminomethyl, 2-(*N,N*-dimethylamino)-1-methyl-ethylaminomethyl, 3-aminopropylaminomethyl, 3-(*N,N*-dimethylamino)-propylaminomethyl, 3-(*N,N*-diethylamino)-propylaminomethyl, *N*-(*N,N*-diisopropylaminoethyl)-aminomethyl, *N*-(*N,N*-dimethylaminobutyl)-aminomethyl, *N*-(3-hydroxypropyl)-aminomethyl, *N*-(2-hydroxypropyl)-aminomethyl, *N*-(1,2-dihydroxypropyl)-aminomethyl, *N*-(1-amino-2-hydroxy-prop-3-yl)-aminomethyl, *N*-(*N*-ethoxycarbonyl-piperidin-4-yl)-aminomethyl, *N*-(*N*-benzylpiperidin-4-yl)-aminomethyl, *N*-(homopiperidin-3-yl)-aminomethyl, *N*-(*N*-benzylpyrrolidin-3-yl)-aminomethyl, *N*-(*N*-ethylpiperidin-3-yl)aminomethyl, 2,2,2-trifluoroethylaminomethyl, 3,3,3-trifluoropropylaminomethyl, 2,2,3,3,3-pentafluoropropylaminomethyl, $-CH_2N(CH_2CH_2OH)_2$, $-CH_2N(CH_3)(CH_2CH_2OH)$, $-CH_2NH(CH_2CH_2OH)$, $-CH_2NH(CH_2CH_2CH_2CH_2OH)$, $-CH_2N(CH_3)$(*N*-methyl-pyrrolidin-3-yl), $-CH_2NH(C(CH_3)_2CH_2OH)$, $-NHC(O)CH(CH_3)_2$, $-NHC(O)CH_2N(CH_2CH_3)_2$, $-NHC(O)CH_2NH(CH_3)$, -NHC(O)H, $-NHC(O)CH_2CH(OH)CH_2OH$, $-NHC(O)CH_2NH_2$, $-NHC(O)CH_2N(CH_2CH_2OH)_2$, $-NHC(O)CH_2CH_2N(CH_2CH_2OH)_2$, $-NHC(O)CH_2$(4-alkyl-piperazinyl), $-NHC(O)CH_2$(piperidinyl), *N*-(phenyloxyethyl)-aminomethyl, cyclopentyl, 1-amino-cyclopentyl, (*cis,trans*)-2-amino-cyclopentyl, (*cis,trans*)-2-amino-cyclopentyl, *cis*-2-amino-cyclopentyl, *trans*-2-amino-cyclopentyl, (*cis,trans*)-2-hydroxy-cyclohexyl,

cis-2-hydroxy-cyclohexyl, *trans*-2-hydroxy-cyclohexyl, (*cis,trans*)-2-amino-cyclohexyl, *cis*-2-amino-cyclohexyl, *trans*-2-amino-cyclohexyl, azetidin-3-yl, pyrrolidinyl, *N*-alkyl-pyrrolidinyl, 3-(dialkylamino)-pyrrolidinyl, piperidinyl, 2-methyl-piperidin-6-yl, *N-tert*-butoxycarbonylpiperidin-2-yl, piperazinyl, $-CH_2NHC(O)CH_3$, $-CH(CH_3)NHC(O)CH_3$, $-CH(CH_3)NHC(O)C(OCH_3)(CF_3)$phenyl, pyrrol-1-yl, pyrrol-2-yl, pyrrol-3-yl, imidazol-1-yl, imidazol-2-yl, imidazol-4-yl, imidazol-5-yl, *N*-methyl-imidazol-2-yl, 5-methyl-imidazol-2-yl, 1,2,4-triazol-3-yl, thiazol-2-yl, 2-aminopyrimidin-3-yl, pyridinyl, benzimidazolyl, imidazol-1-ylmethyl, imidazol-2-ylmethyl, triazolylmethyl, (5-amino-3-methylpyrazol-1-yl)-methyl, phenoxymethyl, methylsulfonylaminomethyl, 1-(methoxycarbonylamino)-ethyl, 1-amino-1-phenyl-methyl, or 1-amino-3-hydroxy-propyl.

[0066] A more specific embodiment of embodiment A10 is that wherein X and R^7 are halo; A is phenylene optionally substituted with R^{10} and R^{12}, wherein R^{10} and R^{12} are independently hydrogen or halo; R^1, R^2, R^5 and R^6 are hydrogen; and R^3 is hydrogen, halo, hydroxy, alkoxy, or amino.

[0067] A more specific embodiment of embodiment A10 is that wherein R^3 is hydrogen and R^4 is

a) hydrogen;

b) $-NR^8R^{8'}$ (wherein R^8 and $R^{8'}$ are independently hydrogen; alkyl; alkenyl; alkyl substituted with one or two hydroxy; alkyl substituted with one or two $-NR^{30}R^{30'}$, wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; alkyl substituted with optionally substituted heteroaryl; or alkyl substituted with optionally substituted cycloalkyl);

c) $-C(O)NR^8R^{8'}$ (wherein R^8 is hydrogen, alkyl, or alkenyl; and $R^{8'}$ is hydrogen; hydroxy; alkyl; alkenyl; alkyl substituted with one or two hydroxy; alkyl substituted with heterocycloalkyl; alkyl substituted with $-NR^{30}R^{30'}$, wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; or optionally substituted alkoxy);

d) $-NR^8C(O)OR^{8'}$ (wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl);

e) $-NR^8C(O)R^{8'}$ (wherein R^8 is hydrogen, alkyl, or alkenyl; and $R^{8'}$ is hydrogen; alkyl; alkyl substituted with one or two hydroxy; alkyl substituted with optionally substituted heterocycloalkyl; alkyl substituted with $-NR^{30}R^{30'}$, wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, hydroxyalkyl, or alkenyl);

f) alkyl;

g) alkyl substituted with one or two -OR^8 (wherein R^8 is hydrogen);

h) alkyl substituted with -$NR^8R^{8'}$ (wherein R^8 is hydrogen, alkyl, alkenyl, alkynyl, or alkyl substituted with one or two hydroxy; and $R^{8'}$ is hydrogen; alkyl; alkenyl; alkynyl; alkyl substituted with one or two hydroxy; heterocycloalkyl substituted with alkyl; or alkyl substituted with -$NR^{30}R^{30'}$, wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl);

i) heterocycloalkyl; or

j) heterocycloalkyl substituted with -$NR^8R^{8'}$ (wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl).

[0068] Even more specifically, R^3 is hydrogen and R^4 is hydrogen, hydroxymethyl, -NH_2, -$NH(CH_2)_3CH_3$, -$NHCH_3$, -$NH(CH_2CH_3)$, -$NHCH_2CH(CH_3)_2$, -$NHCH_2CH_2OH$, -$NHCH_2CH_2CH_2NH_2$, -$N(CH_3)CH_2CH_2$(pyridin-2-yl), -$NHCH_2$(cyclopropyl), -$NHCH_2$(cyclopentyl), -$NHCH_2$(cyclohexyl), -C(O)NHOH, -$C(O)NH(OCH_2CH(OH)CH_2OH)$, -$C(O)NH(CH_2)_3CH_3$, -$C(O)NHCH_2CH{=}CH_2$, -$C(O)NHCH_2CH_3$, -$C(O)NHCH_2CH_2OH$, -$C(O)NHCH_2CH(OH)CH_2OH$, -$C(O)NHCH_2CH_2CH(OH)CH_2OH$, -$C(O)NHCH_2CH_2$(piperidin-1-yl), -C(O)NH(phenyl), -$C(O)NHCH_2CH_2N(CH_2CH_3)_2$, *N*-(isopropyl)-aminomethyl, *N,N*-dimethylaminomethyl, *N*-(2-aminoethyl)-aminomethyl, -$NHC(O)OC(CH_3)_3$, -$NHC(O)OCH_3$, -$NHC(O)CH(CH_3)_2$, -$NHC(O)CH_2NH_2$, -$NHC(O)CH_2N(CH_2CH_3)_2$, -$NHC(O)CH_2NH(CH_3)$, -NHC(O)H, -$NHC(O)CH_2CH(OH)CH_2OH$, -$NHC(O)CH_2N(CH_2CH_2OH)_2$, -$NHC(O)CH_2CH_2N(CH_2CH_2OH)_2$, -$NHC(O)CH_2$(4-alkyl-piperazinyl), -$NHC(O)CH_2$(piperidinyl), pyrrolidinyl, 3-(dialkylamino)-pyrrolidinyl, piperidinyl, 2-methyl-piperidin-6-yl, *N*-methylpiperidin-2-yl, or piperazin-2-yl.

[0069] A more specific embodiment of embodiment A10 is that wherein R^3 is alkoxy and R^4 is alkyl substituted with -$NR^8R^{8'}$ (wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl). More specifically, R^3 is methoxy and R^4 is alkyl substituted with -$NR^8R^{8'}$ (wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl).

[0070] A more specific embodiment of embodiment A10 is that wherein R^3 is halo and R^4 is alkyl substituted with -$NR^8R^{8'}$ (wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl). More specifically, R^3 is fluoro and R^4 is alkyl substituted with -$NR^8R^{8'}$ (wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl).

[0071] A more specific embodiment of embodiment A10 is that wherein R^3 is amino and R^4 is alkyl substituted with $-NR^8R^{8'}$ (wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl).

[0072] A more specific embodiment of embodiment A10 is that wherein R^3 is hydroxy and R^4 is

a) hydrogen;

b) $-CH_2N(R^{25})(NR^{25a}R^{25b})$;

c) $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$;

d) $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$;

e) $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$;

f) $-CH_2NR^{25}C(=NH)(R^{25})$;

g) $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$;

h) alkyl;

i) alkenyl;

j) alkyl substituted with one or two $-OR^8$, wherein R^8 is hydrogen, aryl, or alkyl wherein the alkyl is substituted with one or two hydroxy;

k) alkyl substituted with one, two, or three halo;

l) alkyl substituted with nitro;

m) alkyl substituted with $-S(O)_mR^9$ (wherein m is 0 and R^9 is aryl);

n) alkyl substituted with optionally substituted heterocycloalkyl;

o) alkyl substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen, alkyl, alkenyl, alkynyl, or alkyl substituted with one or two hydroxy; and $R^{8'}$ is hydrogen; hydroxy; alkoxy; alkyl; alkenyl; alkynyl; optionally substituted alkoxy; alkyl substituted with one or two hydroxy; alkyl substituted with $-NR^{30}R^{30'}$ wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; alkyl substituted with one or two hydroxy and one or two $-NR^{30}R^{30'}$ wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; heterocycloalkyl substituted with alkyl, alkoxycarbonyl, or optionally substituted arylalkyl; alkyl substituted with one, two, three, four, or five halo; alkyl substituted with optionally substituted cycloalkyl; alkyl substituted with optionally substituted aryl; alkyl substituted with one or two hydroxy and one optionally substituted aryl; alkyl substituted with optionally substituted heterocycloalkyl; alkyl substituted with optionally substituted heteroaryl; heteroaryl; aryl; aryl substituted with one or two hydroxy; aryl substituted with one or two

alkoxy; aryl substituted with one or two halo; aryl substituted with one or two $-NR^{32}C(O)R^{32a}$ wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl; aryl substituted with $-NR^{34}SO_2R^{34a}$ wherein R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl; cycloalkyl; cycloalkyl substituted with one or two hydroxy; cycloalkyl substituted with one or two hydroxy and one or two hydroxyalkyl; cycloalkyl substituted with one or two alkoxy; cycloalkyl substituted with carboxy; cycloalkyl substituted with $-C(O)NR^{33}R^{33a}$ wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl; cycloalkyl substituted with optionally substituted cycloalkyl; heterocycloalkyl; heterocycloalkyl substituted with one or two hydroxy; heterocycloalkyl substituted with one or two alkoxy; heterocycloalkyl substituted with one or two hydroxyalkyl; heterocycloalkyl substituted with one or two hydroxy, one or two alkoxy, and one or two hydroxyalkyl; alkyl substituted with $-C(O)NR^{33}R^{33a}$, wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl; alkyl substituted with optionally substituted aryloxy; alkyl substituted with $-S(O)_nR^{31}$, wherein n is 0 and R^{31} is alkyl; alkyl substituted with carboxy; alkyl substituted with alkoxycarbonyl; or alkyl substituted with $-NR^{32}C(O)R^{32a}$, wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl);

p) heterocycloalkyl;

q) $-C(O)NR^8R^{8'}$ (wherein R^8 is hydrogen, alkyl, or alkenyl; and $R^{8'}$ is hydrogen; alkyl; alkyl; alkenyl; or substituted with one or two hydroxy;);

r) alkyl substituted with $-NR^8C(O)R^{8'}$ (wherein R^8 is hydrogen, alkyl, or alkenyl and $R^{8'}$ is alkyl; alkenyl; or alkyl substituted with alkoxy, aryl, and one, two, or three halo);

s) cycloalkyl;

t) cycloalkyl substituted with $-NR^8R^{8'}$, wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl;

u) cycloalkyl substituted with $-C(O)NR^{33}R^{33a}$, wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl;

v) heterocycloalkyl;

w) heterocycloalkyl substituted with one or two alkyl;

x) heterocylcloalkyl substituted with $-C(O)OR^8$, wherein R^8 is alkyl or alkenyl;

y) heteroaryl;

z) heteroaryl optionally substituted with $-NR^8R^{8'}$, wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl;

aa) alkyl substituted with optionally substituted heteroaryl;

bb) alkyl substituted with $-NR^8S(O)_2R^9$, wherein R^8 is hydrogen, alkyl, or alkenyl and R^9 is alkyl or alkenyl;

cc) alkyl substituted with $-NR^8C(O)OR^{8'}$, wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl;

dd) alkyl substituted with one aryl and one $-NR^8R^{8'}$, wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl; or

ee) alkyl substituted with one or two $-OR^8$ (wherein R^8 is hydrogen) and one or two $-NR^8R^{8'}$ wherein R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl.

[0073] Even more specifically in embodiment (A10), R^3 is hydroxy and R^4 is hydrogen, $-CH_2N(H)(NHCH_3)$, $-CH_2NHC(=NH)(NH_2)$, $-CH_2NHC(=NH)(NHNO_2)$, $-CH_2NHC(=NH)(NHCN)$, $-CH_2NHC(=NH)(phenyl)$, $-CH_2NHC(NH_2)=CH(NO_2)$, methyl, ethyl, hydroxymethyl, 2,3-dihydroxypropyl, 3-hydroxy-2-methyl-prop-2-yl, *N*-(1-methoxy-prop-2-yl)-aminomethyl, *N*-(ethoxypropyl)-aminomethyl, *N*-(ethoxyethyl)-aminomethyl, *N*-(2,2-dimethoxyethyl)-aminomethyl, *N*-(methoxyethyl)-aminomethyl, *N*-(isopropxyethyl)-aminomethyl, trifluoromethyl, 1-nitro-ethyl, 1-methyl-1-nitro-ethyl, 1-nitro-propyl, 3-methyl-1-nitro-butyl, phenylthiomethyl, allyl, ethenyl, 2-methylthio-ethylaminomethyl, 3-methylthio-propylaminomethyl, *N*-(*tert*-butoxycarbonylaminopropyl)-aminomethyl, *N*-(1-carboxyethyl)-aminomethyl, *N*-(1*R*-carboxyethyl)-aminomethyl, *N*-(1*S*-carboxyethyl)-aminomethyl, *N*-(1-methoxycarbonylethyl)-aminomethyl, azetidinylmethyl, pyrrolidinylmethyl, 3-hydroxy-pyrrolidinylmethyl, 2-(methoxymethyl)-pyrrolidinylmethyl, 2*S*-(methoxymethyl)-pyrrolidinylmethyl, 2*R*-(methoxymethyl)-pyrrolidinylmethyl, morpholinylmethyl, 4-hydroxypiperidinylmethyl, 4-methyl-piperazinylmethyl, 4-methyl-homopiperazinylmethyl, 4-(piperidinyl)-piperidinylmethyl, 4-[2-(*N,N*-diethylamino)-ethyl]-piperazinylmethyl, *N*-hydroxyaminomethyl, *N*-methoxyaminomethyl, *N*-ethoxyaminomethyl, *N*-ethylaminomethyl, 1-(*N*-ethyl-amino)-ethyl, *N,N*-diethylaminomethyl, *N,N*-dimethylaminomethyl, aminomethyl, 1-amino-ethyl, 1*R*-amino-ethyl, 1*S*-amino-ethyl, 1-(methylamino)-ethyl, 1-(*N,N*-dimethylamino)-ethyl, 1-amino-1-methyl-ethyl, 1-aminopropyl, 1*S*-aminopropyl, 1*R*-aminopropyl, *N*-(n-propyl)-aminomethyl, *N*-(isopropyl)-aminomethyl, 2-(*N*-isopropylamino)-ethyl, 3-(*N*-

isopropylamino)-2-methyl-prop-2-yl, 1-(*N*-ethyl-amino)-propyl, 1-(*N*,*N*-diethyl-amino)-propyl, 1-aminobutyl, 1-amino-isobutyl, *N*-(n-butyl)-aminomethyl, *N*-isobutylaminomethyl, *tert*-butylaminomethyl, 1-(*tert*-butylamino)-ethyl, *sec*-butylaminomethyl, *N*-(2-methyl-but-3-yl)-aminomethyl, *N*-(3,3-dimethyl-butyl)-aminomethyl, *N*-(3-methylbut-3-yl)-aminomethyl, *N*-(2-methylbutyl)-aminomethyl, *N*-(pent-3-yl)-aminomethyl, n-pentylaminomethyl, isopentylaminomethyl, *sec*-pentylaminomethyl, neopentylaminomethyl, *N*-(2,2,4-trimethyl-pent-4-yl)-aminomethyl, *N*-(2-ethyl-butyl)-aminomethyl, *N*-allyl-aminomethyl, 3-methyl-but-1-yn-3-ylaminomethyl, *N*-(2,3-dihydroxypropyloxy)-aminomethyl, *N*-cyclopropylaminomethyl, *N*-cyclopentylaminomethyl, *N*-cyclopenten-4-ylaminomethyl, *N*-(1(*R,S*)-hydroxy-cyclopent-2-yl)-aminomethyl, *N*-(1*S*-hydroxy-cyclopent-2-yl)-aminomethyl, *N*-(1*R*-hydroxy-cyclopent-2-yl)-aminomethyl, *N*-(1(*R,S*)-hydroxy-1-methyl-cyclopent-2-yl)-aminomethyl, *N*-(1*S*-hydroxy-1-methyl-cyclopent-2-yl)-aminomethyl, *N*-(1*R*-hydroxy-1-methyl-cyclopent-2-yl)-aminomethyl, *N*-(3,4-dihydroxy-cyclopentyl)-aminomethyl, *N*-(1-hydroxymethyl-cyclopent-1-yl)-aminomethyl, *N*-(2,3-dihydroxy-4-hydroxymethyl-cyclopentyl)-aminomethyl, *N*-(1(*R,S*)-methoxy-cyclopent-2-yl)-aminomethyl, *N*-(1*S*-methoxy-cyclopent-2-yl)-aminomethyl, *N*-(1*R*-methoxy-cyclopent-2-yl)-aminomethyl, *N*-(1-carboxy-cyclopentyl)-aminomethyl, *N*-cyclohexylaminomethyl, *N*-(1(*R,S*)-hydroxy-cyclohex-2-yl)-aminomethyl, *N*-(1(*R*)-hydroxy-cyclohex-2-yl)-aminomethyl, *N*-(1(*S*)-hydroxy-cyclohex-2-yl)-aminomethyl, *N*-(*cis*-4-hydroxy-cyclohexyl)-aminomethyl, *N*-(*trans*-4-hydroxy-cyclohexyl)-aminomethyl, 1-[*N*-(*cis*-4-hydroxy-cyclohexyl)-amino]-ethyl, 1-[*N*-(*trans*-4-hydroxy-cyclohexyl)-amino]-ethyl, *N*-(1-hydroxymethyl-cyclohexyl)-aminomethyl, *N*-(2-cyclohexyl-cyclohexyl)-aminomethyl, *N*-{(2*R*,3*S*,4*R*,6*R*)-2-(hydroxymethyl)-3,4-dihydroxy-6-methoxy-tetrahydro-2*H*-pyran-5-yl}-aminomethyl, *N*-(cycloheptyl)-aminomethyl, *N*-(cyclooctyl)-aminomethyl, [(1r,3r,5*R*,7*R*)-tricyclo[3.3.1.1~3,7~]dec-2-ylamino]methyl, *N*-(1-benzyloxy-cyclopent-2-yl)-aminomethyl, *N*-[1-(cyclopropylaminocarbonyl)-cyclopentyl]-aminomethyl, $-CH_2NHC(CH_3)_2C(O)NH$(cyclohexyl), $-CH_2NHC(CH_3)_2C(O)NH(CH_2CH_3)$, *N*-(cyclopropylmethyl)-aminomethyl, *N*-(cyclohexylmethyl)-aminomethyl, *N*-(1-cyclohexylethyl)-aminomethyl, *N*-(imidazolyl)-aminomethyl, *N*-(1,3,5-triazinyl)-aminomethyl, *N*-(5-hydroxy-pyrazol-3-yl)-aminomethyl, *N*-(5-methyl-pyrazol-3-yl)-aminomethyl, *N*-(benzimidazolyl)-aminomethyl, *N*-(pyrimidin-2-yl)-aminomethyl,

N-(pyridin-2-yl)-aminomethyl, *N*-(pyridin-3-yl)-aminomethyl, *N*-(pyridin-4-yl)-aminomethyl, *N*-indan-1-yl-aminomethyl, *N*-indan-2-yl-aminomethyl, phenylaminomethyl, *N*-(2-hydroxyphenyl)-aminomethyl, *N*-(3-hydroxyphenyl)-aminomethyl, *N*-(4-hydroxyphenyl)-aminomethyl, *N*-(2-methoxyphenyl)-aminomethyl, *N*-(3-methoxyphenyl)-aminomethyl, *N*-(4-methoxyphenyl)-aminomethyl, *N*-(2-fluorophenyl)-aminomethyl, *N*-(3-fluorophenyl)-aminomethyl, *N*-(4-fluorophenyl)-aminomethyl, *N*-(2-chlorophenyl)-aminomethyl, *N*-(3-chlorophenyl)-aminomethyl, *N*-(4-chlorophenyl)-aminomethyl, *N*-(3-methylcarbonylamino-phenyl)-aminomethyl, *N*-(4-methylcarbonylamino-phenyl)-aminomethyl, *N*-(2-aminophenyl)-aminomethyl, *N*-(3-aminophenyl)-aminomethyl, *N*-(4-aminophenyl)-aminomethyl, *N*-(2-methylsulfonylaminophenyl)-aminomethyl, *N*-(3-methylsulfonylaminophenyl)-aminomethyl, *N*-(4-methylsulfonylaminophenyl)-aminomethyl, *N*-(2-fluoro-4-hydroxy-phenyl)-aminomethyl, *N*-(3-fluoro-4-hydroxy-phenyl)-aminomethyl, *N*-(benzyl)-aminomethyl, *N*-(2-hydroxyphenylmethyl)-aminomethyl, *N*-(3-hydroxyphenylmethyl)-aminomethyl, *N*-(4-hydroxyphenylmethyl)-aminomethyl, *N*-(2-(*N*-methylpiperazin-1-yl)-phenylmethyl)-aminomethyl, *N*-(4-methyl-phenethyl)-aminomethyl, *N*-(1-hydroxy-3-phenyl-prop-2-yl)-aminomethyl, *N*-(pyrrolidin-2-ylmethyl)-aminomethyl, *N*-(*N*-ethyl-pyrrolidinylmethyl)-aminomethyl, *N*-(*N*-methyl-pyrrolidin-2-ylethyl)-aminomethyl, *N*-(pyrrolidinylpropyl)-aminomethyl, *N*-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-aminomethyl, *N*-(tetrahydrofuranylmethyl)-aminomethyl, *N*-(tetrahydro-2*H*-pyran-4-ylmethyl)-aminomethyl, *N*-(tetrahydro-2*H*-pyranylethyl)-aminomethyl, *N*-(piperidin-4-ylmethyl)-aminomethyl, *N*-(*N*-methylpiperidin-4-ylmethyl)-aminomethyl, *N*-(*N*-*tert*-butoxycarbonylpiperidin-4-ylmethyl)-aminomethyl, *N*-(*N*-methylimidazol-5-ylmethyl)-aminomethyl, *N*-(*N*-methylimidazol-4-ylmethyl)-aminomethyl, *N*-[2-(imidazol-4-yl)-ethyl]-aminomethyl, *N*-[3-(imidazolyl)-propyl]-aminomethyl, *N*-(pyridin-3-ylethyl)-aminomethyl, *N*-(pyridin-4-ylethyl)-aminomethyl, *N*-(thien-2-ylethyl)-aminomethyl, *N*-(furan-2-ylethyl)-aminomethyl, *N*-(5-methyl-1,3,4-oxadiazol-2-ylmethyl)-aminomethyl, *N*-(2-indolin-3-ylethyl)-aminomethyl, 2-(*N,N*-dimethylamino)-ethylaminomethyl, 2-(*N,N*-dimethylamino)-1-methyl-ethylaminomethyl, 3-aminopropylaminomethyl, 3-(*N,N*-dimethylamino)-propylaminomethyl, 3-(*N,N*-diethylamino)-propylaminomethyl, *N*-(*N,N*-diisopropylaminoethyl)-aminomethyl, *N*-(*N,N*-dimethylaminobutyl)-aminomethyl, 3-hydroxypropylaminomethyl, *N*-(1,2-dihydroxypropyl)-aminomethyl, *N*-(1-amino-2-hydroxy-prop-3-yl)-aminomethyl, *N*-(*N*-

ethoxycarbonyl-piperidin-4-yl)-aminomethyl, *N*-(*N*-benzylpiperidin-4-yl)-aminomethyl, *N*-(homopiperidin-3-yl)-aminomethyl, *N*-(*N*-benzylpyrrolidin-3-yl)-aminomethyl, *N*-(*N*-ethylpiperidin-3-yl)aminomethyl, 2,2,2-trifluoroethylaminomethyl, 3,3,3-trifluoropropylaminomethyl, 2,2,3,3,3-pentafluoropropylaminomethyl, $-CH_2N(CH_2CH_2OH)_2$, $-CH_2N(CH_3)(CH_2CH_2OH)$, $-CH_2NH(CH_2CH_2OH)$, $-CH_2NH(CH_2CH_2CH_2CH_2OH)$, $-CH_2NH(C(CH_3)_2CH_2OH)$, $-CH_2N(CH_3)$(*N*-methyl-pyrrolidin-3-yl), $-C(O)NH_2$, $-C(O)NHCH_2CH{=}CH_2$, $-C(O)NHCH_2CH(OH)CH_2OH$, *N*-(phenyloxyethyl)-aminomethyl, $-CH_2NHC(O)CH_3$, $-CH(CH_3)NHC(O)CH_3$, $-CH(CH_3)NHC(O)C(OCH_3)(CF_3)$phenyl, cyclopentyl, 1-amino-cyclopentyl, (*cis,trans*)-2-amino-cyclopentyl, (*cis,trans*)-2-amino-cyclopentyl, *cis*-2-amino-cyclopentyl, *trans*-2-amino-cyclopentyl, (*cis,trans*)-2-hydroxy-cyclohexyl, *cis*-2-hydroxy-cyclohexyl, *trans*-2-hydroxy-cyclohexyl, (*cis,trans*)-2-amino-cyclohexyl, *cis*-2-amino-cyclohexyl, *trans*-2-amino-cyclohexyl, azetidin-3-yl, pyrrolidinyl, *N*-methyl-pyrrolidin-2-yl, *N*-ethyl-pyrrolidin-2-yl, 3-(dimethylamino)-pyrrolidinyl, piperidinyl, 2-methyl-piperidin-6-yl, *N*-methylpiperidin-2-yl, *N*-*tert*-butoxycarbonylpiperidin-2-yl, piperazin-2-yl, pyrrol-1-yl, pyrrol-2-yl, pyrrol-3-yl, imidazol-1-yl, imidazol-2-yl, imidazol-4-yl, imidazol-5-yl, *N*-methyl-imidazol-2-yl, 5-methyl-imidazol-2-yl, 1,2,4-triazol-3-yl, thiazol-2-yl, 2-aminopyrimidin-3-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, benzimidazolyl, imidazol-1-ylmethyl, imidazol-2-ylmethyl, triazol-1-ylmethyl, (5-amino-3-methyl-pyrazol-3-yl)-methyl, phenoxymethyl, 2-hydroxyethyloxymethyl, methylsulfonylaminomethyl, 1-(methoxycarbonylamino)-ethyl, 1-amino-1-phenyl-methyl, or 1-amino-3-hydroxy-propyl.

[0074] Another specific embodiment of the MEK compound (A11) is that wherein the compound of Formula I(M) or Formula I(N) is selected from Group A, wherein R^3 and R^4 together with the carbon to which they are attached, form -C(O)- or -C(=NOH)-. More specifically, X and R^7 are halo; A is phenylene optionally substituted with R^{10} and R^{12}, wherein R^{10} and R^{12} are each independently hydrogen or halo; R^1, R^2, R^5 and R^6 are hydrogen; and R^3 and R^4 together with the carbon to which they are attached form -C(O)- or -C(=NOH)-.

[0075] Another specific embodiment of the MEK compound (A12) is that wherein the compound of Formula I(M) or Formula I(N) is selected from Group A, wherein X and R^7 are halo; A is phenylene optionally substituted with R^{10} and R^{12}, wherein R^{10} and R^{12} are independently hydrogen or halo; and R^1, R^2, R^4, R^5 and R^6 are hydrogen.

[0076] Another specific embodiment of the MEK compound (A13) is that wherein the compound of Formula I(M) or Formula I(N) is selected from Group A, wherein A is phenylene.

[0077] Another specific embodiment of the MEK compound (A14) is that wherein the compound of Formula I(M) or Formula I(N) is selected from Group A, wherein R^1 is hydrogen and R^2 is alkyl substituted with $-NR^8R^{8'}$, wherein R^8 and $R^{8'}$ and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group A.

[0078] Another specific embodiment of the MEK compound (A15) is that wherein the compound of Formula I(M) or Formula I(N) is selected from Group A, wherein A is phenylene; R^7 is iodo or bromo; X is fluoro or chloro; and R^1, R^2, R^5, and R^6 are hydrogen; and R^{10}, R^{12}, R^{14}, and R^{16} are independently hydrogen or fluoro. More specifically, R^{10} is 3-fluoro and R^{12}, R^{14}, and R^{16} are hydrogen or halo; R^{10} is 3-fluoro, R^{12} is 4-fluoro, and R^{14} and R^{16} are hydrogen; R^{10} is 4-fluoro, R^{12} is 5-fluoro, and R^{14} and R^{16} are hydrogen; R^{10} is 4-fluoro, R^{12} is 6-fluoro, and R^{14} and R^{16} are hydrogen; or R^{12} is 4-fluoro and R^{10}, R^{14}, and R^{16} are hydrogen.

[0079] Another embodiment of the MEK compound is a compound of Formula I(M) or Formula I(N) selected form Group A, wherein R^3 is hydroxy and R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. Specifically, R^3 is hydroxy and R^4 is heterocycloalkyl or alkyl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with groups independently selected from hydroxy and alkyl).

[0080] In another embodiment of the MEK compound (B1), the compound of Formula I(M) or Formula I(N) is selected from Group B, wherein all groups are as defined in the compound of Formula I(M) or Formula I(N).

[0081] In another embodiment of the MEK compound (B2), X and R^7 are halo; and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. Specifically, X is fluoro or chloro and R^7 is iodo or bromo.

[0082] In another embodiment of the MEK compound (B3), the compound is selected from Group B, wherein R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$ and R^4 is as defined in the compound of Formula I(M) or Formula I(N); or R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH); and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. More specifically, R^1, R^2, R^5 and R^6 are hydrogen; and X and R^7 are halo.

[0083] In another embodiment of the MEK compound (B4), the compound is selected from Group B, wherein R^3 and R^4 are independently halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or R^3 and R^4 together

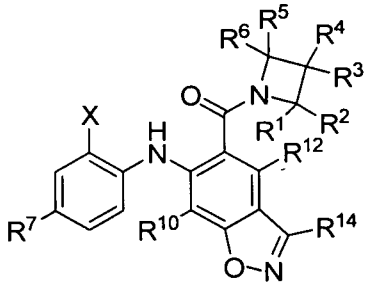
with the carbon to which they are attached form C(O) or C(=NOH); and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. More specifically, R^1, R^2, R^5 and R^6 are hydrogen; and X and R^7 are halo.

[0084] In another embodiment of the MEK compound (B5), A is heteroarylene selected from thien-diyl, benzo[*d*]isoxazol-diyl, benzo[*d*]isothiazol-diyl, 1*H*-indazol-diyl (optionally substituted at the N1 position with R^{19}, wherein R^{19} is as defined in the compound of Formula I(M) for a compound of Group B), benzo[*d*]oxazol-diyl, benzo[*d*]thiazol-diyl, 1*H*-benzo[*d*]imidazol-diyl (optionally substituted at the N1 position with R^{19}, wherein R^{19} is as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B), 1*H*-benzo[*d*][1,2,3]triazol-diyl (optionally substituted at the N1 position with R^{19}, wherein R^{19} is as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B), imidazo[1,2-*a*]pyridin-diyl, cinnolin-diyl, quinolin-diyl, pyridin-diyl, 1-oxido-pyridin-diyl, [1,2,4]triazolo[4,3-a]pyridin-diyl, and 2,3-dihydroimidazo[1,2-a]pyridin-diyl; and A is further optionally substituted with one, two, three, or four groups selected from R^{10}, R^{12}, R^{14}, and R^{16}, wherein R^{10}, R^{12}, R^{14}, and R^{16} and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. More specifically, A is selected from thien-3,4-diyl, benzo[*d*]isoxazol-5,6-diyl, benzo[*d*]isothiazol-5,6-diyl, 1*H*-indazol-5,6-diyl (optionally substituted at the N1 position with R^{19}, wherein R^{19} is alkyl or alkenyl), benzo[*d*]oxazol-5,6-diyl, benzo[*d*]thiazol-5,6-diyl, 1*H*-benzo[d]imidazol-5,6-diyl (optionally substituted at the N1 position with R^{19}, wherein R^{19} is alkyl or alkenyl), 1*H*-benzo[*d*][1,2,3]triazol-5,6-diyl (optionally substituted at the N1 position with R^{19}, wherein R^{19} is alkyl or alkenyl), imidazo[1,2-*a*]pyridin-5,6-diyl, cinnolin-6,7-diyl, quinolin-6,7-diyl, pyridin-3,4-diyl, 1-oxido-pyridin-3,4-diyl, [1,2,4]triazolo[4,3-a]pyridin-6,7-diyl, and 2,3-dihydroimidazo[1,2-a]pyridin-6,7-diyl.

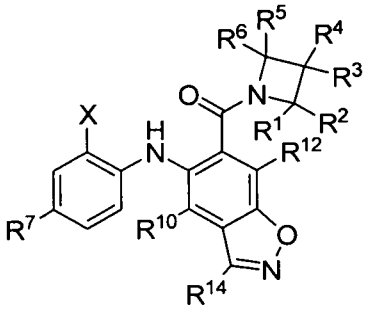
[0085] In another embodiment of the MEK compound (B6), the compound of Formula I(M) or Formula I(N) is selected from Group B, wherein A is thien-diyl and X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, and R^{12} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. More specifically, A is thien-3,4-diyl; R^{10} and R^{12} are hydrogen; X and R^7 are halo; and R^1, R^2, R^5, and R^6 are hydrogen. Even more specifically, X is fluoro or chloro; R^7 is iodo or bromo; R^3 is hydrogen or hydroxy; and R^4 is $-NR^8R^{8'}$ (wherein R^8 and $R^{8'}$ are independently hydrogen or alkyl), heterocycloalkyl, heteroaryl (optionally substituted with alkyl), or alkyl, wherein the alkyl is optionally

substituted with -$NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl).

[0086] In another embodiment, the MEK compound (B7), the compound is of Formula I(c) or I(d)



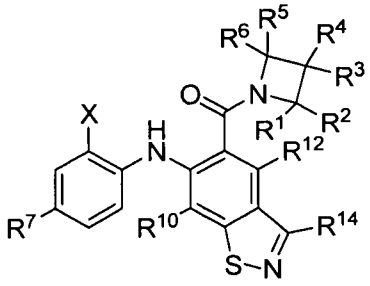
I(c);



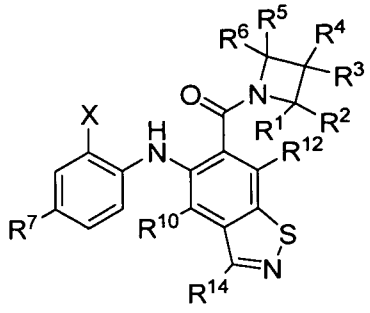
I(d);

wherein X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{12} and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. More specifically, R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the compound of Formula I(M) or Formula I(N) for Group B; and R^{10}, R^{12}, and R^{14} are independently hydrogen, halo, or alkyl. Even more specifically, X is fluoro or chloro and R^7 is iodo or bromo; R^{10} is hydrogen or halo, more specifically hydrogen or fluoro; R^{12} is hydrogen; R^{14} is hydrogen or alkyl; and R^3 is hydroxy. Yet even more specifically, R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with -$NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl wherein the cycloalkyl is optionally substituted with groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. Yet even more specifically, R^4 is piperidinyl, pyrrolidinyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-(3,4-*cis*-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-*cis*-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-*cis*-dihydroxy-cyclopentylamino)-ethyl.

[0087] In another embodiment of the MEK compound (B8), the compound is of Formula I(e) or I(f):



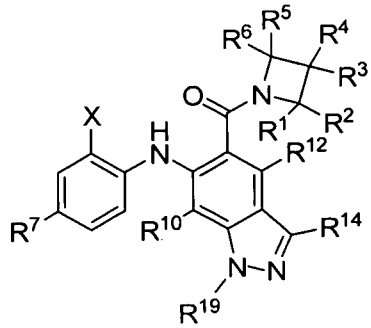
I(e);



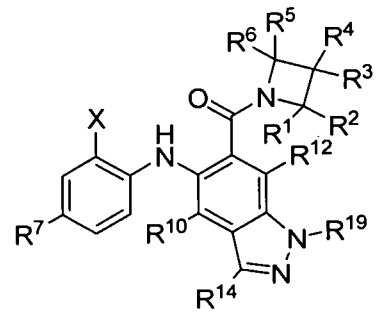
I(f);

wherein X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{12} and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. More specifically, R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the compound of Formula I(M) or Formula I(N) for Group B; and R^{10}, R^{12}, and R^{14} are independently hydrogen, halo, or alkyl. Even more specifically, X is fluoro or chloro and R^7 is iodo or bromo; R^{10} is hydrogen or halo, more specifically hydrogen or fluoro; R^{12} and R^{14} are hydrogen; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

[0088] In another embodiment of the MEK compound (B9), the compound is of Formula I(g) or I(h):



I(g);



I(h);

wherein X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{12}, R^{14}, and R^{19} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B.

[0089] In a more specific embodiment of embodiment B9, the compound is of formula I(g) or I(h), wherein

R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$,

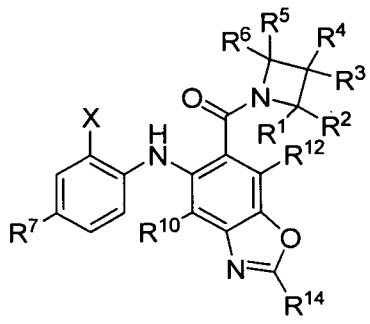
$-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the cycloalkyl, heteroaryl, and heterocycloalkyl are optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; and R^4 is as defined in the compound of Formula I(M) or Formula I(N); or R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH); and

all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B.

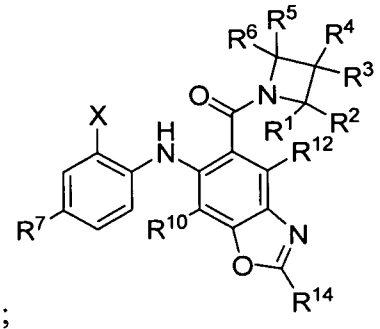
[0090] In a more specific embodiment of embodiment B9, the compound is of formula I(g) or I(h), wherein R^3 is hydroxy and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B.

[0091] In a more specific embodiment of embodiment B9, the compound is of Formula I(g) or I(h), wherein R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the compound of Formula I(M) or Formula I(N) for Group B; R^{10}, R^{12}, and R^{14} are independently hydrogen, halo, or alkyl; and R^{19} is hydrogen or methyl. Even more specifically, X is fluoro or chloro and R^7 is iodo or bromo; R^{10} is hydrogen or halo, more specifically hydrogen or fluoro; R^{12} and R^{14} are hydrogen; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

[0092] In another embodiment of the MEK compound, (B10), the compound is of Formula I(i) or I(j):



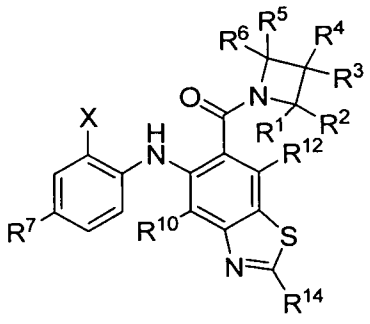
I(i);



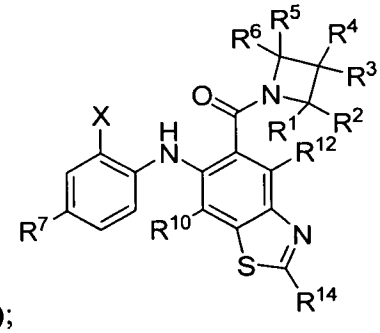
I(j);

wherein X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{12} and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. More specifically, R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the compound of Formula I(M) or Formula I(N) for Group B; and R^{10}, R^{12}, and R^{14} are independently hydrogen, halo, or alkyl. Even more specifically, X is fluoro or chloro and R^7 is iodo or bromo; R^{10} is hydrogen or halo, more specifically hydrogen or fluoro; R^{12} and R^{14} are hydrogen; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

[0093] In another embodiment of the MEK compound (B11), the compound is of Formula I(k) or I(m):



I(k);

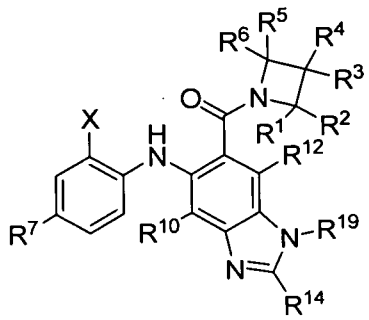


I(m);

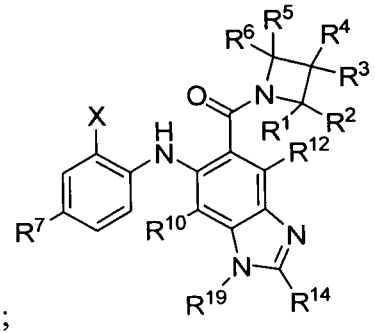
wherein X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{12} and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. The compounds of Formula I(M) and Formula I(m) are two different formulae and are defined separately hereinabove. More specifically, R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3

and R^4 are as defined in the compound of Formula I(M) or Formula I(N) for Group B; and R^{10}, R^{12}, and R^{14} are independently hydrogen, halo, or alkyl. Even more specifically, X is fluoro or chloro and R^7 is iodo or bromo; R^{10} is hydrogen or halo, more specifically hydrogen or fluoro; R^{12} and R^{14} are hydrogen; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

[0094] In another embodiment of the MEK compound, the compound is of Formula I(n) or I(o):



I(n);



I(o);

wherein X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{12}, R^{14}, and R^{19} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B.

[0095] In a more specific embodiment of embodiment B12, the compound is of formula I(n) or I(o), wherein R^7 is halo or alkyl; and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. More specifically, R^7 is iodo or bromo.

[0096] In a more specific embodiment of embodiment B12, the compound is of formula I(n) or I(o), wherein X is halo, haloalkyl, or haloalkoxy; and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. More specifically, X is halo. Even more specifically X is fluoro or chloro.

[0097] In a more specific embodiment of embodiment B12, the compound is of formula I(n) or I(o), wherein

R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl,

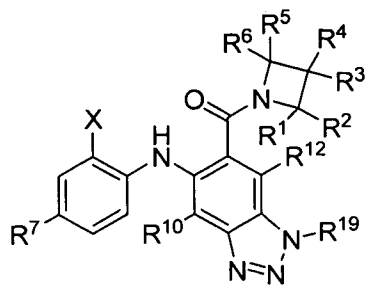
alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; and R^4 is as defined in the compound of Formula I(M) or Formula I(N); or

R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH); and

unless otherwise indicated, R^8 and $R^{8'}$ are as defined in the compound of Formula I(M) or Formula I(N); and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B.

[0098] In a more specific embodiment of embodiment B12, the compound is of formula I(n) or I(o), wherein R^{19} is alkyl; R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the compound of Formula I(M) or Formula I(N) for Group B; and R^{10}, R^{12}, and R^{14} are independently hydrogen or halo. Even more specifically, R^{19} is methyl; X is fluoro or chloro and R^7 is iodo or bromo; R^{10} is hydrogen or fluoro; R^{12} and R^{14} are hydrogen; and R^3 is hydroxy. Yet even more specifically, R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. Yet even more specifically, R^4 is piperidinyl, pyrrolidinyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

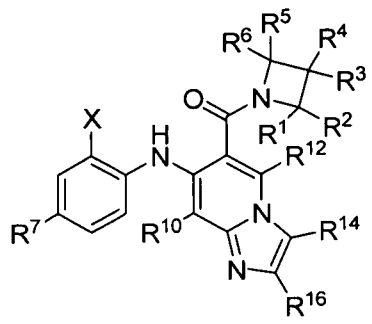
[0099] In another embodiment of the MEK compound (B13), the compound is of Formula I(p):



I(p)

wherein X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{12}, and R^{19} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. More specifically, R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the compound of Formula I(M) or Formula I(N) for Group B; and R^{10} and R^{12} are independently hydrogen, halo, or alkyl. Even more specifically, X is fluoro or chloro; R^7 is iodo or bromo; R^{10} is hydrogen or halo, more specifically hydrogen or fluoro; R^{12} is hydrogen; R^{19} is hydrogen or alkyl, more specifically hydrogen or methyl; R^3 is hydroxy. Even more specifically, R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. Yet even more specifically, R^4 is piperidinyl, pyrrolidinyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00100] In another embodiment of the MEK compound (B14), the compound is of Formula I(q):



I(q)

wherein X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{12} R^{14}, and R^{16} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B.

[00101] In a more specific embodiment of embodiment B14, the compound is of formula I(q) wherein

R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; and R^4 is as defined in the compound of Formula I(M) or Formula I(N); or

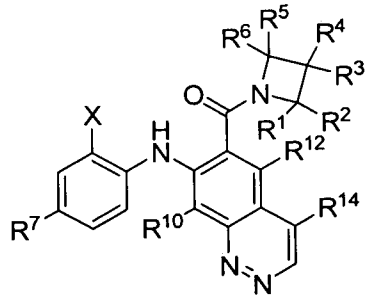
R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH); and

all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B.

[00102] In a more specific embodiment of embodiment B14, the compound is of formula I(q), wherein R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined

in the compound of Formula I(M) or Formula I(N) for Group B; and R^{10}, R^{12}, R^{14}, and R^{16} are independently hydrogen or halo. Even more specifically, R^{10} is halo and R^{12}, R^{14}, and R^{16} are hydrogen. Even more specifically, X is fluoro or chloro; R^7 is iodo or bromo; R^{10} is chloro; and R^3 is hydroxy. Even more specifically, R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. Yet even more specifically, R^4 is piperidinyl, pyrrolidinyl, benzimidazolyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00103] In another embodiment of the MEK compound (B15), the compound is of Formula I(r):

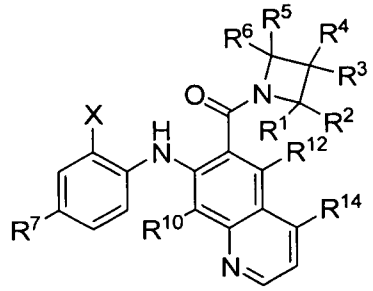


I(r)

wherein X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{12} and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. More specifically, R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the compound of Formula I(M) or Formula I(N) for Group B; R^{10} and R^{12} are independently hydrogen, halo, or alkyl; and R^{14} is hydrogen, halo, alkyl, or amino. Even more specifically, X is fluoro or chloro; R^7 is iodo or bromo; R^{10} is hydrogen or halo, more specifically hydrogen or fluoro; R^{12} is hydrogen; R^{14} is hydrogen, alkyl, or amino, more specifically hydrogen, methyl, or amino; R^3 is hydroxy. Even more specifically, R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and

alkyl) and the heteroaryl is optionally substituted with alkyl. Yet even more specifically, R^4 is piperidinyl, pyrrolidinyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

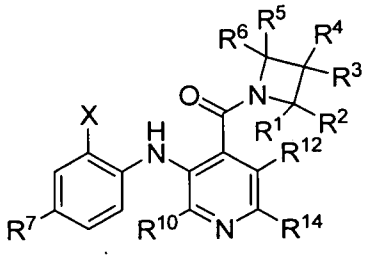
[00104] In another embodiment of the MEK compound (B16), the compound is of Formula I(s):



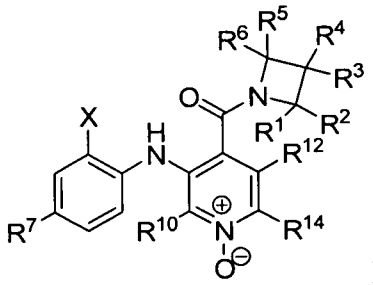
I(s)

wherein X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{12} and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. More specifically, R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the compound of Formula I(M) or Formula I(N) for Group B; and R^{10} and R^{12} are independently hydrogen, halo, or alkyl; and R^{14} is hydrogen, halo, alkyl, or amino. Even more specifically, X is fluoro or chloro and R^7 is iodo or bromo; R^{10} is hydrogen or halo, more specifically hydrogen or fluoro; R^{12} is hydrogen; R^{14} is hydrogen, methyl, or amino; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

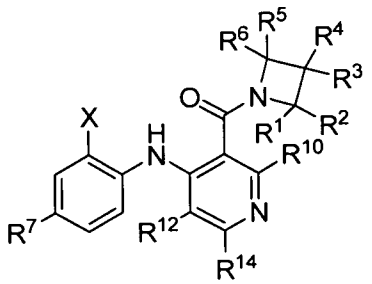
[00105] In another embodiment of the MEK compound (B18), the compound is of Formula I(u), I(v), I(w), or I(x):



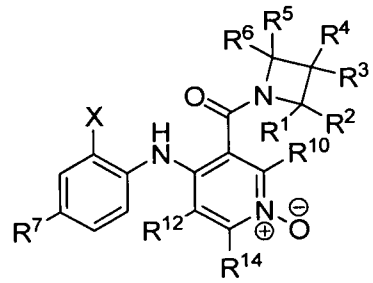
I(u);



I(v);



I(w);



I(x);

wherein X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, R^{12} and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B.

[00106] In a more specific embodiment of embodiment B18, the compound is of formula I(u), I(v), I(w), or I(x), wherein R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl,

[00107] $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; and R^4 is as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B; or R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH); and all

other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B.

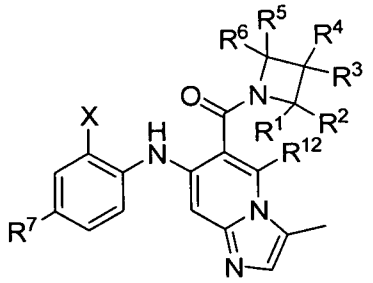
[00108] In a more specific embodiment of embodiment B18, the compound is of formula I(t), I(u), I(v), or I(w), wherein R^3 and R^4 are independently halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH); and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B.

[00109] In a more specific embodiment of embodiment B18, the compound is of formula I(u), I(v), I(w), or I(x), wherein R^4 is heterocycloalkyl, heteroaryl (optionally substituted with alkyl), or alkyl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl). More specifically, R^4 is piperidinyl, pyrrolidinyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-propyl, 1(*R*)-(3,4-*cis*-dihydroxy-cyclopentylamino)-propyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-propyl.

[00110] In a more specific embodiment of embodiment B18, the compound is of formula I(u), I(v), I(w), or I(x), wherein R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the compound of Formula I(M) or Formula I(N) for Group B; and R^{10}, R^{12}, and R^{14} are independently hydrogen, halo, or alkyl. Even more specifically,

X is fluoro or chloro; R^7 is iodo or bromo; R^{10} is hydrogen or halo, more specifically hydrogen or fluoro; R^{12} and R^{14} are hydrogen; and R^3 is hydroxy. Even more specifically R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

[00111] In another embodiment of the MEK compound (B19), the compound is of Formula I(cc)

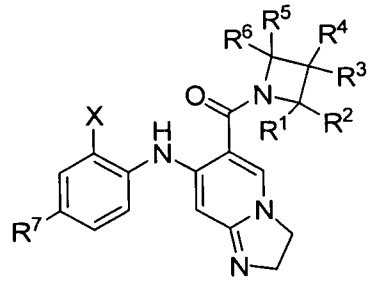


I(cc)

wherein X, R^1, R^2, R^3, R^4, R^5, R^6, and R^7 are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. Specifically, R^1, R^2, R^5, and R^6 are hydrogen; and X and R^7 are halo. More specifically, X is fluoro or chloro; and R^3 is hydrogen or hydroxy; R^7 is iodo or bromo. Even more specifically, R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. Yet even more specifically, R^4 is piperidinyl, pyrrolidinyl, benzimidazolyl, *N*-methyl-benzimidazolyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00112] A specific embodiment (B19a) of embodiment B19 is that wherein R^4 is heterocycloalkyl or alkyl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl). Specifically, R^4 is piperidinyl, pyrrolidinyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00113] In another embodiment of the MEK compound (B20), the compound is of Formula I(dd)



I(dd)

wherein X, R^1, R^2, R^3, R^4, R^5, R^6, and R^7 are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group B. Specifically, R^1, R^2, R^5, and R^6 are hydrogen; and X and R^7 are halo. More specifically, X is fluoro or chloro; R^3 is hydrogen or hydroxy; and R^7 is iodo or bromo. Even more specifically, R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. Yet even more specifically, R^4 is piperidinyl, pyrrolidinyl, benzimidazolyl, *N*-methyl-benzimidazolyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl,

1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00114] A specific embodiment (B20a) of embodiment B20 is that wherein R^4 is heterocycloalkyl or alkyl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl). Specifically, R^4 is piperidinyl, pyrrolidinyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00115] In another embodiment of the MEK compound (C1), the compound of Formula I(M) or Formula I(N) is selected from Group C, wherein all groups are as defined in the compound of Formula I(M) or Formula I(N).

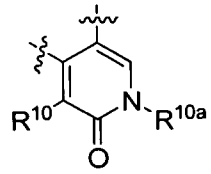
[00116] In another embodiment of the MEK compound (C2), X and R^7 are halo; and all other groups are as defined for a compound selected from Group C.

[00117] In another embodiment of the MEK compound (C3), the compound is selected from Group C, wherein R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl,

haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; and R^4 is as defined in the compound of Formula I(M) or Formula I(N); or R^3 and R^4, together with the carbon to which they are attached, form C(O) or C(=NOH); and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group C. More specifically, R^1, R^2, R^5 and R^6 are hydrogen; and X and R^7 are halo.

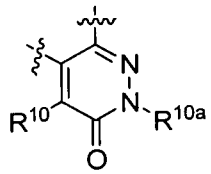
[00118] In another embodiment of the MEK compound (C4), the compound is selected from Group C, wherein R^3 and R^4 are independently halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH); and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group C. More specifically, R^1, R^2, R^5 and R^6 are hydrogen; and X and R^7 are halo.

[00119] In another embodiment of the MEK compound (C5), A is



and X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, and R^{10a} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group C. More specifically, R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^{10} is hydrogen or halo; and R^{10a} is alkyl. Even more specifically, X is fluoro or chloro; R^3 is hydroxy; R^7 is iodo or bromo; R^{10} is hydrogen or fluoro; and R^{10a} is methyl. Even more specifically, R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. Yet even more specifically, R^4 is piperidinyl, pyrrolidinyl, benzimidazolyl, *N*-methyl-benzimidazolyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

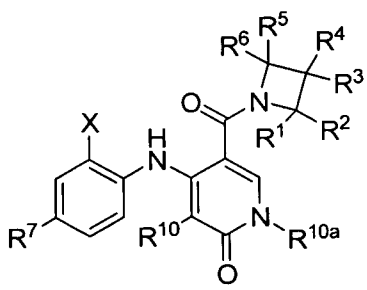
[00120] In another embodiment of the MEK compound (C6), A is



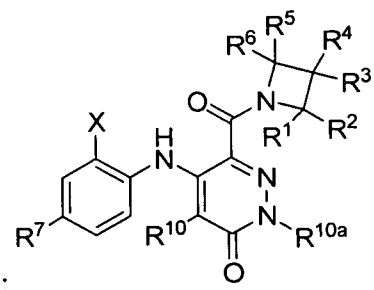
and X, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^{10}, and R^{10a} are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group C. More specifically, R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^{10} is hydrogen or halo; and R^{10a} is alkyl. Even more specifically, X is fluoro or chloro; R^3 is hydroxy; R^7 is iodo or bromo; R^{10} is hydrogen or fluoro; and R^{10a} is methyl. Even more specifically, R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is

hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. Yet even more specifically, R^4 is piperidinyl, pyrrolidinyl, benzimidazolyl, *N*-methylbenzimidazolyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-propyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-propyl, 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00121] In another embodiment of the MEK compound (C7), the compound is of Formula I(y) or I(z):



I(y);



I(z)

wherein R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3, R^4, R^{10}, R^{10a}, and Y^1 are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group C. In a more specific embodiment, X is fluoro or chloro; R^7 is iodo or bromo; R^{10} is hydrogen, halo, or alkyl, more specifically hydrogen or halo; and R^{10a} is alkyl, more specifically methyl. Even more specifically R^{10} is hydrogen or fluoro; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

[00122] In another embodiment of the MEK compound (D), the compound of Formula I(M) or Formula I(N) is selected from Group D, wherein all groups are as defined in the compound of Formula I(M) or Formula I(N).

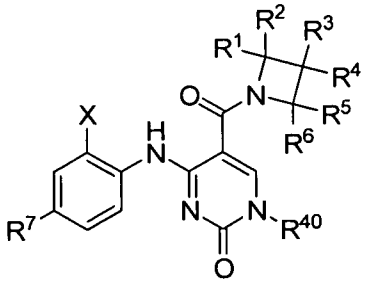
[00123] In another embodiment of the MEK compound (D1), X and R^7 are halo; and all other groups are as defined for a compound selected from Group D.

[00124] In another embodiment of the MEK compound (D2), the compound is selected from Group D, wherein R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; and R^4 is as defined in the compound of Formula I(M) or Formula I(N); or R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH); and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group C. More specifically, R^1, R^2, R^5 and R^6 are hydrogen; and X and R^7 are halo.

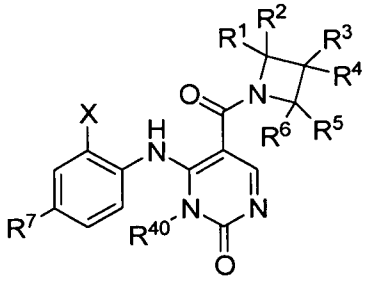
[00125] In another embodiment of the MEK compound, (D3), the compound is selected from Group D, wherein R^3 and R^4 are independently halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, -CN, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or R^3 and R^4 together with the carbon to which they are attached form

C(O) or C(=NOH); and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group C. More specifically, R^1, R^2, R^5 and R^6 are hydrogen; and X and R^7 are halo.

[00126] In another embodiment of the MEK compound (D4), A is



I(aa) or



I(bb)

wherein R^{40} is hydrogen or methyl (specifically, R^{40} is hydrogen) and all other groups are as defined in the compound of Formula I(M) or Formula I(N). Specifically, R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; and R^{40} is hydrogen or methyl. More specifically, X is fluoro or chloro; and R^3 is hydrogen or hydroxy; R^7 is iodo or bromo. Even more specifically, R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. Yet even more specifically, R^4 is piperidinyl, pyrrolidinyl, benzimidazolyl, *N*-methyl-benzimidazolyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00127] A specific embodiment (D4a) of D4 is that wherein R^4 is heterocycloalkyl or alkyl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ (wherein R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl, wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl). Specifically, R^4 is piperidinyl, pyrrolidinyl, methylaminomethyl, 1(*R,S*)-amino-ethyl,

1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00128] Another embodiment of the MEK compound (E) is directed to a compound selected from Group A, Group B, and Group C, wherein

Group A

A is phenylene optionally substituted with one or two groups selected from R^{10}, R^{12}, R^{14}, and

R^{16}, wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen or halo;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen, halo, hydroxy, alkoxy, or amino;

R^4 is hydrogen, $-NR^8R^{8'}$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, cycloalkyl, heterocycloalkyl, or heteroaryl; wherein the R^4 alkyl is optionally substituted with one, two, or three groups independently selected from $-OR^8$, halo, nitro, $-S(O)_mR^9$, optionally substituted heterocycloalkyl, $-NR^8R^{8'}$, $-NR^8C(O)R^{8'}$, $-NR^8S(O)_2R^9$, $-NR^8C(O)OR^{8'}$, and aryl; wherein the R^4 cycloalkyl is optionally substituted with one or two groups selected from $-OR^8$ and $-NR^8R^{8'}$; wherein the R^4 heterocycloalkyl is optionally substituted with one or two groups independently selected from alkyl and $-C(O)OR^8$; and wherein the R^4 heteroaryl is optionally substituted with $-NR^8R^{8'}$; or

R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH);

m is 0;

R^7 is halo;

R^8 and $R^{8'}$ are independently selected from hydrogen, hydroxy, alkyl, alkenyl, alkynyl, aryl, heterocycloalkyl, heteroaryl, and cycloalkyl;

wherein the R^8 and $R^{8'}$ alkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, $-NR^{30}R^{30'}$ (wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), optionally substituted heteroaryl, optionally substituted cycloalkyl), optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, $-C(O)NR^{33}R^{33a}$ (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), optionally substituted aryloxy, $-S(O)_nR^{31}$ (wherein n is 0 and R^{31} is alkyl), carboxy, alkoxycarbonyl, and $-NR^{32}C(O)R^{32a}$ (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl); or wherein the alkyl is optionally substituted with one, two, three, four, or five halo;

wherein the R^8 and $R^{8'}$ heteroaryl are independently optionally substituted with one or two groups indendently selected from amino and alkyl;

wherein the R^8 and $R^{8'}$ heterocycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from alkyl, alkoxycarbonyl, optionally substituted arylalkyl, hydroxy, alkoxy, and hydroxyalkyl;

wherein the R^8 and $R^{8'}$ aryl are independently optionally substituted with one or two groups indendently selected from hydroxy, alkoxy, halo, $-NR^{32}C(O)R^{32a}$ (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl), and $-NR^{34}SO_2R^{34a}$ (wherein R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl); and

wherein the R^8 and $R^{8'}$ cycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, hydroxyalkyl, alkoxy, carboxy, $-C(O)NR^{33}R^{33a}$ (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), and optionally substituted cycloalkyl; and

R^9 is alkyl or aryl;

Group B

A is thien-3,4-diyl, benzo[*d*]isoxazol-5,6-diyl, 1*H*-indazol-5,6-diyl (optionally substituted at the N1 position with R^{19}, wherein R^{19} is alkyl or alkenyl), benzo[*d*]oxazol-5,6-diyl, benzo[*d*]thiazol-5,6-diyl, 1*H*-benzo[d]imidazol-5,6-diyl (optionally substituted at the N1

position with R^{19}, wherein R^{19} is alkyl or alkenyl), 1*H*-benzo[*d*][1,2,3]triazol-5,6-diyl (optionally substituted at the N1 position with R^{19}, wherein R^{19} is alkyl or alkenyl), imidazo[1,2-*a*]pyridin-6,7-diyl, cinnolin-6,7-diyl, quinolin-6,7-diyl, pyridin-3,4-diyl, or 1-oxido-pyridin-3,4-diyl; wherein A is optionally substituted with one, two, or three groups independently selected from R^{10}, R^{12}, R^{14}, R^{16} and R^{19}, wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen, alkyl, halo, or amino; and R^{19} is hydrogen or alkyl;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

R^4 is $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ and wherein the heteroaryl is optionaly substituted with alkyl;

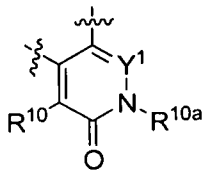
R^7 is halo;

R^8 is hydrogen or alkyl; and

$R^{8'}$ is hydrogen, alkyl, or cycloalkyl; wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl;

Group C

A is



(a)

wherein R^{10} is hydrogen or halo;

R^{10a} is hydrogen or alkyl;

Y^1 is =CH- or =N-;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

R^4 is $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ and wherein the heteroaryl is optionaly substituted with alkyl;

R^7 is halo;

R^8 is hydrogen or alkyl; and

$R^{8'}$ is hydrogen, alkyl, or cycloalkyl; wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl.

[00129] The MEK compound can be in the form of a pharmaceutical composition which comprises the MEK compound of Formula I(M) or Formula I(N) selected from Group A, Group B, Group C and Group D, or a pharmaceutically acceptable salt or solvate therof, and a pharmaceutically acceptable carrier, excipient, or diluent. Non-limiting examples of the MEK compound of Formula I which can be used in the pharmaceutical composition include a compound of Formula I(c), I(d), I(e), I(f), I(g), I(h), I(i), I(j), I(k), I(m), I(n), I(o), I(p), I(q), I(r), I(s), I(t), I(u), I(v), I(w), I(x), I(cc), or I(dd).

Representative MEK Compounds

[00130] Representative MEK compounds of Formula I(M) or I(N) that can be used in the methods of the invention are depicted below in Table 1. The examples are merely illustrative and do not limit the scope of the MEK compounds or MEK inhibitors in any way.

Table 1

Name
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}-carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one
6-(azetidin-1-ylcarbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(hydroxymethyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(trifluoromethyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-prop-2-en-1-ylazetidin-3-ol
3-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]propane-1,2-diol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-ethylazetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-methylazetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-ethenylazetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one oxime
[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]methanol
1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethane-1,2-diol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine

Name
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-hydroxyazetidine-3-carboxamide
1,1-dimethylethyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(pyrrolidin-1-ylmethyl)azetidin-3-ol
3-[(diethylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(dimethylamino)methyl]azetidin-3-ol
N-butyl-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-prop-2-en-1-ylazetidine-3-carboxamide
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-methylpropanamide
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]formamide
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-3,4-dihydroxybutanamide
methyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate
N-butyl-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine
1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-amine
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*R*)-piperidin-2-yl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-pyrrolidin-2-ylazetidin-3-ol

Name
3-(aminomethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
3-[(1*S*)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
3-[(1*R*)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
(3-(1-aminopropyl)-3-hydroxyazetidin-1-yl)(3,4-difluoro-2-(2-fluoro-4-iodophenylamino)phenyl)methanone
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-ethylazetidine-3-carboxamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2-hydroxyethyl)azetidine-3-carboxamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2-piperidin-1-ylethyl)azetidine-3-carboxamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-phenylazetidine-3-carboxamide
N-[2-(diethylamino)ethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(morpholin-4-ylmethyl)azetidin-3-ol
1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}piperidin-4-ol
3-{[bis(2-hydroxyethyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-(4-methylpiperazin-1-yl)acetamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(4-methylpiperazin-1-yl)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(4-methyl-1,4-diazepan-1-yl)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[methyl(1-methylpyrrolidin-3-yl)amino]methyl}azetidin-3-ol
3-(1,4'-bipiperidin-1'-ylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

Name
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N*,*N*-bis(2-hydroxyethyl)glycinamide
3-({4-[2-(diethylamino)ethyl]piperazin-1-yl}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxyethyl)(methyl)amino]methyl}azetidin-3-ol
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-piperidin-1-ylacetamide
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N*3-(2-hydroxyethyl)-*N*3-methyl-beta-alaninamide
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N*3,*N*3-bis(2-hydroxyethyl)-beta-alaninamide
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N*2,*N*2-diethylglycinamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-methylazetidin-3-amine
1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N*,*N*-dimethylpyrrolidin-3-amine
2-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]amino}ethanol
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]propane-1,3-diamine
3-[(dimethylamino)methyl]-1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-methyl-*N*-(2-pyridin-2-ylethyl)azetidin-3-amine
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N*2-methylglycinamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-ethylazetidin-3-amine
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2-methylpropyl)azetidin-3-amine
N-(cyclopropylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine
N-(cyclohexylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine

Name
N-(cyclopentylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine
3-(azetidin-1-ylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-[(2,3-dihydroxypropyl)oxy]azetidine-3-carboxamide
2-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-2-yl]methyl}amino)ethanol
N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-2-yl]methyl}ethane-1,2-diamine
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]glycinamide
6-({3-[(dimethylamino)methyl]azetidin-1-yl}carbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-methylethyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(3,4-dihydroxybutyl)azetidine-3-carboxamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2,3-dihydroxypropyl)azetidine-3-carboxamide
1-({2,4-difluoro-6-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine
1-({4,5-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidine-3-carboxamide
6-{[3-(aminomethyl)-3-(methyloxy)azetidin-1-yl]carbonyl}-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline
N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}acetamide
2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)-6-[(3-{[(1-methylethyl)amino]methyl}azetidin-1-yl)carbonyl]aniline
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(ethylamino)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{2-[(1-methylethyl)amino]ethyl}azetidin-3-ol

Name
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(2-hydroxy-1,1-dimethylethyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1,1-dimethyl-2-[(1-methylethyl)amino]ethyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-methylethyl)amino]methyl}azetidin-3-amine
3-[(cyclopropylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2,2,2-trifluoroethyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-imidazol-1-ylmethyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,1-dimethylethyl)amino]methyl}azetidin-3-ol
3-[(cyclopentylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxy-*N*-prop-2-en-1-ylazetidine-3-carboxamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2,3-dihydroxypropyl)-3-hydroxyazetidine-3-carboxamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-1,2,3-triazol-1-ylmethyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2,2-dimethylpropyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(propylamino)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-methylpropyl)amino]methyl}azetidin-3-ol
3-{[(cyclopropylmethyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(phenylmethyl)amino]methyl}azetidin-3-ol
3-{[(cyclohexylmethyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
3-[(butylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

Name
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1-ethylpyrrolidin-2-yl)methyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxyethyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(dimethylamino)ethyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxy-1,1-dimethylethyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(4-methylphenyl)ethyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(prop-2-en-1-ylamino)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(1-methylpyrrolidin-2-yl)ethyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2,3-dihydro-1*H*-inden-2-ylamino)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(tetrahydrofuran-2-ylmethyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(tetrahydro-2*H*-pyran-4-yl)ethyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1*S*,2*S*)-2-hydroxycyclopentyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,1-dimethylprop-2-yn-1-yl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-pyrrolidin-1-ylpropyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,2-dimethylpropyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(1*H*-imidazol-4-yl)ethyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-methyl-2-(methyloxy)ethyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(ethyloxy)propyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-ethylpropyl)amino]methyl}azetidin-3-ol

Name
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3,3-dimethylbutyl)amino]methyl}azetidin-3-ol
ethyl 4-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)piperidine-1-carboxylate
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-methylbutyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(ethyloxy)ethyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(dimethylamino)propyl]amino}methyl)azetidin-3-ol
3-[(cyclobutylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
3-({[3-(diethylamino)propyl]amino}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(1*H*-imidazol-1-yl)propyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(methylthio)ethyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-(phenylmethyl)piperidin-4-yl]amino}methyl)azetidin-3-ol
3-({[2,2-bis(methyloxy)ethyl]amino}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,1,3,3-tetramethylbutyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,1-dimethylpropyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2,3-dihydro-1*H*-inden-1-ylamino)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[({2-[(phenylmethyl)oxy]cyclopentyl}amino)methyl]azetidin-3-ol
3-{[(3-amino-2-hydroxypropyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-hydroxy-1-(phenylmethyl)ethyl]amino}methyl)azetidin-3-ol
3-[(cyclooctylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

Name
3-{[(1-cyclohexylethyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
3-[(cycloheptylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-pyridin-3-ylethyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(methylthio)propyl]amino}methyl)azetidin-3-ol
N-cyclohexyl-N^2-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-2-methylalaninamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(tetrahydro-2*H*-pyran-4-ylmethyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-hydroxypropyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-pyridin-4-ylethyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-(phenylmethyl)pyrrolidin-3-yl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(2-thienyl)ethyl]amino}methyl)azetidin-3-ol
3-[({2-[bis(1-methylethyl)amino]ethyl}amino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(phenyloxy)ethyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(phenylamino)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxypropyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[({2-[(1-methylethyl)oxy]ethyl}amino)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-ethylpiperidin-3-yl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(methyloxy)ethyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-nitropropyl)azetidin-3-ol

Name
3-(1-aminoethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1-methylpiperidin-4-yl)methyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[4-(dimethylamino)butyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-furan-2-ylethyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1-[(1,1-dimethylethyl)amino]ethyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-ethylbutyl)amino]methyl}azetidin-3-ol
1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}pyrrolidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({(2*S*)-2-[(methyloxy)methyl]pyrrolidin-1-yl}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxyphenyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-hydroxyphenyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(phenyloxy)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1r,3r,5*R*,7*R*)-tricyclo[3.3.1.1~3,7~]dec-2-ylamino]methyl}azetidin-3-ol
3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)propane-1,2-diol
N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-L-alanine
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(phenylthio)methyl]azetidin-3-ol
N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-D-alanine
methyl *N*-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}alaninate
3-[({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)oxy]propane-1,2-diol

Name
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-methylbutyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-methylpropyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-methylbutyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(pentylamino)methyl]azetidin-3-ol
3-[(cyclohexylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(ethylamino)ethyl]azetidin-3-ol
3-[(azepan-3-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(dimethylamino)-1-methylethyl]amino}methyl)azetidin-3-ol
N-cyclopropyl-1-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)cyclopentanecarboxamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(2,3-dihydro-1*H*-indol-3-yl)ethyl]amino}methyl)azetidin-3-ol
N^2-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-*N*-ethyl-2-methylalaninamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2-methylhydrazino)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(hydroxyamino)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(methyloxy)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(ethyloxy)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(ethylamino)propyl]azetidin-3-ol
3-[(azetidin-3-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

Name
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1,3-thiazol-2-ylamino)methyl]azetidin-3-ol
1,1-dimethylethyl [3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-[illegible]
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(pyrrolidin-2-ylmethyl)amino]methyl}azetidin-3-ol
1,1-dimethylethyl 4-[({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-[illegible]
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(2-hydroxyphenyl)methyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(3-hydroxyphenyl)methyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(4-hydroxyphenyl)methyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(4-hydroxybutyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxyethyl)oxy]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1*S*,2*S*)-2-hydroxycyclohexyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,1-dimethyl-2-pyrrolidin-1-ylethyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1-methyl-1*H*-imidazol-4-yl)methyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1-methyl-1*H*-imidazol-5-yl)methyl]amino}methyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(2*S*)-2-(methyloxy)cyclopentyl]amino}methyl)azetidin-3-ol
3-{[1,1'-bi(cyclohexyl)-2-ylamino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(methyloxy)phenyl]amino}methyl)azetidin-3-ol
1-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)cyclopentanecarboxylic acid
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(4-fluorophenyl)amino]methyl}azetidin-3-ol

Name
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1,3,5-triazin-2-ylamino)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(*trans*-4-hydroxycyclohexyl)amino]methyl}azetidin-3-ol
3-[(cyclopent-3-en-1-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
N-[4-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)phenyl]acetamide
N-[3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)phenyl]acetamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methylpyrrolidin-2-yl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1*H*-1,2,4-triazol-3-ylamino)methyl]azetidin-3-ol
3-[1-(diethylamino)propyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)-5-(hydroxymethyl)cyclopentane-1,2-diol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-piperidin-2-ylazetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-fluorophenyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methylpiperidin-2-yl)azetidin-3-ol
1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}guanidine
1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-3-nitroguanidine
N-{1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}acetamide
(2*R*)-*N*-{1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(piperidin-4-ylmethyl)amino]methyl}azetidin-3-ol
3-{[(3-aminopropyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

Name
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[({[2-(4-methylpiperazin-1-yl)phenyl]methyl}amino)methyl]azetidin-3-ol
3-{[(1,1-dimethylethyl)amino]methyl}-1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxycyclohexyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2,2,3,3,3-pentafluoropropyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3,3,3-trifluoropropyl)amino]methyl}azetidin-3-ol
N-[3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)phenyl]methanesulfonamide
N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}methanesulfonamide
3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)-1*H*-pyrazol-5-ol
(1*R*,2*S*)-4-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)cyclopentane-1,2-diol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-(hydroxymethyl)cyclohexyl]amino}methyl)azetidin-3-ol
3-{[(3-chlorophenyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
3-{[(4-chlorophenyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
3-[(5-amino-3-methyl-1*H*-pyrazol-1-yl)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(5-methyl-1*H*-pyrazol-3-yl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-ethylpyrrolidin-2-yl)azetidin-3-ol
(2*R*)-*N*-{(1*S*)-1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanamide
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[4-(methyloxy)phenyl]amino}methyl)azetidin-3-ol
3-(1-amino-2-methylpropyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

Name
3-{[(4-aminophenyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxy-2-methylcyclopentyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1-[(4-hydroxycyclohexyl)amino]ethyl}azetidin-3-ol
methyl (2xi)-2-deoxy-2-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)-beta-D-[illegible]
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-pyridin-2-ylazetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-(hydroxymethyl)cyclopentyl]amino}methyl)azetidin-3-ol
1-cyano-3-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}guanidine
6-({3-[(ethylamino)methyl]-3-fluoroazetidin-1-yl}carbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-nitroethyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-fluoro-4-hydroxyphenyl)amino]methyl}azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-fluoro-4-hydroxyphenyl)amino]methyl}azetidin-3-ol
3-(1-aminoethyl)-1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(methylamino)ethyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-imidazol-2-yl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-pyrrol-2-yl)azetidin-3-ol
N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}benzenecarboximidamide
3-({[(E)-1-amino-2-nitroethenyl]amino}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methyl-1-nitroethyl)azetidin-3-ol

Name
3-(1-amino-1-methylethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
3-[(1*H*-benzimidazol-2-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1*H*-imidazol-2-ylamino)methyl]azetidin-3-ol
methyl {1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}carbamate
3-(1*H*-benzimidazol-2-yl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(dimethylamino)ethyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(pyrimidin-2-ylamino)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(pyridin-2-ylamino)methyl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methyl-1*H*-imidazol-2-yl)azetidin-3-ol
3-(1-aminobutyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
3-[amino(phenyl)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(5-methyl-1*H*-imidazol-2-yl)azetidin-3-ol
1,1-dimethylethyl (2*S*)-2-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate
1-({2-[(4-bromo-2-chlorophenyl)amino]-3,4-difluorophenyl}carbonyl)-3-piperidin-2-ylazetidin-3-ol
3-(1-amino-3-hydroxypropyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-imidazol-2-ylmethyl)azetidin-3-ol
3-(1-aminocyclopentyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
3-(2-aminocyclohexyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

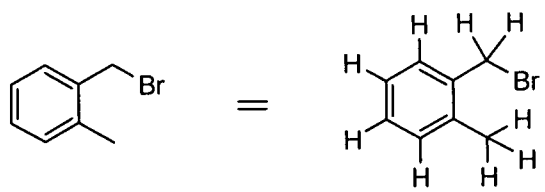
Name
3-(2-aminocyclopentyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-azetidin-3-ol
1-({4-fluoro-5-[(2-fluoro-4-iodophenyl)amino]-1-methyl-1*H*-benzimidazol-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol
1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol
1-({2-[(4-bromo-2-fluorophenyl)amino]-3,4-difluorophenyl}carbonyl)-3-piperidin-2-ylazetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(3-methyl-1-nitrobutyl)azetidin-3-ol
3-(2-aminopyrimidin-4-yl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
1-({7-[(4-bromo-2-chlorophenyl)amino]-8-chloroimidazo[1,2-a]pyridin-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol
1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol
1-({7-[(4-bromo-2-chlorophenyl)amino]-8-chloroimidazo[1,2-a]pyridin-6-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol
1--({4-fluoro-5-[(2-fluoro-4-iodophenyl)amino]-1-methyl-1*H*-benzimidazol-6-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol
4-[(4-bromo-2-fluorophenyl)amino]-3-fluoro-5-({3-hydroxy-3-[(2*S*)-piperidin-2-yl]azetidin-1-yl}carbonyl)pyridin-2(1*H*)-one
(±)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(*trans*)-2-hydroxycyclohexyl]azetidin-3-ol
(±)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(*cis*)-2-hydroxycyclohexyl]azetidin-3-ol
1-({3-fluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol
1-({4-fluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol
1-({6-[(4-bromo-2-chlorophenyl)amino]-7-fluoro-3-methyl-1,2-benzisoxazol-5-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(6-methylpiperidin-2-yl)azetidin-3-ol
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-piperazin-2-ylazetidin-3-ol

Name
5-[(2-fluoro-4-iodophenyl)amino]-6-({3-hydroxy-3-[(2*S*)-piperidin-2-yl]azetidin-1-yl}carbonyl)-2-methylpyridazin-3(2*H*)-one
6-({3-[(1*S*)-1-aminoethyl]-3-hydroxyazetidin-1-yl}carbonyl)-5-[(2-fluoro-4-iodophenyl)amino]-2-methylpyridazin-3(2*H*)-one
1-({3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol
1-({3-[(2-fluoro-4-iodophenyl)amino]-1-oxidopyridin-4-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol

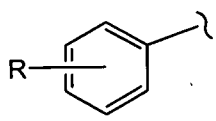
MEK Definitions

[00131] The following definitions apply to the MEK compounds described above only. These definitions are not to be considered when determining the scope and meaning of the JAK-2 compounds. To the same extent, the JAK-2 definitions are not to be considered when determining the scope and meaning of the MEK compounds.

[00132] When chemical structures are depicted or described, unless explicitly stated otherwise, all carbons are assumed to have hydrogen substitution to conform to a valence of four. For example, in the structure on the left-hand side of the schematic below there are nine hydrogens implied. The nine hydrogens are depicted in the right-hand structure. Sometimes a particular atom in a structure is described in textual formula as having a hydrogen or hydrogens as substitution (expressly defined hydrogen), for example, -CH_2CH_2-. It is understood by one of ordinary skill in the art that the aforementioned descriptive techniques are common in the chemical arts to provide brevity and simplicity to description of otherwise complex structures.

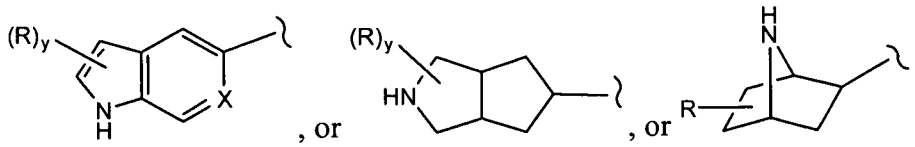


[00133] If a group "R" is depicted as "floating" on a ring system, as for example in the formula:



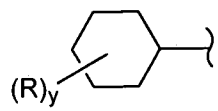
then, unless otherwise defined, a substituent "R" may reside on any atom of the ring system, assuming replacement of a depicted, implied, or expressly defined hydrogen from one of the ring atoms, so long as a stable structure is formed.

[00134] If a group "R" is depicted as floating on a fused ring system, as for example in the formulae:

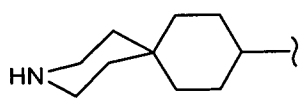


then, unless otherwise defined, a substituent "R" may reside on any atom of the fused ring system, assuming replacement of a depicted hydrogen (for example the -NH- in the formula above), implied hydrogen (for example as in the formula above, wherein the hydrogens are not shown but understood to be present), or expressly defined hydrogen (for example where in the formula above, "X" equals =CH-) from one of the ring atoms, so long as a stable structure is formed. In the example depicted, the "R" group may reside on either the 5-membered or the 6-membered ring of the fused ring system. In the formula depicted above, when y is 2 for example, then the two "R's" may reside on any two atoms of the ring system, again assuming each replaces a depicted, implied, or expressly defined hydrogen on the ring.

[00135] When a group "R" is depicted as existing on a ring system containing saturated carbons, as for example in the formula:



where, in this example, "y" can be more than one, assuming each replaces a currently depicted, implied, or expressly defined hydrogen on the ring; then, unless otherwise defined, where the resulting structure is stable, two "R's" may reside on the same carbon. A simple example is when R is a methyl group; there can exist a geminal dimethyl on a carbon of the depicted ring (an "annular" carbon). In another example, two R's on the same carbon, including that carbon, may form a ring, thus creating a spirocyclic ring (a "spirocyclyl" group) structure with the depicted ring as for example in the formula:



[00136] "Acyl" means a -C(O)R radical, wherein R is optionally substituted alkyl, optionally substituted alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, or heterocycloalkylalkyl, as defined herein, e.g., acetyl, benzoyl, trifluoromethylcarbonyl, or 2-methoxyethylcarbonyl, and the like.

[00137] "Acylamino" means a -NRR' group, wherein R is acyl, as defined herein, and R' is hydrogen or alkyl.

[00138] "Administration" and variants thereof (e.g., "administering" a compound) in reference to a compound of the invention means introducing the compound or a prodrug of the compound into the system of the animal in need of treatment. When a compound of the invention or prodrug thereof is provided in combination with one or more other active agents (e.g., surgery, radiation, and chemotherapy, etc.), "administration" and its variants are each understood to include concurrent and sequential introduction of the compound or prodrug thereof and other agents.

[00139] "Alkenyl" means a means a linear monovalent hydrocarbon radical of one to six carbon atoms or a branched monovalent hydrocarbon radical of three to 6 carbon atoms which radical contains at least one double bond, e.g., ethenyl, propenyl, 1-but-3-enyl, 1-pent-3-enyl, 1-hex-5-enyl and the like.

[00140] "Alkenylcarbonyl" means a -C(O)R group, wherein R is alkenyl, as defined herein.

[00141] "Alkenyloxycarbonyl" means a -C(O)OR group, wherein R is alkenyl, as defined herein.

[00142] "Alkoxy" means an -OR group, wherein R is alkyl group as defined herein. Examples include methoxy, ethoxy, propoxy, isopropoxy, and the like. Lower-alkoxy refers to groups containing one to six carbons.

[00143] "Alkoxyalkyl" means an alkyl group, as defined herein, substituted with at least one, preferably one, two, or three, alkoxy groups as defined herein. Representative examples include methoxymethyl and the like.

[00144] "Alkoxycarbonyl" means a -C(O)OR group, wherein R is alkyl as defined herein.

[00145] "Alkoxycarbonylamino" means a -NR'R" group, wherein R' is hydrogen, alkyl, hydroxy, or alkoxy and R" is alkoxycarbonyl, as defined herein.

[00146] "Alkyl" means a linear saturated monovalent hydrocarbon radical of one to eight carbon atoms or a branched saturated monovalent hydrocarbon radical of three to

eight carbon atoms, e.g., methyl, ethyl, propyl, 2-propyl, butyl (including all isomeric forms), or pentyl (including all isomeric forms), and the like.

[00147] "Alkylamino" means a -NHR radical, wherein R is alkyl as defined herein, or an N-oxide derivative, or a protected derivative thereof, e.g., methylamino, ethylamino, *n*-propylamino, *iso*-propylamino, *n*-butylamino, *iso*-butylamino, *tert*-butylamino, or methylamino-N-oxide, and the like.

[00148] "Alkylaminoalkyl" means an alkyl group substituted with one or two alkylamino groups, as defined herein.

[00149] "Alkylaminocarbonyl" means a -C(O)R group, wherein R is alkylamino, as defined herien.

[00150] "Alkylcarbonyl" means a -C(O)R group, wherein R is alkyl, as defined herein.

[00151] "Alkylcarbonylamino" means a -NRR' group, wherein R is hydrogen or alkyl as defined herein and R' is alkylcarbonyl, as defined herein.

[00152] "Alkylcarbonyloxy" means an -OC(O)R group, wherein R is alkyl, as defined herein.

[00153] "Alkylsulfonylamino" means a $-NRS(O)_2R'$ group, wherein R is hydrogen or alkyl as defined herein, and R' is alkyl, as defined herein.

[00154] "Alkynyl" means a straight or branched hydrocarbon radical having from 2 to 8 carbon atoms and at least one triple bond and includes ethynyl, propynyl, butynyl, pentyn-2-yl and the like.

[00155] "Aminoalkyl" means an alkyl group substiuted with at least one, specifically one, two or three, amino groups.

[00156] "Aminocarbonyl" means a $-C(O)NH_2$ group.

[00157] "Aryl" means a monovalent six- to fourteen-membered, mono- or bi-carbocyclic ring, wherein the monocyclic ring is aromatic and at least one of the rings in the bicyclic ring is aromatic. Unless stated otherwise, the valency of the group may be located on any atom of any ring within the radical, valency rules permitting. Representative examples include phenyl, naphthyl, and indanyl, and the like.

[00158] "Arylene" means a divalent six- to fourteen-membered, mono- or bi-carbocyclic ring, wherein the monocyclic ring is aromatic and at least one of the rings in the bicyclic ring is aromatic. Representative examples include phenylene, naphthylene, and indanylene, and the like.

[00159] "Arylalkyl" means an alkyl group, as defined herein, substituted with one or two aryl groups, as defined herein. Examples include benzyl, phenethyl, and the like.

[00160] "Carboxy ester" means a -C(O)OR group, wherein R is lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, aryl or arylalkyl, each of which is defined herein. Representative examples include methoxycarbonyl, ethoxycarbonyl, and benzyloxycarbonyl, and the like.

[00161] "Cycloalkyl" means a monocyclic or fused bicyclic, saturated or partially unsaturated (but not aromatic), monovalent hydrocarbon radical of three to ten carbon ring atoms. Fused bicyclic hydrocarbon radical includes bridged ring systems. Unless stated otherwise, the valency of the group may be located on any atom of any ring within the radical, valency rules permitting. One or two ring carbon atoms may be replaced by a -C(O)-, -C(S)-, or -C(=NH)- group. More specifically, the term cycloalkyl includes, but is not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexyl, or cyclohex-3-enyl, and the like.

[00162] "Dialkylamino" means a -NRR' radical, wherein R and R' are alkyl as defined herein, or an N-oxide derivative, or a protected derivative thereof, e.g., dimethylamino, diethylamino, *N,N*-methylpropylamino or *N,N*-methylethylamino, and the like.

[00163] "Dialkylaminoalkyl" means an alkyl group substituted with one or two dialkylamino groups, as defined herein.

[00164] "Dialkylaminocarbonyl" means a -C(O)R group, wherein R is dialkylamino, as defined herien.

[00165] "Fused-polycyclic" or "fused ring system" means a polycyclic ring system that contains fused rings and, unless otherwise indicated, can contain bridged rings; that is, wherein two rings have more than one shared atom in their ring structures. In this application, fused-polycyclics and fused ring systems are not necessarily all aromatic ring systems. Typically, but not necessarily, fused-polycyclics share a vicinal set of atoms, for example naphthalene or 1,2,3,4-tetrahydro-naphthalene. A spiro ring system is not a fused-polycyclic by this definition, but fused polycyclic ring systems of the invention may themselves have spiro rings attached thereto via a single ring atom of the fused-polycyclic. In some examples, as appreciated by one of ordinary skill in the art, two adjacent groups on an aromatic system may be fused together to form a ring structure. The fused ring structure may contain heteroatoms and may be optionally substituted with

one or more groups. It should additionally be noted that saturated carbons of such fused groups (*i.e.* saturated ring structures) can contain two substitution groups.

[00166] "Haloalkoxy" means an -OR' group, wherein R' is haloalkyl as defined herein, e.g., trifluoromethoxy or 2,2,2-trifluoroethoxy, and the like.

[00167] "Halogen" or "halo" means fluoro, chloro, bromo and iodo.

[00168] "Haloalkyl" means an alkyl group, as defined herein, that is substituted with one or more halogens, preferably one to five halo atoms. Representative examples include trifluoromethyl, difluoromethyl, 1-chloro-2-fluoro-ethyl, and the like.

[00169] "Heteroaryl" means a monocyclic, fused bicyclic, or fused tricyclic, monovalent radical of 5 to 14 ring atoms containing one or more, preferably one, two, three, or four ring heteroatoms independently selected from -O-, -S(O)$_n$- (n is 0, 1, or 2), -N-, -N(R^x)-, and the remaining ring atoms being carbon, wherein the ring comprising a monocyclic radical is aromatic and wherein at least one of the fused rings comprising a bicyclic or tricyclic radical is aromatic. One or two ring carbon atoms of any nonaromatic rings comprising a bicyclic or tricyclic radical may be replaced by a -C(O)-, -C(S)-, or -C(=NH)- group. R^x is hydrogen, alkyl, hydroxy, alkoxy, acyl, or alkylsulfonyl. Unless stated otherwise, the valency may be located on any atom of any ring of the heteroaryl group, valency rules permitting. In particular, when the point of valency is located on the nitrogen, R^x is absent. More specifically, the term heteroaryl includes, but is not limited to, 1,2,4-triazolyl, 1,3,5-triazolyl, phthalimidyl, pyridinyl, pyrrolyl, imidazolyl, thienyl, furanyl, indolyl, 2,3-dihydro-1*H*-indolyl (including, for example, 2,3-dihydro-1*H*-indol-2-yl or 2,3-dihydro-1*H*-indol-5-yl, and the like), isoindolyl, indolinyl, isoindolinyl, benzimidazolyl, benzodioxol-4-yl, benzofuranyl, cinnolinyl, indolizinyl, naphthyridin-3-yl, phthalazin-3-yl, phthalazin-4-yl, pteridinyl, purinyl, quinazolinyl, quinoxalinyl, tetrazoyl, pyrazolyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isooxazolyl, oxadiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, tetrahydroisoquinolinyl (including, for example, tetrahydroisoquinolin-4-yl or tetrahydroisoquinolin-6-yl, and the like), pyrrolo[3,2-c]pyridinyl (including, for example, pyrrolo[3,2-c]pyridin-2-yl or pyrrolo[3,2-c]pyridin-7-yl, and the like), benzopyranyl, thiazolyl, isothiazolyl, thiadiazolyl, benzothiazolyl, benzothienyl, and the derivatives thereof, or N-oxide or a protected derivative thereof.

[00170] "Heteroarylene" means a monocyclic, fused bicyclic, or fused tricyclic, divalent radical of 5 to 14 ring atoms containing one or more, preferably one, two, three, or four

ring heteroatoms independently selected from -O-, -S(O)$_n$- (n is 0, 1, or 2), -N-, -N(R^{19})-, and the remaining ring atoms being carbon, wherein the ring comprising a monocyclic radical is aromatic and wherein at least one of the fused rings comprising a bicyclic or tricyclic radical is aromatic. One or two ring carbon atoms of any nonaromatic rings comprising a bicyclic or tricyclic radical may be replaced by a -C(O)-, -C(S)-, or -C(=NH)- group. R^{19} is hydrogen, alkyl, or alkenyl. Unless stated otherwise, the valencies may be located on any atom of any ring of the heteroarylene group, valency rules permitting. In particular, when the point of valency is located on the nitrogen, R^x is absent. More specifically, the term heteroaryl includes, but is not limited to, thien-diyl, benzo[*d*]isoxazol-diyl, benzo[*d*]isothiazol-diyl, 1*H*-indazol-diyl (optionally substituted at the N1 position with R^{19}), benzo[*d*]oxazol-diyl, benzo[*d*]thiazol-diyl, 1*H*-benzo[*d*]imidazol-diyl (optionally substituted at the N1 position with R^{19}), 1*H*-benzo[*d*][1,2,3]triazol-diyl (optionally substituted at the N1 position with R^{19}), imidazo[1,2-*a*]pyridin-diyl, cinnolin-diyl, quinolin-diyl, pyridin-diyl, 1-oxido-pyridin-diyl, [1,2,4]triazolo[4,3-a]pyridin-diyl, and 2,3-dihydroimidazo[1,2-a]pyridin-diyl, and the like.

[00171] "Heterocycloalkyl" means a saturated or partially unsaturated (but not aromatic) monovalent monocyclic group of 3 to 8 ring atoms or a saturated or partially unsaturated (but not aromatic) monovalent fused bicyclic group of 5 to 12 ring atoms in which one or more, specifically one, two, three, or four ring heteroatoms independently selected from O, S(O)$_n$ (n is 0, 1, or 2), N, N(R^y) (wherein R^y is hydrogen, alkyl, hydroxy, alkoxy, acyl, or alkylsulfonyl), the remaining ring atoms being carbon. One or two ring carbon atoms may be replaced by a -C(O)-, -C(S)-, or -C(=NH)- group. Fused bicyclic radical includes bridged ring systems. Unless otherwise stated, the valency of the group may be located on any atom of any ring within the radical, valency rules permitting. When the point of valency is located on a nitrogen atom, R^y is absent. More specifically the term heterocycloalkyl includes, but is not limited to, azetidinyl, pyrrolidinyl, 2-oxopyrrolidinyl, 2,5-dihydro-1*H*-pyrrolyl, piperidinyl, 4-piperidonyl, morpholinyl, piperazinyl, 2-oxopiperazinyl, tetrahydropyranyl, 2-oxopiperidinyl, thiomorpholinyl, thiamorpholinyl, perhydroazepinyl, pyrazolidinyl, imidazolinyl, imidazolidinyl, dihydropyridinyl, tetrahydropyridinyl, oxazolinyl, oxazolidinyl, isoxazolidinyl, thiazolinyl, thiazolidinyl, quinuclidinyl, isothiazolidinyl, octahydroindolyl,

octahydroisoindolyl, decahydroisoquinolyl, tetrahydrofuryl, and tetrahydropyranyl, and the derivatives thereof and N-oxide or a protected derivative thereof.

[00172] "Hydroxyalkyl" means an alkyl, as defined herein, substituted with at least one, preferably one, two, or three, hydroxy group(s), provided that if two hydroxy groups are present they are not both on the same carbon atom. Representative examples include, but are not limited to, hydroxymethyl, 2-hydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, 1-(hydroxymethyl)-2-methylpropyl, 2-hydroxybutyl, 3-hydroxybutyl, 4-hydroxybutyl, 2,3-dihydroxypropyl, 1-(hydroxymethyl)-2-hydroxyethyl, 2,3-dihydroxybutyl, 3,4-dihydroxybutyl and 2-(hydroxymethyl)-3-hydroxypropyl, preferably 2-hydroxyethyl, 2,3-dihydroxypropyl, and 1-(hydroxymethyl)-2-hydroxyethyl, and the like.

[00173] "Hydroxyamino" means a -NH(OH) group.

[00174] "Optional" or "optionally" means that the subsequently described event or circumstance may or may not occur, and that the description includes instances wherein said event or circumstance occurs and instances in which it does not. One of ordinary skill in the art would understand that with respect to any molecule described as containing one or more optional substituents, only sterically practical and/or synthetically feasible compounds are meant to be included. "Optionally substituted " refers to all subsequent modifiers in a term. So, for example, in the term "optionally substituted arylC_{1-8} alkyl," both the "C_{1-8} alkyl" portion and the "aryl" portion of the molecule may or may not be substituted. A list of exemplary optional substitutions is presented below in the definition of "substituted."

[00175] "Optionally substituted alkoxy" means an -OR radical wherein R is optionally substituted alkyl as defined herein. Representative examples include $-OCH_2CH_2OCH_3$, $-OCH_2CH_2OH$, $-OCH_2CH(NH_2)CH_3$, and the like.

[00176] "Optionally substituted alkyl" means an alkyl radical, as defined herein, optionally substituted with one or more group(s), specifically one, two, three, four, or five groups, independently selected from alkylcarbonyl, alkenylcarbonyl, cycloalkylcarbonyl, alkylcarbonyloxy, alkenylcarbonyloxy, amino, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, cyano, cyanoalkylaminocarbonyl, alkoxy, alkenyloxy, halo, hydroxy, hydroxyalkoxy, carboxy, alkylcarbonylamino, alkylcarbonyloxy, $-S(O)_{0-2}$-alkyl, $-S(O)_{0-2}$-alkenyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, $-NR^cS(O)_2$-alkyl (wherein R^c is hydrogen, alkyl, optionally

substituted alkenyl, optionally substituted alkynyl, hydroxy, alkoxy, alkenyloxy, or cyanoalkyl), alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylaminoalkyloxy, dialkylaminoalkyloxy, alkoxycarbonyl, alkenyloxycarbonyl, alkoxycarbonylamino, alkylaminocarbonylamino, dialkylaminocarbonylamino, alkoxyalkyloxy, and $-C(O)NR^aR^b$ (wherein R^a and R^b are independently hydrogen, alkyl, optionally substituted alkenyl, optionally substituted alkynyl, hydroxy, alkoxy, alkenyloxy, or cyanoalkyl).

[00177] "Optionally substituted aryl" means an aryl group, as defined herein, which is optionally substituted with one, two, three, four, of five groups selected from halo, haloalkyl, haloalkoxy, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, carboxy, carboxy ester, amino, alkylamino, dialkylamino, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, -C(O)NR'R" (wherein R' is hydrogen or alkyl and R" is hydrogen, alkyl, aryl, heteroaryl, or heterocycloalkyl), -NR'C(O)R" (wherein R' is hydrogen or alkyl and R" is alkyl, aryl, heteroaryl, or heterocycloalkyl), and $-NHS(O)_2R'$ (wherein R' is alkyl, aryl, or heteroaryl).

[00178] "Optionally substituted arylalkyl means an alkyl group substituted with one or two optionally substituted aryl group(s) as defined herein.

[00179] "Optionally substituted arylalkyloxy" means an -OR group, wherein R is optionally substituted arylalkyl, as defined herein.

[00180] "Optionally substituted arylalkyloxycarbonyl" means a -C(O)R group, wherein R is optionally substituted arylalkyloxy, as defined herein.

[00181] "Optionally substituted aryloxy" means an -OR group, wherein R is optionally substituted aryl, as defined herein.

[00182] "Optionally substituted aryloxycarbonyl" means a -C(O)R group, wherein R is optionally substituted aryloxy as defined herein.

[00183] "Optionally substituted cycloalkyl" means a cycloalkyl radical, as defined herein, that is optionally substituted with one, two, three, or four groups independently selected from alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkoxy, oxo, hydroxy, cyano, nitro, amino, mono(C_1-C_6)alkylamino, dialkylamino, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl dialkylaminoalkyl, carboxy, carboxy ester, cycloalkyl, hydroxyalkyl, -C(O)NR'R" (wherein R' is hydrogen, alkyl, hydroxy, or alkoxy and R" is hydrogen, alkyl, aryl, heteroaryl, or heterocycloalkyl), optionally substituted heterocycloalkyl, optionally substituted heteroaryl, -NR'C(O)R" (wherein R' is hydrogen

or alkyl and R" is alkyl, aryl, heteroaryl, or heterocycloalkyl), and -$NHS(O)_2R$' (wherein R' is alkyl, aryl, or hetercyclyl).

[00184] "Optionally substituted cycloalkyloxycarbonyl" means a -C(O)OR group, wherein R is optionally substituted cycloalkyl as defined herein.

[00185] "Optionally substituted heteroaryl" means a heteroaryl group, as defined herein, optionally substituted with one, two, three, four, or five groups selected from halo, haloalkyl, haloalkoxy, alkyl, alkenyl, alkynyl, alkoxy, hydroxy, oxo (valency rules permitting), carboxy, carboxy ester, amino, alkylamino, dialkylamino, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, heteroaryl, optionally substituted aryl, -C(O)NR'R" (wherein R' is hydrogen or alkyl and R" is hydrogen, alkyl, aryl, heteroaryl, or heterocycloalkyl), -NR'C(O)R" (wherein R' is hydrogen or alkyl and R" is alkyl, aryl, heteroaryl, or heterocycloalkyl), and -$NHS(O)_2R$' (wherein R' is alkyl, aryl, or heteroaryl).

[00186] "Optionally substituted heterocycloalkyl" means a heterocycloalkyl ring, as defined herein, optionally substituted with one, two, three, four, or five groups selected from halo, haloalkyl, haloalkoxy, hydroxy, oxo, alkyl, alkenyl, alkynyl, alkoxy, optionally substituted cycloalkyl, heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, alkylaminoalkyl, dialkylaminoalkyl, carboxy, alkoxycarbonyl, aryloxycarbonyl, arylalkyloxycarbonyl, cycloalkyloxycarbonyl, cycloalkylalkyloxycarbonyl, -C(O)NR'R" (wherein R' is hydrogen or alkyl and R" is hydrogen, alkyl, aryl, heteroaryl, or heterocycloalkyl), -NR'C(O)R" (wherein R' is hydrogen or alkyl and R" is alkyl, aryl, heteroaryl, or heterocycloalkyl), amino, alkylamino, dialkylamino, and -$NHS(O)_2R$' (wherein R' is alkyl, aryl, or heteroaryl).

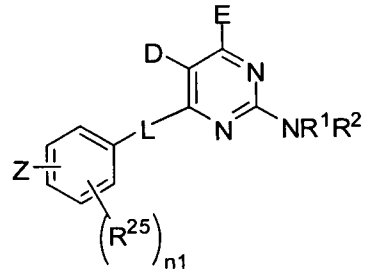
[00187] "Saturated bridged ring system" refers to a bicyclic or polycyclic ring system that is not aromatic. Such a system may contain isolated or conjugated unsaturation, but not aromatic or heteroaromatic rings in its core structure (but may have aromatic substitution thereon). For example, hexahydro-furo[3,2-b]furan, 2,3,3a,4,7,7a-hexahydro-1H-indene, 7-aza-bicyclo[2.2.1]heptane, and 1,2,3,4,4a,5,8,8a-octahydro-naphthalene are all included in the class "saturated bridged ring system."

JAK-2 COMPOUNDS

[00188] The JAK-2 compounds regulate and/or modulate the signal transduction of JAK-2 aminopyrimidine derivatives. The JAK-2 compounds described below are non-

limiting examples of "JAK-2 inhibitors" defined hereinabove. All of the substituents for the JAK-2 compounds described below are defined separately from the MEK compounds so that every substituent in the JAK-2 compounds that also appears in the MEK compounds has a separate and distinct meaning for each of these two compounds. For instance, R^1 for the JAK-2 compounds has a separate and distinct meaning from R^1 for the MEK compounds.

[00189] The JAK-2 compound is a compound of Formula I(J):



I(J)

or a pharmaceutically acceptable salt thereof, wherein

D is hydrogen, halo, $-CF_3$, heterocycloalkyl or alkyl;

E is hydrogen, halo, $-CF_3$, heterocycloalkyl or alkyl; or

D and E, together with the carbon atoms to which they are attached, form a 5-7 membered heteroaryl or a 5-7 membered heterocycloalkyl, wherein the 5-7 membered heteroaryl or 5-7 membered heterocycloalkyl are each fused to the pyrimidinyl moiety to which D and E are attached;

L is a bond, -O- or -N(H)-;

Z is selected from alkoxy, cycloalkyl, heteroaryl optionally substituted with alkyl, halo, $-C(O)OR^{26}$, -C(=N-OH)alkyl, $-C(O)R^8$, $-C(O)NR^{30}R^{30a}$, $-CH_2R^2$, $-(CH_2)_{n5}NR^{26}R^{26a}$, $-CF_3$, -CN, $-SO_2R^{12}$, $-S-R^{12a}$, $-OR^{32a}$, $-NHC(O)R^{32}$, aryl, and heterocycloalkyl optionally substituted with 1 or 2 oxo, or

Z and R^{25}, together with the carbon atoms to which they are attached, join to form a 5 or 6 membered heterocycloalkyl, a 5 or 6 membered heteroaryl, or a 5 or 6 membered cycloalkyl ring, wherein the 5 or 6 membered heterocycloalkyl, 5 or 6 membered heteroaryl, or 5 or 6 membered cycloalkyl ring are fused to the phenyl moiety to which Z and R^{25} are attached, and wherein the 5 or 6 membered heterocycloalkyl, 5 or 6 membered heteroaryl, or 5 or 6 membered cycloalkyl ring are each optionally substituted with 1, 2, or 3 groups independently selected from oxo, alkyl, alkoxy and halo;

n1 is 0, 1, 2, 3, or 4, and each n1 is independently selected when more than one n1 is present;

n2 is 0, 1, 2, 3, or 4, and each n2 is independently selected when more than one n2 is present;

n3 is 0, 1, 2, or 3, and each n3 is independently selected when more than one n3 is present;

n4 is 0, 1, 2, 3 or 4, and each n4 is independently selected when more than one n4 is present;

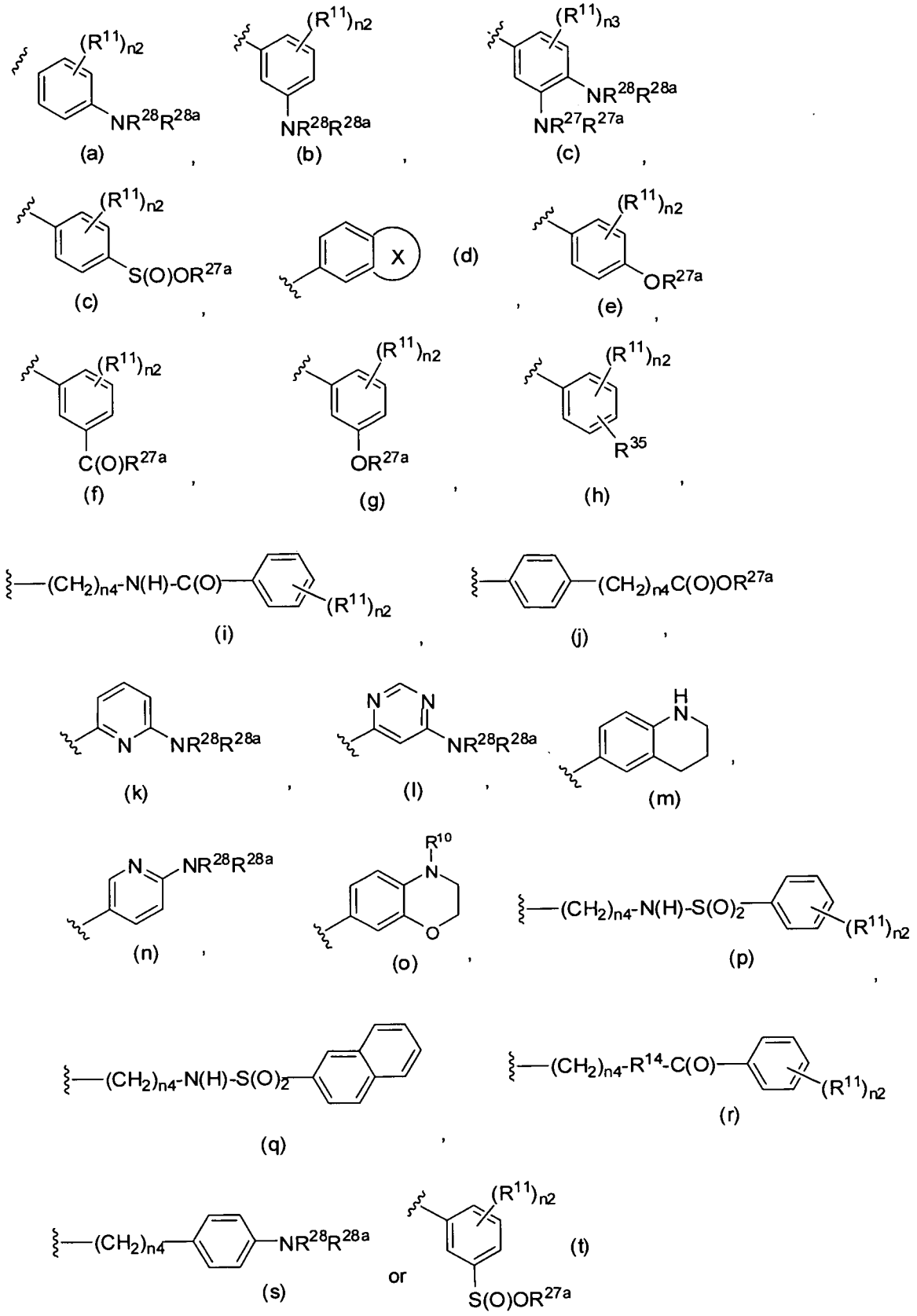
n5 is 0, 1, 2, 3 or 4, and each n5 is independently selected when more than one n5 is present;

p is 0-3;

r is 1-3;

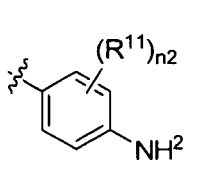
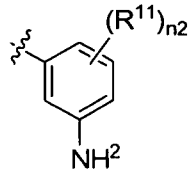
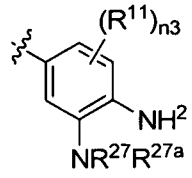
R^1 is hydrogen;

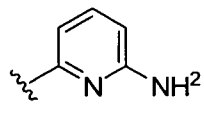
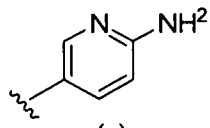
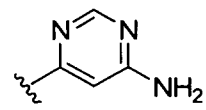
R^2 is selected from one of the following groups:



;

or R^2 is selected from one of the following groups:


(u) ,

(v) ,

(w) ,


(x) ,

(y) , or

(z) ;

ring X in formula (d) of R^2 is a 5 or 6 membered unsaturated heterocyclic ring fused to the two carbon atoms of the phenyl moiety to which ring X is attached, wherein ring X contains 1 or 2 nitrogen atoms;

R^7, $R^{7'}$, R^9, R^{10}, R^{12} and R^{15} are each independently hydrogen, alkyl, alkoxy, or alkoxyalkyl;

R^8 is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, hydroxyalkyl, alkoxyalkyl, dihydroxyalkyl, alkylamino, dialkylamino, aminoalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, alkylaminoalkyl, dialkylaminoalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl;

each R^{11}, when R^{11} is present, is independently selected from alkyl, alkenyl, lower alkynyl,

$-CF_3$, alkoxy, halo, haloalkoxy, haloalkyl, aminoalkyl, aminoalkoxy, alkylaminoalkyl, alkylaminoalkoxy, dialkylaminoalkyl, dialkylaminoalkoxy, oxo, thioalkyl, alkylthioalkyl, $-(CH_2)_p-OR^{17}$, -CN, $-O-CH_2-C(O)-R^{17}$, $-C(O)R^{16}$, $-(CH_2)_p-C(O)OR^{17}$, $-S(O)_2R^{17}$, $-S(O)_2NR^{15}R^{17}$, aryl, heteroaryl, cycloalkyl, arylalkyl, arylalkoxy, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl,

cycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at any ring position with 1, 2, 3 or 4 R^{21};

R^{12} is hydrogen or alkyl;

R^{12a} is hydrogen or alkyl;

R^{13} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with 1, 2, 3, 4 or 5 groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl are independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

R^{14} is a bond, heterocycloalkyl or cycloalkyl;

R^{16} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, dialkylaminoalkyl,
$-(CH_2)_r-C(O)OR^7$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl

of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl is optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

R^{17} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, dialkylaminoalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl is optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

each R^{21}, when R^{21} is present, is independently selected from alkyl, alkenyl, lower alkynyl, cyano, halo, haloalkoxy, haloalkyl, hydroxyalkyl, amino, alkylamino, dialkylamino, dialkylaminoalkyl, dialkylaminoalkyloxy, haloalkyl, oxo, $-OR^{13}$, $-NHS(O)_2R^{17}$, $-S(O)_2R^{17}$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-C(O)NR^{15}R^{17}$, $-NR^{15}C(O)R^{17}$, aryl, arylalkyl, heteroarylalkyl, aryloxy, and heteroaryl; wherein each of the aryl, arylalkyl, heteroarylalkyl, aryloxy, and heteroaryl within R^{21} are optionally substituted at any ring position with 1, 2, or 3 groups selected from alkyl, lower alkoxy halo, phenyl, heteroaryl and alkylheteroalkyl;

R^{25} is selected from alkyl, alkenyl, lower alkyl, halo, haloalkyl, haloalkoxy, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, $-OR^{12}$, cyano, $-CH_2NHC(O)OR^7$, $-CH_2NHC(O)R^7$, $-SR^7$, $-S(O)_2R^7$, $-S(O)_2NR^7R^8$, $-C(O)OR^8$, $-C(O)NR^7R^8$, cycloalkyl, heterocycloalkyl, aryl and heteroaryl; wherein the cycloalkyl, heterocycloalkyl, aryl and heteroaryl are each optionally substituted with one, two or three groups independently selected from alkyl, alkenyl, halo, haloalkoxy, haloalkyl, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, $-OR^8$, $-NHS(O)_2R^8$, cyano, $-C(O)R^8$, $-CH_2NHC(O)OR^7$, $-CH_2NHC(O)R^7$, $-SR^7$, $-S(O)_2R^7$, $-S(O)_2NR^7R^8$,

$-C(O)OR^8$, $-C(O)NR^7R^8$, $-NR^{7'}C(O)-CHR^3-OR^8$, $-NR^{7'}C(O)-CHR^3-NR^7-R^8$, and $-NR^7C(O)R^8$;

R^{26} is hydrogen, -C(O)-phenyl or alkyl, wherein the -C(O)-phenyl is optionally substituted at any ring position with 1, 2 or 3 halo;

R^{26a} is hydrogen, alkyl, heteroaryl, $-C(O)R^{32}$, $-C(O)NHR^{32a}$, $-S(O)_2R^9$, $-SR^9$, $-C(O)OR^{32}$, or $-C(O)NR^{32a}R^{32}$;

R^{27} and R^{28} are each independently selected from alkyl, alkenyl, hydroxy, alkoxy, and alkoxyalkyl;

R^{27a} and R^{28a} are independently selected from hydrogen, alkyl, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, dialkylaminoalkyl, arylcarbonylalkyl, aryloxyalkyl, dialkylaminoalkyl, alkyl-O-C(O)heterocylcoalkyl, $-(CH_2)_{n4}$heterocycloalkyl, heterocycloalkylalkyl, heteroaryl, heteroarylalkyl, $-(CH_2)_{n4}-C(O)R^{29}$, $-(CH_2)_{n4}NR^{28}R^{28a}$, $-(CH_2)_{n4}NHR^{28a}$, $-CH(phenyl)_2$, $-S(O)_2R^{29}$, $-C(O)R^{29}$, $-C(O)OR^{29}$, and $-C(O)NR^{29a}R^{29}$, wherein the aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{27a} and R^{28a} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkylcarbonyl, phenyl, phenoxy, arylcarbonyl, $-CF_3$, oxo, $-OCF_3$, alkoxyphenyl, and heteroaryl optionally substituted with alkyl or halo;

or R^{27} and R^{27a}, together with the nitrogen to which they are attached, form heterocycloalkylamino, heterocycloalkyl or heteroaryl, wherein the heterocycloalkylamino and heteroaryl are each independently optionally substituted with 1, 2, 3, 4, or 5 R^{31};

or R^{28} and R^{28a} together with the nitrogen to which they are attached form heterocycloalkyl or heteroaryl, wherein the heterocycloalkyl and heteroaryl are each optionally substituted with 1, 2, 3, 4, or 5 R^{31};

R^{29a} is hydrogen or alkyl;

R^{29} is selected from alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{29} are each optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkylcarbonyl,

phenyl, phenoxy, arylcarbonyl, -CF_3, oxo, -OCF_3, alkoxyphenyl, and heteroaryl optionally substituted with alkyl or halo;

R^{30a} is hydrogen or alkyl;

R^{30} is selected from hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkoxycarbonylalkyl, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, aryl, arylalkyl, phenoxyalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, arylheteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, arylalkyl, phenoxyalkyl, cycloalkyl, arylheteroarylalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{30} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkoxyalkyl, -$C(O)OCH_3$, -CF_3, -OCF_3, alkylcarbonyl, phenyl, phenoxy, alkylphenoxy, dialkylaminoalkoxy and heteroaryl;

R^{31} is selected from alkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkylthioalkyl, -$C(O)R^{30}$, -$C(O)NR^{30}R^{30a}$, -$C(O)OR^{30}$, -$S(O)_2R^{30}$, amino, dihydroxyalkyl, arylcarbonyl, alkylcarbonylamino, alkoxyphenyl, phenylalkoxyalkyl, arylheteroarylalkyl, alkylamino, -O-dialkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, dialkylaminoalkoxy, oxo, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, spirocyclic cycloalkyl, spirocyclic heterocycloalkyl, and heterocycloalkylalkyl, wherein the aryl, arylalkyl, cycloalkyl, arylheteroarylalkyl, arylalkoxyalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{31} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, -CF_3, -OCF_3, cyano, alkoxy, alkoxyalkyl, -$C(O)OCH_3$, alkylcarbonyl, phenyl optionally substituted at any ring position with halo, phenoxy, alkylphenoxy, arylalkoxyalkyl, dialkylaminoalkoxy and heteroaryl;

R^{32a} is hydrogen, -OCF_3, -CF_3, or alkyl;

R^{32} is selected from aryl, arylalkyl, arylalkoxy, arylcycloalkyl, alkoxycarbonylalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkylhydroxyalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl, wherein the aryl, arylalkyl, cycloalkyl, arylcycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from hydroxy, oxo, alkyl, alkoxy, amino, hydroxyalkyl, alkylcarbonyl, alkoxycarbonyl, halo, -CF_3, -OCF_3, aminoalkyl,

alkylaminoalkyl, aryl and dialkylaminoalkyl, and wherein the alkyl portion of the heteroarylalkyl can be substituted with amino;

or R^{32} is alkyl optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from hydroxy, alkoxycarbonyl, alkoxy, $-CF_3$, halo, aminocarbonyl, alkylaminocarbonyl, alkoxycarbonylalkylamino, dialkylaminocarbonyl, $-NR^{34}R^{34a}$ and phenyl optionally substituted with 1, 2, or 3 halo;

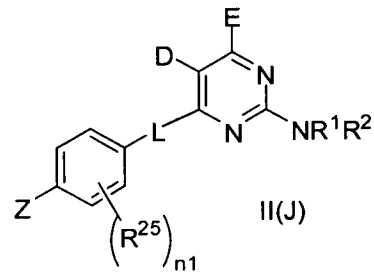
or R^{32} is alkylamino or arylalkylamino;

R^{34} is hydrogen or alkyl;

R^{34a} is selected from hydrogen, alkyl, heteroaryl, aryl, aminoalkyl, aminocarbonylalkyl, heteroarylalkyl, arylalkoxy and arylalkyloxycarbonylalkyl; wherein the heteroaryl, aryl, heteroarylalkyl, arylalkoxy or arylalkyloxycarbonylalkyl are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from hydroxy, oxo, alkyl, amino, hydroxyalkyl, alkylcarbonyl, alkoxycarbonyl, halo, aminoalkyl, alkylaminoalkyl, and dialkylaminoalkyl; and

R^{35} is selected from halo, $-(CH_2)_pC(O)OR_{17}$, cycloalkyl, heterocycloalkyl, and heterocycloalklylalkyl; wherein the heterocycloalkyl and heterocycloalklylalkyl are each optionally substituted with 1, 2, 3, 4, or 5 groups each independently selected from alkyl, alkoxy, and halo.

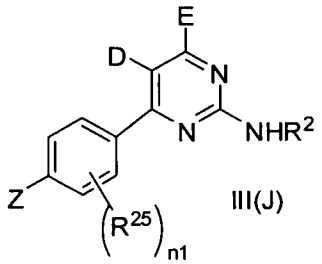
[00190] In a specific embodiment of the JAK compound of Formula I(J) is a compound of Formula II(J):



II(J)

wherein E, D, L, Z, R^1, R^2 and R^{25} are as defined above for the compound of Formula I(J).

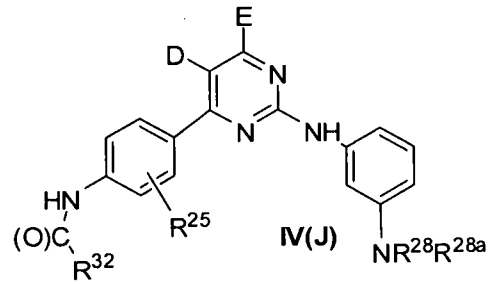
[00191] Another specific embodiment of the the JAK compound of Formula I(J) is a compound of Formula III(J):



III(J)

wherein E, D, L, Z, R^1, R^2 and R^{25} are as defined above for the compound of Formula I(J).

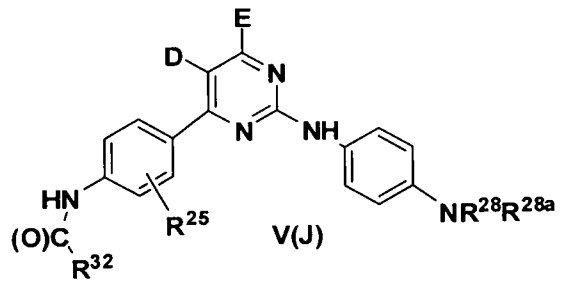
[00192] Another specific embodiment of the JAK compound of Formula I(J) is a compound of Formula IV(J):



IV(J)

wherein D, E, R^{25} and R^{32} are as defined above for Formula I(J), and R^{28} and R^{28a}, together with the nitrogen atom to which they are attached, form a heterocycloalkyl, wherein the heterocycloalkyl is optionally substituted with one or two R^{31}, and wherein R^{31} is as defined above in Formula I(J).

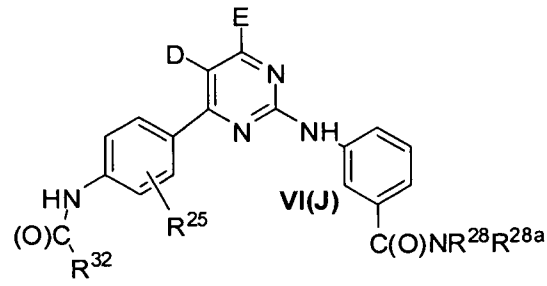
[00193] Another specific embodiment of the JAK-2 compound of Formula I(J) is a compound of Formula V(J):



V(J)

wherein D, E, R^{25} and R^{32} are as defined above for Formula I, and R^{28} and R^{28a}, together with the nitrogen atom to which they are attached, form a heterocycloalkyl, wherein the heterocycloalkyl is optionally substituted with one or two R^{31}, and wherein R^{31} is as defined above in Formula I(J).

[00194] Another specific embodiment of the JAK compound of Formula I(J) is a compound of Formula VI(J):



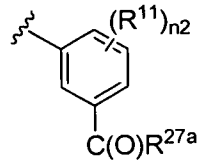
wherein D, E, R^{25} and R^{32} are as defined above for Formula I(J), and R^{28} and R^{28a}, together with the nitrogen atom to which they are attached, form a heterocycloalkyl, wherein the heterocycloalkyl is optionally substituted with one or two R^{31}, and wherein R^{31} is as defined above in Formula I(J).

[00195] In other embodiments of JAK-2 compound D, E and R^{25} for Formula IV(J), Formula V(J) or Formula VI(J) are each hydrogen.

[00196] In other embodiments of the JAK-2 compound, R^{32} for Formula IV(J), Formula V(J) or Formula VI(J) is heterocycloalkyl.

[00197] In other embodiments of the JAK-2 compound, R^{32} for Formula IV(J), Formula V(J) or Formula VI(J) is alkyl optionally substituted with alkoxy, hydroxy, amino, alkylamino, or dialkylamino.

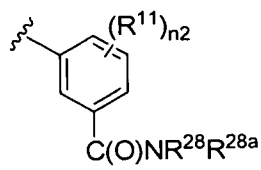
[00198] In other embodiments of the JAK-2 compound, R^2 in Formula I(J), II(J) or III(J) is



(f)

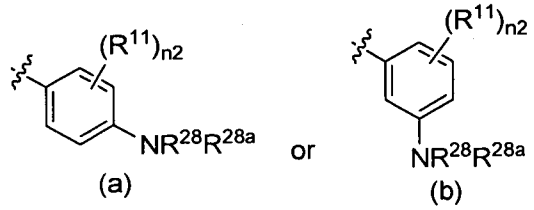
wherein R^{27a}, R^{11} and n2 are as defined above for the compound of Formula I(J).

[00199] In other embodiments of the JAK-2 compound, R^2 in Formula I(J), II(J) or III(J) is



wherein R^{28}, R^{11} and n2 are as defined above for the compound of Formula I(J), and R^{28a} is arylalkyl or heteroarylalkyl, wherein the arylalkyl or heteroarylalkyl are each optionally substituted with 1, 2, 3, 4, or 5 substituents selected from halo or lower alkyl.

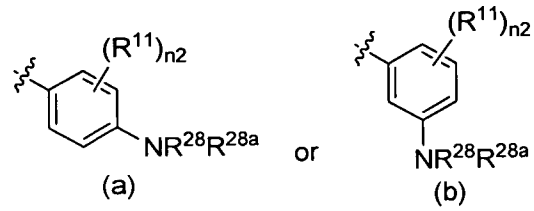
[00200] In other embodiments of the JAK compound, R^2 in Formula I(J), II(J) or III(J) is



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wherein R^{28}, R^{28a}, R^{11} and n2 are as defined above for the compound of Formula I(J).

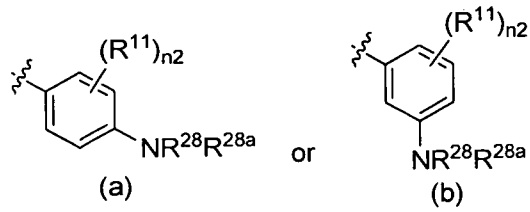
[00201] In the embodiments of the JAK-2 compound, R^2 in Formula I(J), II(J) or III(J) is



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wherein R^{28}, R^{11} and n2 are as defined above for the compound of Formula I(J), and R^{28a} is selected from lower alkyl, dialkylaminoalkyl, alkoxyalkyl, arylalkyl, heteroarylalkyl, and hetercycloalkylalkyl.

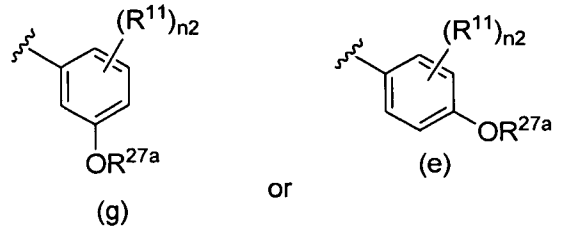
[00202] In other embodiments of the JAK-2 compound, R^2 in Formula I(J), II(J) or III(J) is



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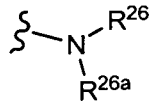
wherein R^{11} and n2 are as defined above for the compound of Formula I(J), and R^{28} and R^{28a}, together with the nitrogen atom to which they are attached, join together to form a ring structure selected from thiazolidinyl, piperazinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyrimidinyl, and pyridinyl, wherein the ring structure is optionally substituted with 1, 2, 3, 4 or 5 subsituents selected from halo, lower alkyl or alkoxy.

[00203] In other embodiments of the JAK-2 compound, R^2 in Formula I(J), II(J) or III(J) is

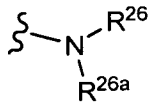


wherein R^{27a}, R^{11} and $_{n2}$ are as defined above for the compound of Formula I(J).

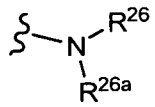
[00204] Other embodiments of the JAK compound are of Formula I(J), II(J) or III(J),

wherein L is a bond, and Z is  .

[00205] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J) ,

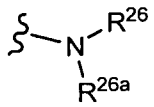
wherein Z is  and R^{25} is hydrogen.

[00206] Other embodiment of the JAK-2 compound are of Formula I(J), II(J) or III(J),

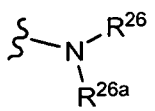
wherein Z is  , R^{25} is hydrogen and E and D are hydrogen.

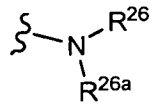
[00207] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J), wherein R^{25} is on the 3 position.

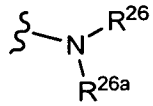
[00208] Other embodiment of the JAK-2 compound aer of Formula I(J), II(J) or III(J),

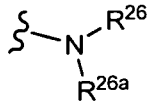
wherein Z is  , and R^{26a} is $-C(O)R^{32}$.

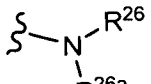
[00209] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J),

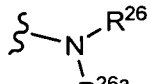
wherein Z is  , R^{26a} is $-C(O)R^{32}$, and R^{32} is selected from lower alkyl, cylcoalkyl, diaminoalkyl, aminoalkyl, arylalkyl, heterocycloalkyl, alkoxyalkyl, alkylamino, and hydroxyalkyl optionally substituted with amino.

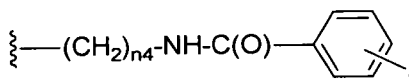
[00210] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J), wherein Z is  , R^{26a} is $-C(O)R^{32}$, and R^{32} is cycloalkyl.

[00211] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J), wherein Z is  , R^{26a} is $-C(O)R^{32}$, and R^{32} is lower alkyl.

[00212] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J) wherein Z is  , R^{26a} is $-C(O)R^{32}$, R^{26} is hydrogen, wherein R^{32} selected from aryl, arylalkyl, cycloalkyl, alkoxycarbonylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl, wherein R^{32} optionally substituted with 1, 2, 3, 4 or 5 groups selected from hydroxyl, oxo, alkyl, alkoxy, amino, hydroxyalkyl or halo.

[00213] Other embodiments of the JAK compound are of Formula I(J), II(J) or III(J), wherein Z is  , R^{26a} is $-C(O)R^{32}$, R^{26} is hydrogen, wherein R^{32} selected from tetrahydrofuran, pyrrolidinyl or pryimidinyl, wherein R^{32} optionally substituted with 1, 2, 3, 4 or 5 groups selected from hydroxyl, oxo, alkyl, alkoxy, amino, hydroxyalkyl or halo.

[00214] Other embodiments of the JAK compound are of Formula I(J), II(J) or III(J), wherein Z is  , R^{26a} is $-C(O)R^{32}$, R^{26} is hydrogen, wherein R^{32} is lower alkyl optionally substituted with 1, 2, 3, 4 or 5 groups selected from dialkylaminocarbonyl, hydroxy and $-NR^{34}R^{34a}$, wherein R^{34} and R^{34a} are as defined above for Formula I(J).

[00215] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J), wherein R^2 is  .

[00216] In another embodiment of the JAK-2 compound, R^{32} is methyl.

[00217] In another embodiment of the JAK-2 compound, R^{32} is alkyl substituted with $-NR^{34}R^{34a}$.

[00218] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J), wherein R^{32} is U or $-CH_2$-U, wherein U is selected from pyrolidinyl, thiazolidinyl, morpholinyl, azetidinyl, cyclobutyl, cyclopropyl, tetrahydofuranyl, pyrazinyl, imidazolyl, piperazinyl, thienyl, thienylmethyl, furanyl, phenyl, prolinamidyl, pyridinyl,

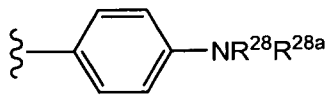
tetrahydronaphthalene, tetrazolyl, isoindolinyl, pyranyl, cyclopentyl, and octahydro-1H-indolyl.

[00219] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J), wherein R^{11}, when present, is halo or lower alkyl.

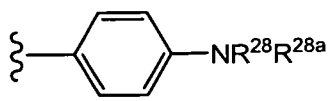
[00220] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J), wherein R^{11}, when present, is lower alkyl.

[00221] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J), wherein R^{35} is heterocycloalkylalkyl, wherein the heterocyloalkyl is selected from piperazinyl, piperidinyl, morpholinyl and dioxanyl.

[00222] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J), wherein n2 is 0.

[00223] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J), wherein R^2 is 

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[00224] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J), wherein R^2 is 

, and wherein R^{28} and R^{28a}, together with the nitrogen atom to which they are attached, form a heterocycloalkyl.

[00225] Other embodiments of the JAK-2 compound are of Formula I(J), II(J) or III(J), IV(J) or V(J), wherein R^{25} is hydrogen.

[00226] Representative JAK-2 compounds of Formula I(J) are depicted below in Table 2 (Part A and Part B). The examples are merely illustrative and do not limit the scope of the JAK-2 compounds or JAK-2 inhibitors in any way.

TABLE 2 (Part A)

Name
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2,6-dichlorobenzamide
2,6-dichloro-*N*-(3-{[4-(2,3-dihydro-1-benzofuran-6-yl)pyrimidin-2-yl]amino}propyl)benzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-fluoro-6-iodobenzamide
N-(3-{[4-(4-aminophenyl)pyrimidin-2-yl]amino}propyl)-2,6-dichlorobenzamide
N-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide

Name
N-{4-[2-({3-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(dimethylamino)ethyl]benzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-fluorobenzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-fluoro-6-iodobenzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dimethylbenzamide
N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]pyridine-4-carboxamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,3,4,5,6-pentafluorobenzamide
4-(4-chlorophenyl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
4-(2,4-dichlorophenyl)-*N*-{3-[(2-piperidin-1-ylethyl)oxy]phenyl}pyrimidin-2-amine
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-chlorobenzamide
N-(4-{2-[(3-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-piperidin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-bromobenzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-3-fluorobenzamide
N-[3-({4-[4-(acetylamino)phenyl]-5-methylpyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide
N-(4-{2-[(3-{[(2,6-dichlorophenyl)sulfonyl]amino}phenyl)amino]-5-methylpyrimidin-4-yl}phenyl)acetamide
2,6-dichloro-*N*-(3-{[4-(1*H*-indol-5-yl)pyrimidin-2-yl]amino}phenyl)benzamide
N-[3-({4-[4-(acetylamino)phenyl]-5-fluoropyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-methylbenzamide

Name
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,4-dichlorobenzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,3-dichlorobenzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,5-dichlorobenzamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-piperidin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(2-methyl-4-piperazin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)thiophene-2-carboxamide
N-(4-{5-methyl-2-[(3-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)-2-(phenyloxy)acetamide
N-(4-{6-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)-2-morpholin-4-ylacetamide
N-[4-(2-{[3-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[3-({4-[4-(acetylamino)-2-chlorophenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide
2,6-dichloro-*N*-{3-[(4-phenylpyrimidin-2-yl)amino]phenyl}benzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-difluorobenzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,4,5-trifluorobenzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]benzamide
N-(4-{6-morpholin-4-yl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide

Name
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-3,5-difluorobenzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-chloro-6-fluoro-3-(methyloxy)benzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-chloro-6-fluoro-4-methylbenzamide
N-(4-{2-[(3-{[(2,6-dimethylphenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
4-(2,4-dichlorophenyl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
4-(2,4-dichlorophenyl)-*N*-{3-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}pyrimidin-2-amine
N-(3-{[4-(4-aminophenyl)pyrimidin-2-yl]amino}phenyl)-2,6-dichlorobenzamide
4-(4-aminophenyl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
4-[4-(ethylamino)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
N-[4-(2-{[3-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-aminophenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({3-[4-(pyridin-4-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-[5-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-2-morpholin-4-ylphenyl]-2,6-dichlorobenzamide
N-(4-{5-fluoro-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{[2-(4-ethylpiperazin-1-yl)-2-oxoethyl]oxy}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[3-(morpholin-4-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide

Name
N-{3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-5-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-2,6-dichlorobenzamide
4-[4-(dimethylamino)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
2,6-dichloro-*N*-(3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}phenyl)benzamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]-5-(trifluoromethyl)pyrimidin-4-yl}phenyl)acetamide
N-(3-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)thiophene-2-carboxamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-1-methylpiperidine-4-carboxamide
N-{4-[2-({3-[(phenylmethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(3-aminophenyl)amino]-5-methylpyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-aminophenyl)amino]-5-fluoropyrimidin-4-yl}phenyl)acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(2-ethylphenyl)benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(phenylmethyl)benzamide
N-{4-[2-({3-[(4-cyclopentylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[(4-phenylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(3-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(2-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({3-[(4-pyrazin-2-ylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(3-{[4-(3-chlorophenyl)piperazin-1-yl]carbonyl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(1-methyl-1*H*-benzimidazol-2-yl)methyl]benzamide

Name
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-propylbenzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-cyclopropylbenzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(3-fluorophenyl)methyl]benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(naphthalen-1-ylmethyl)benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(dimethylamino)ethyl]-*N*-methylbenzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(2-methylphenyl)methyl]benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(3-chlorophenyl)methyl]benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(2-phenylethyl)benzamide
N-{4-[2-({3-[(4-methylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(tetrahydrofuran-2-ylmethyl)benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[3-(2-oxopyrrolidin-1-yl)propyl]benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(3s,5s,7s)-tricyclo[3.3.1.1~3,7~]dec-1-yl]benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(methyloxy)ethyl]benzamide
N-[4-(2-{[3-(1,3-thiazolidin-3-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({3-[(4-pyridin-2-ylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{[2-(methyloxy)phenyl]methyl}benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{[3-(methyloxy)phenyl]methyl}benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(2-fluorophenyl)methyl]benzamide

Name
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(4-fluorophenyl)methyl]benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(3,3-dimethylbutyl)benzamide
N-[4-(2-{[3-(thiomorpholin-4-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(2-thienylmethyl)benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[3-(dimethylamino)propyl]benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{[2-(trifluoromethyl)phenyl]methyl}benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{[3-(trifluoromethyl)phenyl]methyl}benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{[4-(trifluoromethyl)phenyl]methyl}benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(2,4-difluorophenyl)methyl]benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-ethyl-*N*-methylbenzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-({4-[(trifluoromethyl)oxy]phenyl}methyl)benzamide
N-{4-[2-({3-[(4-acetylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(cyclopropylmethyl)benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(2-fluorophenyl)ethyl]benzamide
N-[4-(2-{[3-(pyrrolidin-1-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({3-[(4-pyrimidin-2-ylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-methyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide

Name
N-[4-(2-{[3-(1,3-dioxan-2-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[3-(morpholin-4-ylmethyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({3-[(4-ethylpiperazin-1-yl)methyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-3-[(2-morpholin-4-ylethyl)oxy]benzamide
4-[4-(methylamino)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
N-[4-(2-{[4-(4-acetylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(3-amino-2,4,5,6-tetrafluorophenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-{[4-(2-fluorophenyl)piperazin-1-yl]carbonyl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(phenyloxy)ethyl]benzamide
methyl 1-{[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]carbonyl}piperidine-4-carboxylate
N-[4-(2-{[3-({4-[3-(methyloxy)phenyl]piperazin-1-yl}carbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{2-[2-(methyloxy)phenyl]ethyl}benzamide
N-[4-(2-{[3-(1,3-dihydro-2*H*-isoindol-2-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(biphenyl-4-ylmethyl)benzamide
N-(4-{2-[(3-{[4-(phenylcarbonyl)piperazin-1-yl]carbonyl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[3-({4-[4-(methyloxy)phenyl]piperazin-1-yl}carbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-methyl-*N*-{[2-(methyloxy)phenyl]methyl}benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(2-fluorophenyl)methyl]-*N*-methylbenzamide

Name
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(diphenylmethyl)benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(2-pyridin-2-ylethyl)benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(pyridin-2-ylmethyl)benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(2-chlorophenyl)ethyl]benzamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-fluoropyrimidin-4-yl)phenyl]acetamide
N^2-[3-(1*H*-imidazol-1-yl)propyl]-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-N^2-(2-pyridin-3-ylethyl)glycinamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(pyridin-3-ylmethyl)benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(pyridin-4-ylmethyl)benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-methyl-*N*-(phenylmethyl)benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-cyclopentylbenzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(2-chlorophenyl)methyl]benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(4-chlorophenyl)methyl]benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(furan-2-ylmethyl)benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{[4-(methyloxy)phenyl]methyl}benzamide
N-[4-(2-{[3-({4-[2-(methyloxy)phenyl]piperazin-1-yl}carbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[3-(methyloxy)propyl]benzamide
N-(4-{2-[(3-{[(2*R*,6*S*)-2,6-dimethylmorpholin-4-yl]carbonyl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide

Name
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(6-chloropyridin-3-yl)methyl]benzamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-butylbenzamide
N-(4-{2-[(3-{[4-(2-chlorophenyl)piperazin-1-yl]carbonyl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-ethyl-*N*-[2-(methyloxy)ethyl]benzamide
N-(4-(2-(3-(3-morpholinopropoxy)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(3-(2-(dimethylamino)ethoxy)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-[3-({4-[4-(acetylamino)phenyl]-5-methylpyrimidin-2-yl}amino)phenyl]-2,6-dimethylbenzamide
N-[4-(2-{[4-(phenyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
4-(4-aminophenyl)-*N*-[4-(phenyloxy)phenyl]pyrimidin-2-amine
N-{4-[2-({4-[(phenylmethyl)oxy]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
4-(4-aminophenyl)-*N*-[3-(morpholin-4-ylsulfonyl)phenyl]pyrimidin-2-amine
N-(4-{2-[(3,5-dimorpholin-4-ylphenyl)amino]-5-fluoropyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({4-[4-(phenylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(4-{4-[(5-methyl-3-phenylisoxazol-4-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(2-phenyl-1,3-thiazol-4-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(4-{[6-(phenyloxy)pyridin-3-yl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({4-[4-(cyclohexylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide

Name
N-(4-{2-[(4-{4-[(1*S*,4*S*)-bicyclo[2.2.1]hept-5-en-2-ylmethyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(4-pentylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-{4-[(2-chlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(4-{[3,5-bis(methyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-{4-[(4-fluorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(1-methyl-1*H*-pyrrol-2-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(2,4-dichlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({4-[4-(9*H*-fluoren-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(4-{4-[(3-methyl-2-thienyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(5-ethylfuran-2-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(3-{[4-(1,1-dimethylethyl)phenyl]oxy}phenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({4-[4-(3-thienylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
methyl 4-({4-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperazin-1-yl}methyl)benzoate
N-(4-{2-[(4-{4-[3-(methylthio)propyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(4-{[3-(dimethylamino)propyl]oxy}phenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(4-{2-[(phenylmethyl)oxy]ethyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-{4-[(2-chloroquinolin-3-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(4-chloro-2,6-dimethylphenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide

Name
N-{1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]pyrrolidin-3-yl}acetamide
N^2-[3-(4-methylpiperazin-1-yl)propyl]-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide
N^2-(1-methylpiperidin-4-yl)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide
N-{4-[2-({4-[(pyridin-4-ylmethyl)oxy]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(4-{[2-(methyloxy)ethyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
2-(dimethylamino)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)furan-2-carboxamide
2-(methyloxy)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)cyclobutanecarboxamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)azetidine-3-carboxamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-2-carboxamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-3-carboxamide
N-[4-(2-{[4-(dimethylamino)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-chlorophenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-{[(2-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-4-carboxamide
2-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide

Name
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)morpholine-2-carboxamide
N^2-methyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-beta-alaninamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)phenylalaninamide
N-[4-(2-{[4-(3-oxopiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(4-{[5-(3-chlorophenyl)furan-2-yl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(4-{[4-fluoro-2-(trifluoromethyl)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(4-{[4-(1*H*-imidazol-1-yl)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(4-{[2,5-bis(trifluoromethyl)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-{4-[(2,6-dimethylphenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(2,3-dimethylphenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(4-{[2,4-bis(ethyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(4-{[3-(ethyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({4-[4-(2,2'-bithien-5-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-[4-(2-{[4-(4-{[4-(2-thienyl)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-{4-[(4-cyanophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(4-{[2,5-bis(methyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({4-[4-(2,2-diphenylethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide

Name
N-{4-[2-({4-[4-(1*H*-pyrrol-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-(1*H*-indazol-6-ylamino)-5-methylpyrimidin-4-yl]phenyl}acetamide
N-{4-[2-(1*H*-indol-5-ylamino)-5-methylpyrimidin-4-yl]phenyl}acetamide
N-[4-(2-{[4-(morpholin-4-ylmethyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(3-{[(3-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-{[(4-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
4-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-*N*-ethylpiperazine-1-carboxamide
N-{4-[2-({4-[4-(ethylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-(1*H*-indazol-5-ylamino)-5-methylpyrimidin-4-yl]phenyl}acetamide
N-[4-(2-{[4-(4-propylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(4-butylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({4-[4-(cyclopropylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
4-[4-(methylsulfonyl)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
ethyl *N*-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-*N*-methylglycinate
4-[3-(methylsulfonyl)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
4-[4-(methylthio)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
N-(4-{2-[(4-cyclohexylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({4-[(tetrahydrofuran-2-ylmethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide

Name
N-{4-[2-({4-[(phenylmethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-[4-(2-{[4-(acetylamino)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
methyl (4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)carbamate
1-ethyl-3-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)urea
ethyl 1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperidine-3-carboxylate
ethyl [4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]acetate
4-[4-(methyloxy)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
4-[3-(methyloxy)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
4-(1*H*-indol-5-yl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
2-[(2-amino-2-oxoethyl)amino]-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
2-morpholin-4-yl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
2,6-dichloro-*N*-{3-[(4-{4-[(cyclopropylcarbonyl)amino]phenyl}pyrimidin-2-yl)amino]phenyl}benzamide
N^2-(2-aminoethyl)-N^2-methyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-N^2-1*H*-pyrazol-5-ylglycinamide
phenylmethyl *N*-{2-[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]-2-oxoethyl}-L-alaninate
4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzamide
1,1-dimethylethyl [(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)methyl]carbamate
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide

Name
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenylacetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-phenylpropanamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)tetrahydrofuran-2-carboxamide
5-methyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyrazine-2-carboxamide
2-(ethyloxy)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-(phenyloxy)acetamide
N-[4-(2-{[4-(1*H*-pyrrol-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(2,6-dimethylmorpholin-4-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
ethyl 1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperidine-4-carboxylate
2-cyclopentyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-pyridin-3-ylpropanamide
6-(methyloxy)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-3-carboxamide
methyl 4-[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]-4-oxobutanoate
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)butanamide
N-(4-{2-[(4-{bis[2-(methyloxy)ethyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(morpholin-4-ylsulfonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
4-(4-(aminomethyl)phenyl)-*N*-(4-morpholinophenyl)pyrimidin-2-amine
N-[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)methyl]acetamide

Name
N-(4-morpholin-4-ylphenyl)-4-{4-[(propylamino)methyl]phenyl}pyrimidin-2-amine
N-(4-{2-[(4-piperidin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3,5-dimorpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
2-(2-methylphenyl)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)cyclopentanecarboxamide
N,*N*-dimethyl-*N*'-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)butanediamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-N^2-pyrimidin-4-ylglycinamide
3-chloro-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-4-carboxamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-piperidin-1-ylacetamide
N^2-ethyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-pyrrolidin-1-ylacetamide
2-(1*H*-imidazol-1-yl)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-piperazin-1-ylacetamide
N-[4-(2-{[4-(4-phenylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(3-chloro-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-piperazin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
'*N*-[6-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)pyridin-2-yl]-2,6-dichlorobenzamide
'*N*-[6-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)pyrimidin-4-yl]-2,6-dichlorobenzamide

Name
'N-(4-{2-[(6-aminopyridin-2-yl)amino]pyrimidin-4-yl}phenyl)acetamide
'N-(4-{2-[(6-aminopyrimidin-4-yl)amino]pyrimidin-4-yl}phenyl)acetamide
'5-fluoro-N^4-[2-(methyloxy)phenyl]-N^2-[3-(methyloxy)phenyl]pyrimidine-2,4-diamine
'2,6-dichloro-N-{3-[(4-{[3-chloro-4-(methyloxy)phenyl]oxy}pyrimidin-2-yl)amino]phenyl}benzamide
'4-{[2-chloro-4-(methyloxy)phenyl]oxy}-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
'N-[4-({2-[(4-morpholin-4-ylphenyl)amino]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}amino)phenyl]acetamide
'N-[4-({2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}oxy)phenyl]acetamide
N-{4-[2-({4-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({4-[(2R,6S)-2,6-dimethylmorpholin-4-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(4-{4-[(2-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({4-[4-(1H-pyrazol-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(3-piperazin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[3-(4-{[2-(methyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({3-[4-(1,3-thiazol-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(3-bromo-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-{[2-(diethylamino)ethyl]oxy}-3-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzoic acid
4-(4-furan-2-ylphenyl)-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine

Name
4-[4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzonitrile
methyl 4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzoate
4-(4-fluorophenyl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
N-[3-({2-[(4-morpholin-4-ylphenyl)amino]-7*H*-pyrrolo[2,3-d]pyrimidin-4-yl}amino)phenyl]acetamide
N-(4-morpholin-4-ylphenyl)-4-[4-(pyridin-3-ylamino)phenyl]pyrimidin-2-amine
N-(4-morpholin-4-ylphenyl)-4-[4-(pyridin-2-ylamino)phenyl]pyrimidin-2-amine
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)methanesulfonamide
1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-(phenylmethyl)urea
4-(2,3-dihydro-1,4-benzodioxin-6-yl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]-7*H*-pyrrolo[2,3-d]pyrimidin-4-yl}phenyl)acetamide
N-(4-morpholin-4-ylphenyl)-4-quinolin-6-ylpyrimidin-2-amine
4-[4-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
N-(4-morpholin-4-ylphenyl)-4-(4-pyrimidin-5-ylphenyl)pyrimidin-2-amine
N-(4-morpholin-4-ylphenyl)-4-quinoxalin-6-ylpyrimidin-2-amine
2-chloro-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide
2-(2-fluorophenyl)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyrimidine-5-carboxamide

Name
(2*S*)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)azetidine-2-carboxamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-N^2-phenylglycinamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-prolinamide
N-(4-(2-(3-methoxy-4-morpholino-phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-isobutyrylpiperazin-1-yl)phenylamino)-pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-(3-methylbutanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-(cyclopropanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-(cyclobutanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-(cyclopentanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-(2-methoxybenzoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-pentanoylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-picolinoylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-isonicotinoylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-(1-acetylpiperidine-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-(2-cyclopropylacetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-(2-(2-methoxyethoxy)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-(2-(pyridin-3-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide

Name
N-(4-(2-(4-(4-(3-(pyridin-3-yl)propanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(pyridin-3-yl)acetamide
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)isonicotinamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide
N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide
O-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-serinamide
(*S*)-3-hydroxy-*N*-(4-(2-(4-morpholino-phenylamino)-pyrimidin-4-yl)-phenyl)-butanamide
(*R*)-3-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide
(*R*)-2-amino-3-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
2-*H*ydroxy-2-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
2-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-((*R*)-3-(dimethylamino)pyrrolidin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
4-amino-1,1-dioxo-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)tetrahydro-2*H*-thiopyran-4-carboxamide
(*R*)-4-(4-aminophenyl)-*N*-(4-(3-(dimethylamino)-pyrrolidin-1-yl)phenyl)-pyrimidin-2-amine
(*R*)-*N*-(4-(2-(4-(3-(dimethylamino)pyrrolidin-1-yl)phenylamino)-pyrimidin-4-yl)phenyl)-3-methoxy-propanamide
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)piperazine-2-carboxamide
2-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-1,2,3,4-tetrahydronaphthalene-2-carboxamide

Name
4-(4-(1,1-dioxo-isothiazolidin-2-yl)phenyl)-*N*-(4-morpholinophenyl)-pyrimidin-2-amine
4-(4-(1*H*-tetrazol-1-yl)phenyl)-*N*-(4-morpholinophenyl)-pyrimidin-2-amine
(*R*)-*N*-(4-(2-(3-(benzyloxy)-4-morpholino-phenylamino)-pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide
(*S*)-2-amino-3-hydroxy-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(1*H*-tetrazol-1-yl)acetamide
(*R*)-*N*-(4-(2-(3-ethoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(1,2,3,4-tetrahydroquinolin-6-ylamino)-pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide
3-hydroxy-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-3-methylbutanamide
(3*S*,7*S*)-7-(hydroxymethyl)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)quinuclidine-3-carboxamide
1-hydroxy-*N*-(4-(2-(4-morpholino-phenylamino)-pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
(*S*)-2-amino-*N*-(4-(2-(3-methyl-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
(*R*)-*N*-(4-(2-(3-methyl-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-morpholino-3-(trifluoromethyl)-phenylamino)pyrimidin-4-yl)-phenyl)-pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-(4-((*S*)-tetrahydrofuran-2-carbonyl)-piperazin-1-yl)-phenylamino)-pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-(4-((*R*)-tetrahydrofuran-2-carbonyl)-piperazin-1-yl)-phenylamino)-pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide
4-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)piperazine-1-carboxamide
3-methoxy-*N*-(4-(2-(4-morpholino-3-(trifluoromethyl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
3-methoxy-*N*-(4-(2-(4-morpholino-phenylamino)pyrimidin-4-yl)phenyl)-propane-1-sulfonamide

Name
2-methoxy-*N*-(4-(2-(4-morpholino-phenylamino)pyrimidin-4-yl)phenyl)-ethanesulfonamide
(*S*)-3-hydroxy-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide
(*R*)-3-hydroxy-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide
1-(3-(dimethylamino)propyl)-3-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)urea
(*R*)-*N*-(4-(2-(4-(4-((*S*)-pyrrolidin-2-ylmethyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-2-amino-*N*-(4-(2-(4-(4-ethylpiperazin-1-yl)phenylamino)-5-methylpyrimidin-4-yl)phenyl)propanamide
1-(3-methoxypropyl)-3-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)urea
(*R*)-*N*-(4-(2-(4-(4-ethylpiperazin-1-yl)phenylamino)-5-methylpyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*S*)-*N*-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)-3-fluorophenylamino)pyrimidin-4-yl)phenyl)-5-oxopyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(3-chloro-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
1-(2-morpholinoethyl)-3-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)urea
1-(2-(dimethylamino)ethyl)-3-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)urea
(*S*)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(pyrrolidin-2-yl)acetamide
2,3-dihydroxy-*N*-(4-(2-(4-morpholino-phenylamino)pyrimidin-4-yl)phenyl)-propanamide
(*S*)-2-amino-4-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanamide
(*R*)-2-amino-4-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanamide
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)isoindoline-1-carboxamide

Name
N-ethyl-4-(4-(4-(4-(tetrahydrofuran-2-carboxamido)phenyl)pyrimidin-2-ylamino)phenyl)piperazine-1-carboxamide
N-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide
(*R*)-*N*-(4-(2-(4-(4-((*R*)-2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-(4-((*S*)-2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
N-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide
3-methoxy-*N*-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
N-(4-(2-(4-(4-pivaloylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide
(*R*)-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-1-methylpyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-4-(4-(4-(4-(2-aminopropanamido)phenyl)-pyrimidin-2-ylamino)phenyl)-*N*-ethylpiperazine-1-carboxamide
(*R*)-2-amino-*N*-(4-(2-(4-(4-((*R*)-pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
(*R*)-2-amino-*N*-(4-(2-(4-(4-((*S*)-pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
(*R*)-2-amino-*N*-(4-(2-(4-(4-((*S*)-2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
(*R*)-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*S*)-*N*-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
N-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
(*R*)-*N*-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
1-ethyl-3-(4-(5-methyl-2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)urea

Name
(*S*)-*N*-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
(*R*)-*N*-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-methoxypropanamide
(*S*)-3-methoxy-*N*-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
(*R*)-*N*-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
N-(4-(2-(4-(4-(cyclobutanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
N-(4-(2-(4-(4-isobutyrylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
N-(4-(2-(4-(1-butyryl-1,2,4-triazinan-4-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide
1-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-ethylurea
N-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-methoxypropanamide
N-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
N-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide
1-ethyl-3-(4-(2-(4-(4-pivaloylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea
1-(4-(2-(4-(4-(cyclobutanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-ethylurea
1-ethyl-3-(4-(2-(4-(4-isobutyrylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea
N-ethyl-4-(4-(4-(4-(3-ethylureido)phenyl)pyrimidin-2-ylamino)phenyl)piperazine-1-carboxamide
(*S*)-1-ethyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-1-(2-hydroxyethyl)-*N*-(4-(2-(4-morpholinobenzyl)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-1-isopropyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide

Name
(*S*)-2-(dimethylamino)-*N*-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
1-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-ethylurea
(*R*)-1-ethyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
4-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)tetrahydro-2*H*-pyran-4-carboxamide
(*R*)-2-amino-*N*-(4-(2-(4-(4-isobutyrylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
(*R*)-2-amino-*N*-(4-(2-(4-(4-((*R*)-2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
(*R*)-*N*-(4-(5-methyl-2-(4-(4-((1-methyl-1*H*-imidazol-2-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-2-amino-*N*-(4-(5-methyl-2-(4-(4-((1-methyl-1*H*-imidazol-2-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
(*R*)-2-(dimethylamino)-*N*-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
(*R*)-*N*-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*S*)-*N*-(4-(5-methyl-2-(4-(4-((1-methyl-1*H*-imidazol-2-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-2-amino-*N*-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
(2*R*)-*N*-(4-(2-(4-(4-(tetrahydrofuran-3-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*S*)-1-ethyl-3-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea
(*S*)-1-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-ethylurea
N-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide
(*S*)-*N*-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide
3-methoxy-*N*-(4-(5-methyl-2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide

Name
(*R*)-2-amino-*N*-(4-(5-methyl-2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
2-(dimethylamino)-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
1-ethyl-3-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea
3-methoxy-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
(*R*)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-5-oxopyrrolidine-2-carboxamide
(*S*)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-5-oxopyrrolidine-2-carboxamide
(*S*)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-3-carboxamide
(2*R*,3*S*)-2-amino-3-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide
(*R*)-2-amino-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
N-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
N-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butyramide
N-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide
N-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
(*R*)-2-amino-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
(2*S*,3*R*)-2-amino-3-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide
(*R*)-*N*-(4-(2-(4-((2*S*,6*R*)-2,6-dimethylmorpholino)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-(4-(3-hydroxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
1-ethyl-3-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea

Name
(*R*)-1-ethyl-3-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea
3,3,3-trifluoro-2-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
(*R*)-1-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-ethylurea
2-(dimethylamino)-*N*-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
(*R*)-2-amino-*N*-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
(*R*)-*N*-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-2-amino-*N*-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-methoxypropanamide
N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide
N-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide
N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide
(*R*)-*N*-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide
2-(dimethylamino)-*N*-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
(*R*)-*N*-(4-(2-(4-(4-(piperidine-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
3-methoxy-*N*-(4-(2-(4-(4-(piperidine-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
1-ethyl-3-(4-(2-(4-(4-(piperidine-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea
N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropanoyl)piperazin-1-yl)benzyl)pyrimidin-4-yl)phenyl)acetamide
(*S*)-*N*-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide

Name
(*R*)-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide
(4*S*)-4-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide
(*S*)-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide
N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
N-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide
(*S*)-*N*-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide
(2*R*)-*N*-(4-(2-(4-(4-(tetrahydrofuran-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(5-chloro-2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
N-(4-(2-(4-(4-(3-(diethylamino)propanoyl)piperazin-1-yl)benzyl)pyrimidin-4-yl)phenyl)acetamide
(*S*)-1-(2-hydroxyethyl)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-3-carboxamide
(*S*)-2-amino-*N*1-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanediamide
(*R*)-2-amino-*N*1-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanediamide
(*R*)-2-amino-*N*1-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)succinamide
(*R*)-*N*-(4-(2-(4-(4-((4-chloro-1-methyl-1*H*-pyrazol-3-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*S*)-1-ethyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-3-carboxamide
(*R*)-*N*-(4-(2-(4-(4-(2-ethoxyacetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-(4-(2-(pyrrolidin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide

Name
(*R*)-*N*-(4-(2-(4-(4-(2-morpholinoacetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-1*H*-imidazole-4-carboxamide
2-(dimethylamino)-*N*-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
(*S*)-*N*-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide
(*R*)-2-hydroxy-2-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide
(*S*)-2-hydroxy-2-methyl-*N*-(4-(2-(4-morpholinobenzyl)pyrimidin-4-yl)phenyl)butanamide
(*R*)-2-methoxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
(*S*)-2-methoxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
(*R*)-*N*-(4-(2-(4-(4-(2-methoxyacetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-(4-acetylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*S*)-2-amino-*N*-(4-(5-methyl-2-(4-(4-((1-methyl-1*H*-imidazol-2-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide
N-(4-(2-(4-(4-(piperidine-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide
(2*R*,4*S*)-4-hydroxy-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
1-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)cyclopentanecarboxamide
(*R*)-*N*-(4-(2-(4-(4-formylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-1-(2-hydroxyethyl)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-3-carboxamide
1-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-1*H*-pyrrole-2-carboxamide

Name
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-1*H*-imidazole-2-carboxamide
(*S*)-2-hydroxy-3,3-dimethyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide
(*R*)-2-cyclohexyl-2-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide
(*S*)-2-cyclohexyl-2-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide
(*S*)-2-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
1-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)cyclobutanecarboxamide
(*R*)-*N*-(4-(2-(6-morpholinopyridin-3-ylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*S*)-*N*-(4-(2-(3-chloro-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(2*R*,3*R*)-2-amino-3-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanamide
1-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)cyclopentanecarboxamide
(*R*)-*N*-(4-(2-(4-(4-(4-(dimethylamino)butanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-(2-methoxyethyl)-3,4-dihydro-2*H*-benzo[b][1,4]oxazin-7-ylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-2-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide
(*R*)-2-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanamide
(*R*)-2-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)hexanamide
(*R*)-2-amino-3-methoxy-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
(2*S*,3*R*)-2-amino-3-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanamide
(*R*)-*N*-(4-(2-(3-fluoro-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide

Name
N-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(1*H*-tetrazol-1-yl)acetamide
(*S*)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)indoline-2-carboxamide
(*R*)-tert-butyl 2-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenylcarbamoyl)pyrrolidine-1-carboxylate
1-acetyl-4-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)piperidine-4-carboxamide
(*R*)-2-amino-3-methoxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
(*S*)-*N*-(4-(2-(3-fluoro-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-2-amino-*N*-(4-(2-(3-fluoro-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide
2-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide
(*R*)-*N*-(4-(2-(4-(4-(2-hydroxyethyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-(4-((1-methyl-1*H*-pyrrol-2-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(*R*)-*N*-(4-(2-(4-(4-((*R*)-pyrrolidin-2-ylmethyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide
(2*S*,3a*S*,7a*S*)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)octahydro-1*H*-indole-2-carboxamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)cyclopropanecarboxamide
N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)cyclopropanecarboxamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)valinamide
N-(4-{2-[(4-{4-[(1-methyl-1H-imidazol-2-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3,5-dimorpholin-4-ylphenyl)amino]-5-methylpyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-alaninamide

Name
N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
2-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenylacetamide
N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
3-(methyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)prolinamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-alaninamide
N-(4-{2-[(4-{4-[3-(dimethylamino)-2,2-dimethylpropyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1,3-thiazole-4-carboxamide

5

5

Table 2 (Part B)

Name
N-(4-{2-[(2-methyl-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-pyrrolidin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(diethylamino)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-azepan-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({4-[methyl(2-phenylethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-[4-(2-{[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(2-oxopiperidin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(2-methylpiperidin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-valinamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-valinamide
2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)alaninamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)tryptophanamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide
O-(1,1-dimethylethyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-serinamide
3-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)tetrahydrofuran-3-carboxamide
bis(1,1-dimethylethyl) (2R)-2-{[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]carbonyl}piperazine-1,4-dicarboxylate
N-(4-{2-[(4-{4-[2-(2-fluorophenyl)acetyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[2-(2-methylphenyl)acetyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[2-(3-fluorophenyl)acetyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({4-[4-(3-thienylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(4-{4-[(6-chloropyridin-3-yl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(3-methylfuran-2-yl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-(2-(4-(4-(3-fluoro-2-methylbenzoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-(1H-imidazole-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-(4-(2-(4-(4-(2-methoxynicotinoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide

Name
N-(4-(2-(4-(4-(4-fluoro-3-methylbenzoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide
N-{4-[2-({4-[4-(naphthalen-2-ylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({4-[4-(quinolin-8-ylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-[4-(2-{[4-(4-{[4-(1,1-dimethylethyl)phenyl]sulfonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(4-{[5-bromo-2-(methyloxy)phenyl]sulfonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-{4-[(phenylmethyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(4-{[3-(trifluoromethyl)phenyl]sulfonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-{4-[(2-methylphenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(3-fluorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(2,4-difluorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({3-[4-({4-[(trifluoromethyl)oxy]phenyl}methyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(3-{4-[(1-methyl-1H-imidazol-2-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({3-[4-({2-[(trifluoromethyl)oxy]phenyl}methyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(3-{4-[(3-chlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({3-[4-(2,3-dihydroxypropyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(pyridin-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(pyridin-3-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(1H-pyrrol-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
4-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-N-(phenylmethyl)piperazine-1-carboxamide
N-[4-(2-{[3-(4-{[2-(methyloxy)phenyl]carbonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({3-[4-(1H-pyrazol-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(3-pyridin-3-ylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(3-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[3-(4-{2-[(4-fluorophenyl)oxy]acetyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({3-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(pyridin-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(pyridin-2-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide

Name
N-(4-{2-[(3-{4-[(2-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({3-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-3-carboxamide
(2R)-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide
(2S)-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide
N-(4-{2-[(4-{4-[(2-fluorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-{4-[(3,5-dichlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
ethyl 3-[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]-3-oxopropanoate
N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-3-carboxamide
N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-3-carboxamide
N-ethyl-4-{4-[(4-{4-[(tetrahydrofuran-3-ylcarbonyl)amino]phenyl}pyrimidin-2-yl)amino]phenyl}piperazine-1-carboxamide
N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-3-carboxamide
N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-3-carboxamide
N-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-3-carboxamide
N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-3-carboxamide
N-{4-[2-(1H-benzimidazol-6-ylamino)-5-methylpyrimidin-4-yl]phenyl}acetamide
4-(4-furan-2-ylphenyl)-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine
N-(4-morpholin-4-ylphenyl)-4-[4-(pyrimidin-2-ylamino)phenyl]pyrimidin-2-amine
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-methylpyrimidin-4-yl)phenyl]cyclopropanecarboxamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]cyclopropanecarboxamide
N-(4-{2-[(3,5-dimorpholin-4-ylphenyl)amino]-5-methylpyrimidin-4-yl}phenyl)-N^2,N^2-dimethylglycinamide
N^2,N^2-dimethyl-N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide
N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide
N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide
N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide
N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide
N-ethyl-4-[4-({4-[4-(D-prolylamino)phenyl]pyrimidin-2-

Name
yl}amino)phenyl]piperazine-1-carboxamide
N-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide
N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide
1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-2-carboxamide
N-{4-[2-({4-[4-(piperidin-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-prolinamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-pyridin-4-ylacetamide
2-(3-fluorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
3-(4-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide
2-(3-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-phenylpropanamide
(1R,2R)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenylcyclopropanecarboxamide
2-(4-fluorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
3-(2-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide
3-(3-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide
3-(2-fluorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide
Nalpha,Nalpha-dimethyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-phenylalaninamide
2-(2-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-pyridin-2-ylacetamide
2-(4-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-{4-[(trifluoromethyl)oxy]phenyl}acetamide
2-[2-(methyloxy)phenyl]-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
2-[3-(methyloxy)phenyl]-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
2-[4-(methyloxy)phenyl]-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-alaninamide
N-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-3-(methyloxy)propanamide
(2R)-2-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenylethanamide

Name
N^2,N^2-dimethyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-alaninamide
1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide
N^2,N^2-dimethyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-alaninamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1-phenylcyclopropanecarboxamide
2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)butanamide
(2S)-1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)azetidine-2-carboxamide
2,4,6-trichloro-N-(3-{[4-(4-methyl-2-thienyl)pyrimidin-2-yl]amino}propyl)benzamide
N-[3-({4-[3,4-bis(methyloxy)phenyl]pyrimidin-2-yl}amino)propyl]-2,6-dichlorobenzamide
2,6-dichloro-N-[3-({4-[(4-morpholin-4-ylphenyl)amino]pyrimidin-2-yl}amino)propyl]benzamide
2,6-dichloro-N-(3-{[4-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-fluoropyrimidin-2-yl]amino}propyl)benzamide
2,6-dichloro-N-{3-[(4-{3-[(dimethylamino)methyl]phenyl}pyrimidin-2-yl)amino]propyl}benzamide
2,6-dichloro-N-[3-({4-[3-(1-methylethyl)phenyl]pyrimidin-2-yl}amino)propyl]benzamide
2,6-dichloro-N-{3-[(4-{4-[(1-methylethyl)oxy]phenyl}pyrimidin-2-yl)amino]propyl}benzamide
N-[3-({4-[3-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2,6-dichlorobenzamide
2,6-dichloro-N-[3-({4-[(E)-2-phenylethenyl]pyrimidin-2-yl}amino)propyl]benzamide
phenyl (4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)carbamate
phenylmethyl (4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)carbamate
N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-3-(methyloxy)propanamide
N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}cyclopropanecarboxamide
4-{4-[(4-{4-[(cyclopropylcarbonyl)amino]phenyl}pyrimidin-2-yl)amino]phenyl}-N-ethylpiperazine-1-carboxamide
N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-3-(methyloxy)propanamide
3-(methyloxy)-N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}propanamide
N-ethyl-4-(4-{[4-(4-{[3-(methyloxy)propanoyl]amino}phenyl)pyrimidin-2-yl]amino}phenyl)piperazine-1-carboxamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-2-phenylacetamide
1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyrrolidin-2-one
N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-alaninamide
N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-alaninamide
(2S)-2-hydroxy-3-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)butanamide
(2R)-2-hydroxy-3-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-

Name
4-yl}phenyl)butanamide
N-{4-[2-({4-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-alaninamide
(2S)-2-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenylethanamide
2-amino-2-(4-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)morpholine-3-carboxamide
1-ethyl-3-[4-(2-{[4-(4-ethylpiperazin-1-yl)-3-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]urea
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)-3-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)-3-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
1-(2,6-dichlorophenyl)-3-(3-{[4-(4-methyl-2-thienyl)pyrimidin-2-yl]amino}propyl)urea
1-[2-fluoro-5-(trifluoromethyl)phenyl]-3-(3-{[4-(4-methyl-2-thienyl)pyrimidin-2-yl]amino}propyl)urea
2,6-dichloro-N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]benzenesulfonamide
N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2,6-difluorobenzenesulfonamide
N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]naphthalene-2-sulfonamide
N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]-3,4-bis(methyloxy)benzenesulfonamide
3-chloro-N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]propane-1-sulfonamide
N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]propane-1-sulfonamide
methyl (3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}propyl)carbamate
1-methylethyl (3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}propyl)carbamate
phenylmethyl (3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}propyl)carbamate
N-{4-[2-({[3-(3-chlorophenyl)isoxazol-5-yl]methyl}amino)pyrimidin-4-yl]phenyl}acetamide
ethyl 4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)piperidine-1-carboxylate
1,1-dimethylethyl 4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)piperidine-1-carboxylate
N-(4-{2-[(4-cyanophenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyridin-4-yl}phenyl)acetamide
1,1-dimethylethyl {1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperidin-4-yl}carbamate
N-{4-[2-({4-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}cyclopropanecarboxamide
N-{1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperidin-4-yl}acetamide
4-(4-aminophenyl)-N-[4-(4-aminopiperidin-1-yl)phenyl]pyrimidin-2-amine
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-methylpyrimidin-4-yl)phenyl]-3-(methyloxy)propanamide
N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-2-carboxamide

Name
N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-2-carboxamide
N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-2-carboxamide
N-cyclopropyl-4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzamide
N-[2-(methyloxy)ethyl]-4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzamide
2,6-dichloro-N-{3-[(4-pyridin-3-ylpyrimidin-2-yl)amino]propyl}benzamide
2,6-dichloro-N-(3-{[4-(4-methyl-3,4-dihydro-2H-1,4-benzoxazin-7-yl)pyrimidin-2-yl]amino}propyl)benzamide
2,6-dichloro-N-(3-{[4-(2,3-dihydro-1,4-benzodioxin-6-yl)-6-methylpyrimidin-2-yl]amino}propyl)benzamide
N-(4-{2-[(3-{[(2,6-dichlorophenyl)carbonyl]amino}propyl)amino]pyrimidin-4-yl}phenyl)morpholine-4-carboxamide
2,6-dichloro-N-{3-[(4-{4-[(cyclopropylcarbonyl)amino]phenyl}pyrimidin-2-yl)amino]propyl}benzamide
N-(4-{2-[(3-{[(2,6-dichlorophenyl)carbonyl]amino}propyl)amino]pyrimidin-4-yl}phenyl)thiophene-2-carboxamide
2,6-dichloro-N-(3-{[4-(4-{[N-(2-morpholin-4-ylethyl)glycyl]amino}phenyl)pyrimidin-2-yl]amino}propyl)benzamide
1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)ethanone
(1E)-1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)ethanone oxime
N-{4-[2-({4-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-2-phenylacetamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-bromobenzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-fluorobenzamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-chlorobenzamide
N-[4-(2-{[3-(morpholin-4-ylsulfonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({3-[(cyclohexylmethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(3-{[(5-bromo-2-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-{[(2,5-dimethylphenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3,4-dimorpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({4-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}cyclopropanecarboxamide
N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}butanamide
N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}butanamide
N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}butanamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-2-carboxamide
2-hydroxy-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide
3-(methyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide
4-(methyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide

Name
4-chloro-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide
(2R)-N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide
(2S)-N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide
1-(2-hydroxyethyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-prolinamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)thiophene-2-carboxamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-3-carboxamide
2-phenyl-N-{4-[2-({4-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(diphenylmethyl)benzamide
N-[4-(2-{[4-(4-methylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({4-[4-(phenylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({4-[4-(2-cyclopentylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({4-[4-(cyclohexylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(4-{4-[(2-chlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(3-fluorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(3-fluoro-4-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(3,4-dichlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(3,5-dichlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(4-{[3-(methyloxy)phenyl]carbonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-{4-[(4-chlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(4-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({4-[4-(furan-2-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-[4-(2-{[4-(4-{2-[(4-fluorophenyl)oxy]acetyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)furan-3-carboxamide
N-{4-[2-({4-[4-(phenylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({4-[4-(2-thienylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(4-{4-[(4-fluorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[4-(4-{[4-(methyloxy)phenyl]sulfonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide

Name
N-(4-{2-[(4-{4-[(4-chlorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-{4-[(3-chlorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({4-[4-(biphenyl-4-ylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({4-[4-(naphthalen-1-ylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(3-{4-[(2-chlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[4-(2-{[3-(4-{[3-(methyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({3-[4-(3-methylbutyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(2,3-dihydro-1,4-benzodioxin-6-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(cyclopropylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(3-{4-[3-(methylthio)propyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-{4-[(4-{[3-(dimethylamino)propyl]oxy}phenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({3-[4-({3-[(trifluoromethyl)oxy]phenyl}methyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
4-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-N-phenylpiperazine-1-carboxamide
N-[4-(2-{[3-(4-propanoylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({3-[4-(phenylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(2-phenylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(cyclopentylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(2-pyridin-3-ylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(2-cyclopentylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-(4-{2-[(3-{4-[(2-chlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-{4-[(4-chlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-{4-[(3,4-dichlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-{4-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N^2,N^2-dimethyl-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]glycinamide
3-(methyloxy)-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]propanamide
N-(4-{2-[(4-{4-[(2-chlorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-{4-[2-({3-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({3-[4-(2-cyclopropylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-[4-(2-{[3-(4-{[3-(methyloxy)phenyl]carbonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide

Name
N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperidine-3-carboxylic acid
1,1-dimethylethyl methyl{2-[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]-2-oxoethyl}carbamate
1,1-dimethylethyl [4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]carbamate
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-N^2,N^2-dimethylglycinamide
4-(4-aminophenyl)-N-[4-(4-ethylpiperazin-1-yl)phenyl]pyrimidin-2-amine
Nalpha-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-phenylalaninamide
Nalpha-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-phenylalaninamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-phenylalaninamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-phenylalaninamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-L-valinamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-valinamide
1-ethyl-3-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]urea
(2R)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-2-carboxamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-methylpyrimidin-4-yl)phenyl]acetamide
4-{4-[(4-{4-[(N,N-dimethylglycyl)amino]phenyl}pyrimidin-2-yl)amino]phenyl}-N-ethylpiperazine-1-carboxamide
N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-N^2,N^2-dimethylglycinamide
N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-N^2,N^2-dimethylglycinamide
N^2,N^2-dimethyl-N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}glycinamide
N-{4-[2-({4-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-N^2,N^2-dimethylglycinamide
N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-N^2,N^2-dimethylglycinamide
N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-N^2,N^2-dimethylglycinamide
N-(4-{2-[({1-[(2,6-dichlorophenyl)carbonyl]azetidin-3-yl}methyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(3-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)cyclohexyl]-2,6-dichlorobenzamide
N-{4-[2-({[4-(4-methylpiperazin-1-yl)phenyl]methyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide
N-{4-[2-(piperidin-4-ylamino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({1-[(2,6-dichlorophenyl)carbonyl]piperidin-4-yl}amino)pyrimidin-4-yl]phenyl}acetamide
N-{4-[2-({4-[(2-hydroxyethyl)oxy]phenyl}amino)pyrimidin-4-

Name
yl]phenyl}acetamide
1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-phenylurea
N-[5-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-2-(4-ethylpiperazin-1-yl)phenyl]-2,6-dichlorobenzamide
1-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-3-(phenylmethyl)urea
N^2,N^2-dimethyl-N-{4-[2-({4-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}glycinamide
N-(3-fluoro-4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)cyclopropanecarboxamide
N-(4-{2-[(4-{4-[(1-methyl-1H-imidazol-2-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)cyclopropanecarboxamide
N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide
N-{4-[2-({4-[4-(2-piperazin-1-ylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide
N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide
N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide
N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide
N-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide
1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1H-pyrrole-2-carboxamide
3-fluoro-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-4-carboxamide
6-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-3-carboxamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridazine-4-carboxamide
2-cyclopropyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)isoxazole-5-carboxamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-3-carboxamide
4-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]butanamide
1-ethyl-3-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]urea

5

JAK-2 Definitions

[00227] The following definitions apply to the JAK-2 compounds described above only. These definitions are not to be considered when determining the scope and meaning of the MEK compounds. To the same extent, the MEK definitions are not to be considered when determining the scope and meaning of the JAK-2 compounds.

[00228] "Alkyl" is intended to include C_1-C_{20}, more typically, C_1-C_{12} linear or branched structures and combinations thereof, inclusively. "Lower alkyl" is intended to include C_1-C_6 linear or branched structures and combinations thereof, inclusively. For example, "C_6 alkyl" can refer to an *n*-hexyl, *iso*-hexyl, cyclobutylethyl, and the like. Examples of lower alkyl groups include methyl, ethyl, propyl, isopropyl, butyl, *s*-butyl, *t*-butyl, isobutyl, pentyl, hexyl and the like. Higher alkyl refers to alkyl groups containing more that six carbon atoms.

[00229] "Cycloalkyl" means a non-aromatic mono- or multicyclic ring system comprising about 3 to about 14 carbon atoms, 5 to 10 carbon atoms, or 5 to about 7 ring atoms. Non-limiting examples of monocyclic cycloalkyls include cyclopropyl, cyclopentyl, cyclohexyl, cycloheptyl and the like. Non-limiting examples of multicyclic cycloalkyls include 1-decalin, norbornyl, adamantyl and the like. Cycloalkyls can be fused or bridge ring systems or spirocyclic systems.

[00230] "Alkyl substituted with halo and hydroxy" means an alkyl group substituted with 1, 2, or 3 hydroxy and 1, 2, 3, 4, or 5 halo.

[00231] "Alkylene" refers to straight or branched chain divalent group consisting solely of carbon and hydrogen atoms, containing no unsaturation and having from one to ten carbon atoms, for example, methylene, ethylene, propylene, *n*-butylene and the like. Alkylene is a subset of alkyl, referring to the same residues as alkyl, but having two points of attachment and, specifically, fully saturated. Examples of alkylene include ethylene ($-CH_2CH_2-$), propylene ($-CH_2CH_2CH_2-$), dimethylpropylene ($-CH_2C(CH_3)_2CH_2-$), and cyclohexylpropylene ($-CH_2CH_2CH(C_6H_{13})$).

[00232] "Alkoxy" or "alkoxyl" refers to the group -O-alkyl, wherein the term "alkyl" is as defined hereinabove. Examples include methoxy, ethoxy, propoxy, isopropoxy, and the like. Lower alkoxy refers to groups containing one to six carbons.

[00233] "Substituted alkoxy" refers to the group -O-(substituted alkyl), the substitution on the alkyl group generally containing more than only carbon (as defined by alkoxy). Another exemplary substituted alkoxy group is hydroxyalkoxy or –O-alkyl-OH.

[0234] "Alkoxy" or "alkoxyl" refers to the group -O-alkyl, wherein the term "alkyl" is as defined hereinabove. Examples include methoxy, ethoxy, propoxy, isopropoxy, and the like. Lower alkoxy refers to groups containing one to six carbons.

[0235] "Substituted alkoxy" refers to the group -O-(substituted alkyl), the substitution on the alkyl group generally containing more than only carbon (as defined by alkoxy). Another exemplary substituted alkoxy group is hydroxyalkoxy or –O-alkyl-OH.

[0236] "Aryl" means a monovalent six - to fourteen-membered mono- or multicyclic ring, wherein the monocyclic ring is aromatic and at least one of the rings in the multicyclic ring is aromatic. An aryl can also be six- to ten membered, or six membered. Representative non-limiting examples of aryl include phenyl, naphthyl, and the like.

[0237] "Arylalkyl" means a residue in which an aryl moiety, as defined above, is attached to a parent structure via one of an alkylene, alkylidene, or alkylidyne group. Examples include benzyl, phenethyl, phenylvinyl, phenylallyl and the like. The "alkyl" portion of the group can be one to ten carbons, and in another embodiment, one to six carbons; the latter can also be referred to as C_{1-6} arylalkyl. When a group is referred to as or "-(C_1-C_6)alkylaryl," an aryl moiety is attached to a parent structure via an alkylene group. Examples include benzyl, phenethyl, and the like.

[0238] In some examples, as appreciated by one of ordinary skill in the art, two adjacent groups on an aromatic system can be fused together to form a ring structure. The fused ring structure can contain heteroatoms and can be optionally substituted with one or more groups. It should additionally be noted that saturated carbons of such fused groups (*i.e.* saturated ring structures) can contain two substitution groups.

[0239] "Fused-polycyclic" or "fused ring system" refers to a polycyclic ring system that contains bridged or fused rings; that is, where two rings have more than one shared atom in their ring structures. In this application, fused-polycyclics and fused ring systems includes non-aromatic and aromatic systems. Typically, but not necessarily, fused-polycyclics share a vicinal set of atoms, for example naphthalene or 1,2,3,4-tetrahydro-naphthalene. A spiro ring system is not a fused-polycyclic by this definition, but fused polycyclic ring systems of the invention can themselves have spiro rings attached thereto via a single ring atom of the fused-polycyclic.

[0240] "Halogen" or "halo" refers to fluorine, chlorine, bromine or iodine. "Haloalkyl" and "haloaryl" refer generically to alkyl and aryl groups that are substituted with one or more

halogens, respectively. Non-limiting examples of "haloalkyl" include -CH_2F, -$CHCl_2$ or -CF_3.

[0241] "Heteroatom" refers to O, S, N, or P.

[0242] "Heterocyclyl" refers to a stable three- to fifteen-membered ring substituent that consists of carbon atoms and from one to five heteroatoms selected from the group consisting of nitrogen, phosphorus, oxygen and sulfur. For purposes of this invention, the heterocyclyl substituent can be a monocyclic, bicyclic or tricyclic ring system, which can include fused or bridged ring systems as well as spirocyclic systems. The terms "heterocycloalkyl" and "heteroaryl" are groups that are encompassed by the broader term "heterocyclyl." The nitrogen, phosphorus, carbon or sulfur atoms in the heterocyclyl group can be optionally oxidized to various oxidation states. In a specific example, the group -$S(O)_{0-2}$-, refers to -S- (sulfide), -S(O)- (sulfoxide), and -SO_2- (sulfone) respectively. For convenience, nitrogens, particularly but not exclusively, those defined as annular aromatic nitrogens, are meant to include their corresponding *N*-oxide form, although not explicitly defined as such in a particular example. Thus, for a compound of the invention having, for example, a pyridyl ring; the corresponding pyridyl-*N*-oxide is meant to be included as another compound of the invention. In addition, annular nitrogen atoms can be optionally quaternized; and the ring substituent can be partially or fully saturated or aromatic. Examples of heterocyclyl groups include, but are not limited to, azetidinyl, acridinyl, benzodioxolyl, benzodioxanyl, benzofuranyl, carbazoyl, cinnolinyl, dioxolanyl, indolizinyl, naphthyridinyl, perhydroazepinyl, phenazinyl, phenothiazinyl, phenoxazinyl, phthalazinyl, pteridinyl, purinyl, quinazolinyl, quinoxalinyl, quinolinyl, isoquinolinyl, tetrazoyl, tetrahydroisoquinolyl, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, 2-oxoazepinyl, azepinyl, pyrrolyl, 4-piperidonyl, pyrrolidinyl, pyrazolyl, pyrazolidinyl, imidazolyl, imidazolinyl, imidazolidinyl, dihydropyridinyl, tetrahydropyridinyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, oxazolinyl, oxazolidinyl, triazolyl, isoxazolyl, isoxazolidinyl, morpholinyl, thiazolyl, thiazolinyl, thiazolidinyl, isothiazolyl, quinuclidinyl, isothiazolidinyl, indolyl, isoindolyl, indolinyl, isoindolinyl, octahydroindolyl, octahydroisoindolyl, quinolyl, isoquinolyl, decahydroisoquinolyl, benzimidazolyl, thiadiazolyl, benzopyranyl, benzothiazolyl, benzoxazolyl, furyl, tetrahydrofuryl, tetrahydropyranyl, thienyl, benzothienyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, dioxaphospholanyl, oxadiazolyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, and tetrahydroquinolinyl.

[0243] "Heterocycloalkyl" refers to a stable 4-12 membered monocyclic, bicyclic or tricyclic ring containing one or more heteroatoms.

[0244] "Heterocycloalkylalkyl" refers to a heterocycloalkyl, as defined herein, attached to the parent moiety through an "alkyl," as defined herein. One non-limiting example of heterocycloalkyl includes piperadinyl. Another non-limiting example of heterocycloalkyl includes piperadinyl. Another non-limiting example of heterocycloalkyl includes piperazinyl. Another non-limiting example of heterocycloalkyl includes furanyl. Another non-limiting example of heterocycloalkyl includes pyrrolidinyl. Another non-limiting example of heterocycloalkyl includes morpholinyl.

[0245] "Amino" refers to $-NH_2$.

[0246] "Alkylamino" refers to –NH(alkyl), wherein "alkyl" is as defined above, and wherein the the parent moiety is attached to the nitrogen atom.

[0247] "Dialkylamino" refers to $-N(alkyl)_2$, wherein "alkyl" is as defined above, and wherein the parent moiety is attached to the nitrogen atom.

[0248] "Dialkylaminoalkyl refers to $-(alkyl)N(alkyl)_2$, wherein "alkyl" is as defined above. One such non-limiting example of "dialkylaminoalkyl" includes - $CH_2C(CH_3)_2CH_2N(CH_3)_2$.

[0249] "Aminoalkyl" refers to -(alkyl)NH, wherein "alkyl" is as defined above, and wherein the the parent moiety is attached to the alkyl group.

[0250] "Aminoalkyl" refers to $-(alkyl)NH_2$, wherein "alkyl" is as defined above, and wherein the the parent moiety is attached to the alkyl group. The amino group can be attached at any point along the alkyl group. Non-limiting examples of aminoalkyl include - $CH(NH_2)CH_3$,

[0251] Phenoxy refers to a –alkyl-O-phenyl group, wherein "alkyl" is as defined above, and the parent moiety is attached to the alkyl group.

[0252] "Heteroaryl" means a 5- to 12-membered, monocyclic aromatic heterocyclyl (where heterocyclyl is defined herein) or bicyclic heterocyclyl ring system (where at least one of the rings in the bicyclic system is aromatic) where the monocyclic ring and at least one of the rings in the bicyclic ring system contains one, two, three, four, or five heteroatom(s) selected from nitrogen, oxygen, phosphorous, and sulfur. The ring containing the heteroatom can be aromatic or non-aromatic. Representative examples include pyridinyl, imidazolyl, pyrimidinyl, pyrazolyl, triazolyl, pyrazinyl, tetrazolyl, furyl, thienyl, isoxazolyl, thiazolyl, oxazolyl, isothiazolyl, pyrrolyl, quinolinyl, isoquinolinyl, indolyl,

benzimidazolyl, benzdioxolyl, benzofuranyl, cinnolinyl, indazolyl, indolizinyl, phthalazinyl, pyridazinyl, triazinyl, isoindolyl, pteridinyl, purinyl, oxadiazolyl, triazolyl, thiadiazolyl, thiadiazolyl, furazanyl, benzofurazanyl, benzothiophenyl, benzothiazolyl, benzoxazolyl, quinazolinyl, quinoxalinyl, naphthyridinyl, and furopyridinyl. Fused, bridged, and spiro moieties are also included within the scope of this definition.

[0253] "Carbonyl" refers to the group "-C(O)-", which is bivalent.

[0254] "Aminocarbonyl" refers to the group "-C(O)-NH_2," wherein the parent moiety is attached to the amino group.

[0255] "Alkoxycarbonyl" refers to the group "-C(O)alkoxy," wherein alkoxy is as defined above, and the parent moiety is attached to the carbonyl. A non-limiting example includes -C(O)-$OC(CH_3)_3$.

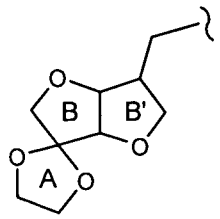
[0256] When a group is referred to as "-C_1-C_6 alkyl heterocyclyl" the heterocyclyl is attached to a parent structure via one of an alkylene, alkylidene, or alkylidyne group. Examples include (4-methylpiperazin-1-yl) methyl, (morpholin-4-yl) methyl, (pyridine-4-yl) methyl, 2-(oxazolin-2-yl) ethyl, 4-(4-methylpiperazin-1-yl)-2-butenyl, and the like. Both the heterocyclyl and the corresponding alkylene, alkylidene, or alkylidyne portion of a heterocyclylalkyl group can be optionally substituted.

[0257] "Hydroxyalkyl" means –alkyl-OH, wherein alkyl is as defined hereinabove.

[0258] "Optional" or "optionally" means that the subsequently described event or circumstance can or can not occur, and that the description includes instances where said event or circumstance occurs and instances in which it does not. One of ordinary skill in the art would understand that with respect to any molecule described as containing one or more optional substituents, only sterically practical and/or synthetically feasible compounds are meant to be included. "Optionally substituted" refers to all subsequent modifiers in a term. So, for example, in the term "optionally substituted arylalkyl," both the "alkyl" portion and the "aryl" portion of the molecule is or is not substituted. A list of exemplary optional substitutions is presented below in the definition of "substituted."

[0259] "Saturated bridged ring system" refers to a bicyclic or polycyclic ring system that is not aromatic. Such a system can contain isolated or conjugated unsaturation, but not aromatic or heteroaromatic rings in its core structure (but can have aromatic substitution thereon). For example, hexahydro-furo[3,2-b]furan, 2,3,3a,4,7,7a-hexahydro-1H-indene, 7-aza-bicyclo[2.2.1]-heptane, and 1,2,3,4,4a,5,8,8a-octahydro-naphthalene are all included in the class "saturated bridged ring system.

[0260] "Spirocyclyl" or "spirocyclic ring" refers to a ring originating from a particular annular carbon of another ring. For example, as depicted below, a ring atom of a saturated bridged ring system (rings B and B'), but not a bridgehead atom, can be a shared atom between the saturated bridged ring system and a spirocyclyl (ring A) attached thereto. A spirocyclyl can be carbocyclic or heteroalicyclic.



[0261] "Substituted" alkyl, aryl, and heterocyclyl, refer respectively to alkyl, aryl, and heterocyclyl, one or more (for example up to about five, in another example, up to about three) hydrogen atoms are replaced by a substituent independently selected from: alkyl (for example, fluoromethyl), aryl (for example, 4-hydroxyphenyl), arylalkyl (for example, 1-phenyl-ethyl), heterocyclylalkyl (for example, 1-pyridin-3-yl-ethyl), heterocyclyl (for example, 5-chloro-pyridin-3-yl or 1-methyl-piperidin-4-yl), alkoxy, alkylenedioxy (for example methylenedioxy), amino (for example, alkylamino and dialkylamino), amidino, aryloxy (for example, phenoxy), arylalkyloxy (for example, benzyloxy), carboxy ($-CO_2H$), carboalkoxy (that is, acyloxy or $-OC(=O)R$), carboxyalkyl (that is, esters or $-CO_2R$), carboxamido, benzyloxycarbonylamino (CBZ-amino), cyano, acyl, halogen, hydroxy, nitro, sulfanyl, sulfinyl, sulfonyl, thiol, halogen, hydroxy, oxo, carbamyl, acylamino, and sulfonamido. And each substituent of a substituted group is optionally substituted, but these optional substituents themselves are not further substituted. Thus, an optionally substituted moiety is one that can or can not have one or more substituents, and each of the substituents can or can not have one or more substituents. But, the substituents of the substituents can not be substituted.

[0262] Some of the compounds of the invention can have imino, amino, oxo or hydroxy substituents off aromatic heterocyclyl systems. For purposes of this disclosure, it is understood that such imino, amino, oxo or hydroxy substituents can exist in their corresponding tautomeric form, *i.e.*, amino, imino, hydroxy or oxo, respectively.

ASSAYS FOR MEK

[0263] Certain compounds above been tested using the assay described in Biological Example 1 and have been determined to be MEK inhibitors. As such compounds of Formula I(M) or I(N) are useful for treating diseases, particularly cancer in which MEK activity contributes to the pathology and/or symptomatology of the disease. For example, cancer in which MEK activity contributes to its pathology and/or symptomatology include malignant melanomas, colorectal cancer, pancreatic cancer, lung cancer, papillary and anaplastic thyroid cancer, and endometriod ovarian cancers, and the like.

[0264] Suitable *in vitro* assays for measuring MEK activity and the inhibition thereof by compounds are known in the art. For example, see WO 2006/061712 for measuring MEK1 and MEK2 *in vitro*. For further details of an *in vitro* assay for measuring MEK activity see Biological Examples, Example 1 *infra*. Following the examples disclosed herein, as well as that disclosed in the art, a person of ordinary skill in the art can determine the inhibitory activity of a compound MEK compound described herein.

[0265] Assays for measurement of *in vitro* efficacy in treatment of cancer are known in the art. For example, see WO 2006/061712, which is herein incorporated by reference, for cell-based assays for colon cancer. In addition, cell-based tumor models are described in Biological Examples, Example 2 and 3 *infra*.

[0266] Suitable *in vivo* models for cancer are known to those of ordinary skill in the art (including WO 2006/061712). For further details of *in vivo* models for colorectal cancer, melanoma, breast adenocarcinoma, and lung anaplastic carcinoma, see Biological Example 4, *infra*.

GENERAL SYNTHESIS OF MEK COMPOUNDS

[0267] The "MEK compounds: described herein can be made by the synthetic procedures described below. The starting materials and reagents used in preparing these compounds are either available from commercial suppliers such as Aldrich Chemical Co. (Milwaukee, Wis.), or Bachem (Torrance, Calif.), or are prepared by methods known to those skilled in the art following procedures set forth in references such as Fieser and Fieser's Reagents for Organic Synthesis, Volumes 1-17 (John Wiley and Sons, 1991); Rodd's Chemistry of Carbon Compounds, Volumes 1-5 and Supplementals (Elsevier Science Publishers, 1989); Organic Reactions, Volumes 1-40 (John Wiley and Sons, 1991), March's Advanced Organic Chemistry, (John Wiley and Sons, 4th Edition) and Larock's Comprehensive Organic

Transformations (VCH Publishers Inc., 1989). These schemes are merely illustrative of some methods by which the MEK compounds can be synthesized, and various modifications to these schemes can be made and will be suggested to one skilled in the art having referred to this disclosure. The starting materials and the intermediates of the reaction may be isolated and purified if desired using conventional techniques, including but not limited to filtration, distillation, crystallization, chromatography and the like. Such materials may be characterized using conventional means, including physical constants and spectral data.

[0268] Unless specified to the contrary, the reactions described herein take place at atmospheric pressure and over a temperature range from about -78 °C to about 150 °C, more preferably from about 0 °C to about 125 °C and most preferably at about room (or ambient) temperature, e.g., about 20 °C. Unless otherwise stated (as in the case of an hydrogenation), all reactions are performed under an atmosphere of nitrogen.

[0269] Prodrugs can be prepared by techniques known to one skilled in the art. These techniques generally modify appropriate functional groups in a given compound. These modified functional groups regenerate original functional groups by routine manipulation or *in vivo*. Amides and esters of the compounds described herein may be prepared according to conventional methods. A thorough discussion of prodrugs is provided in T. Higuchi and V. Stella, "Pro-drugs as Novel Delivery Systems," Vol 14 of the A.C.S. Symposium Series, and in Bioreversible Carriers in Drug Design, ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987, both of which are incorporated herein by reference for all purposes.

[0270] The MEK compounds, or their pharmaceutically acceptable salts, may have asymmetric carbon atoms or quaternized nitrogen atoms in their structure. Compounds of Formula I(N) or Formula I(M) that may be prepared through the syntheses described herein may exist as single stereoisomers, racemates, and as mixtures of enantiomers and diastereomers. The compounds may also exist as geometric isomers. All such single stereoisomers, racemates and mixtures thereof, and geometric isomers are intended to be within the scope of this invention. Some of the compounds described herein may exist as tautomers. For example, wherein a ketone or aldehyde is present, the molecule may exist in the enol form; wherein an amide is present, the molecule may exist as the imidic acid; and wherein an enamine is present, the molecule may exist as an imine. All such tautomers are within the scope of the invention.

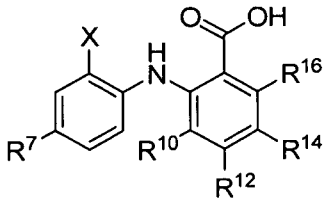
[0271] The MEK compounds also includes N-oxide derivatives and protected derivatives of compounds of Formula I(N) or Formula I(M). For example, when compounds of Formula I(M) or I(N) contain an oxidizable nitrogen atom, the nitrogen atom can be converted to an N-oxide by methods well known in the art. When compounds of Formula I(M) or I(M) contain groups such as hydroxy, carboxy, thiol or any group containing a nitrogen atom(s), these groups can be protected with a suitable "protecting group" or "protective group". A comprehensive list of suitable protective groups can be found in T.W. Greene, *Protective Groups in Organic Synthesis*, John Wiley & Sons, Inc. 1991, the disclosure of which is incorporated herein by reference in its entirety. The protected derivatives of compounds of Formula I can be prepared by methods well known in the art.

[0272] Methods for the preparation and/or separation and isolation of single stereoisomers from racemic mixtures or non-racemic mixtures of stereoisomers are well known in the art. For example, optically active (R)- and (S)- isomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. Enantiomers (R- and S-isomers) may be resolved by methods known to one of ordinary skill in the art, for example by: formation of diastereoisomeric salts or complexes which may be separated, for example, by crystallization; via formation of diastereoisomeric derivatives which may be separated, for example, by crystallization, selective reaction of one enantiomer with an enantiomer-specific reagent, for example enzymatic oxidation or reduction, followed by separation of the modified and unmodified enantiomers; or gas-liquid or liquid chromatography in a chiral environment, for example on a chiral support, such as silica with a bound chiral ligand or in the presence of a chiral solvent. It will be appreciated that where a desired enantiomer is converted into another chemical entity by one of the separation procedures described above, a further step may be required to liberate the desired enantiomeric form. Alternatively, specific enantiomer may be synthesized by asymmetric synthesis using optically active reagents, substrates, catalysts or solvents or by converting on enantiomer to the other by asymmetric transformation. For a mixture of enantiomers, enriched in a particular enantiomer, the major component enantiomer may be further enriched (with concomitant loss in yield) by recrystallization.

[0273] In addition, the MEK compounds can exist in unsolvated as well as solvated forms with pharmaceutically acceptable solvents such as water, ethanol, and the like. In general, the solvated forms are considered equivalent to the unsolvated forms for the purposes of the present invention.

[0274] The chemistry for the preparation of the MEK compounds described herein is known to those skilled in the art.

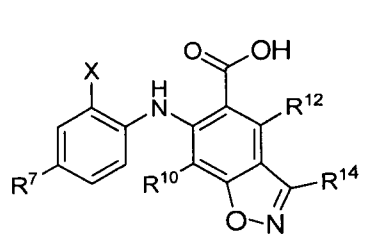
[0275] An intermediate of Formula II:



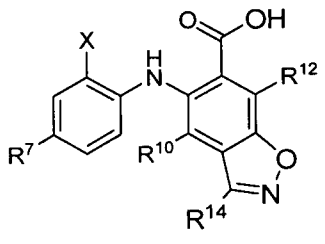
II

wherein R^7, X, R^{10}, R^{12}, R^{14}, and R^{16} are as defined in the compound of Formula I(M) or Formula I(N) for Group A can be prepared using procedures known to one of ordinary skill in the art. In particular, see (for example) US 7,019,033, WO 2002006213, WO 2003062191, WO 2003062189, WO 2002018319, WO2001005392, WO 2000064856, WO 2001005392, WO 9901421, WO 2004056789, Davis, E. M. et al. *Org. Process Res. & Dev.* 2005, 9, 843-6, and Shapiro, N. *et al. Synthetic Commun.* 2005, 35, 2265-9 which are incorporated by reference herein. The following intermediates were prepared using similar procedures as described in the above references: 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid; 2-[(2-chloro-4-iodophenyl)amino]-3,4-difluorobenzoic acid; 4-fluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid; 4,5-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid; and 2-[(4-bromo-2-fluorophenyl)amino]-3,4-difluorobenzoic acid.

An intermediate of Formula III(a) or III(b):



III(a);

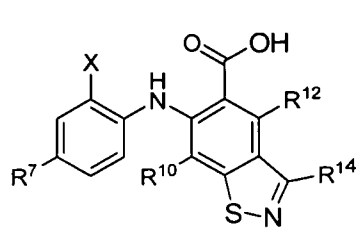


III(b)

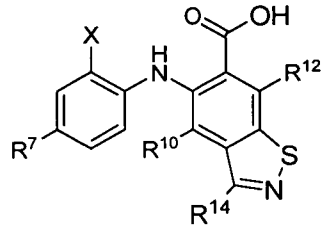
wherein R^7, X, R^{10}, R^{12}, and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for Group B can be prepared using procedures known to one of ordinary skill in the art. In particular for formula III(a), wherein R^{14} is amino or alkyl (particularly methyl); R^{10} is halo (particularly fluoro); R^7 is hydrogen or halo (particularly bromo or chloro); X is halo (particularly chloro); and R^{12} is hydrogen see for example WO2006030610, US2005049419, and US2005/0054701 which are incorporated by reference herein. 6-[(4-bromo-2-chlorophenyl)amino]-7-fluoro-3-methyl-1,2-benzisoxazole-5-carboxylic acid was prepared

using methods similar to those disclosed in WO2006030610, US2005049419, and US2005/0054701.

[0276] An intermediate of Formula IV(a) or IV(b):



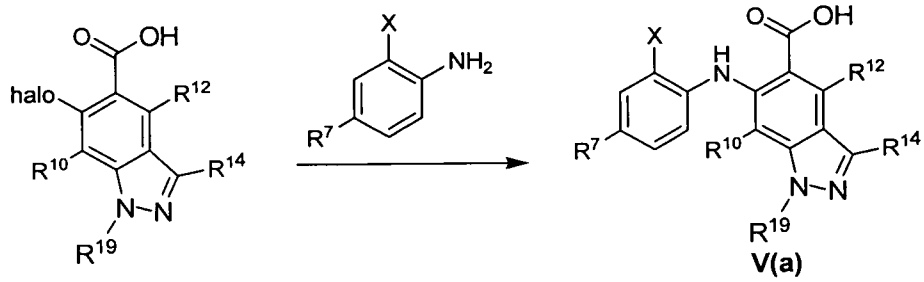
IV(a);



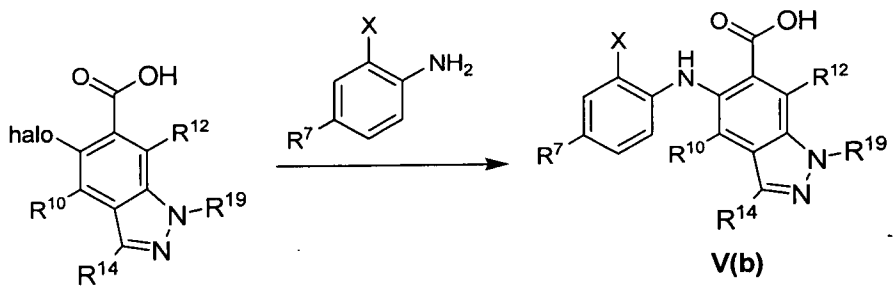
IV(b)

wherein R^7, X, R^{10}, R^{12}, and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for Group B can be prepared using procedures known to one of ordinary skill in the art.

[0277] An intermediate of Formula V(a) or V(b):



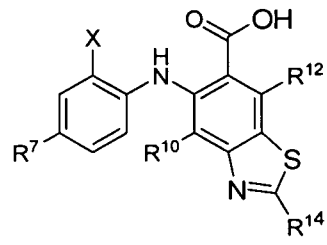
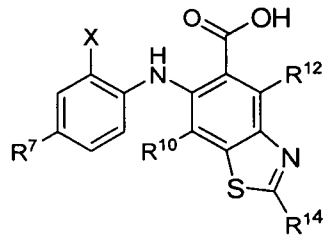
V(a)



V(b)

wherein R^7, X, R^{10}, R^{12}, R^{14}, and R^{19} are as defined in the compound of Formula I(M) or Formula I(N) for Group B can be prepared using procedures known to one of ordinary skill in the art. In particular the halo precursor of V(a) can be prepared using, for example, WO2003101968 and WO2002083648 which are incorporated by reference herein. In particular the halo precursor of V(b) can be prepared using, for example, US2004192653, US2004180896, US2004176325 which are incorporated by reference herein. The halo precursors are then reacted with an appropriate aniline to yield the intermediates of Formula V(a) and V(b).

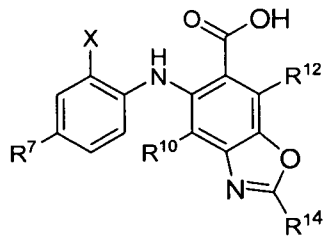
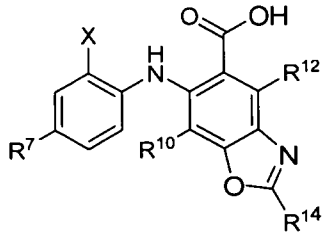
[0278] An intermediate of Formula VI(a) or VI(b):

VI(a); VI(b)

wherein R^7, X, R^{10}, R^{12}, and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for Group B can be prepared using procedures known to one of ordinary skill in the art. In particular, for VI(b) see for example WO2000042022 and WO2001005390 which are incorporated by reference herein.

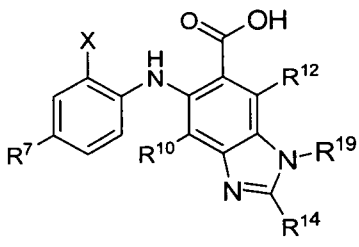
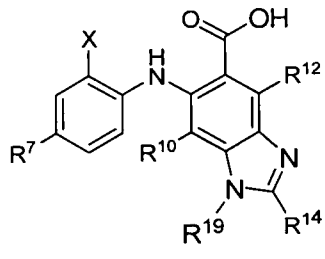
[0279] An intermediate of Formula VII(a) or VII(b):

VII(a); VII(b)

wherein R^7, X, R^{10}, R^{12}, and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for Group B can be prepared using procedures known to one of ordinary skill in the art. For intermediate VII(b) see, for example, WO2001005390 and WO2000042022 which are incorporated by reference herein.

[0280] An intermediate of Formula VIII(a) or VIII(b):

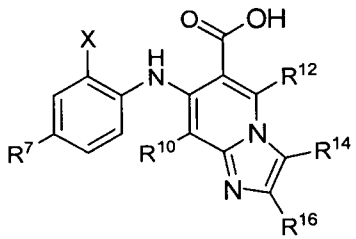



VIII(a); VIII(b)

wherein R^7, X, R^{10}, R^{12}, R^{14}, and R^{19} are as defined in the compound of Formula I(M) or Formula I(N) for Group B can be prepared using procedures known to one of ordinary skill in the art. In particular for formula VIII(b) wherein R^{10} is halo (particularly fluoro), R^{12} is hydrogen, R^{14} is hydrogen, and R^{19} is hydrogen or alkyl (particularly methyl) or alkenyl (particularly allyl), see WO 05/023251, WO2005009975, and WO2001005390 which are incorporated by reference herein. In particular for VIII(a) wherein X is halo (particularly chloro or fluoro) or alkyl (particularly methyl), R^7 is halo (particularly iodo, bromo, or chloro) or haloalkoxy (particularly trifluormethoxy), R^{10} is halo (particularly fluoro or

chloro), R^{14} is hydrogen or alkyl (particularly methyl), and R^{19} is hydrogen or alkyl (particularly methyl), see for example US 2004/0116710, WO 03/077914, WO 03/077855, WO 00/42022, WO2005009975, and WO2001005390 which are incorporated by reference herein. The following intermediates were prepared using similar procedures described in US 2004/0116710, WO 03/077914, WO 03/077855, WO 00/42022, WO2005009975, and WO2001005390: 5-[(4-bromo-2-chlorophenyl)amino]-4-fluoro-1-methyl-1*H*-benzimidazole-6-carboxylic acid and 4-fluoro-5-[(2-fluoro-4-iodophenyl)amino]-1-methyl-1*H*-benzimidazole-6-carboxylic acid.

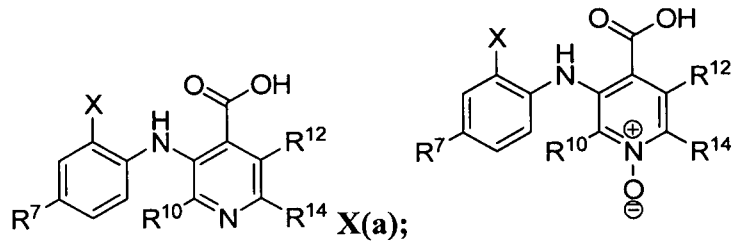
[0281] An intermediate of Formula IX:



IX

wherein R^7, X, R^{10}, R^{12}, R^{14}, and R^{16} are as defined in the compound of Formula I(M) or Formula I(N) for Group B can be prepared using procedures known to one of ordinary skill in the art. In particular, wherein R^{10} is hydrogen or halo (particularly chloro or fluoro); R^{12} is hydrogen; R^{14} is hydrogen, amino, alkylamino, or dialkylamino; R^{16} is hydrogen; X is halo (particularly chloro); and R^7 is halo (particularly bromo) see for example WO 05/023759, US 2005/0054701, US 2006030610, US 2005049419, and US 2005049276 which are incorporated by reference herein. The following intermediates were prepared using similar procedures as those described in WO 05/023759, as well as US 2006030610 and US 2005/0054701: 7-[(4-bromo-2-chlorophenyl)amino]-8-chloroimidazo[1,2-a]pyridine-6-carboxylic acid and 8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridine-6-carboxylic acid. The following intermediates can be prepared using similar procedures described in the references given above: 8-Fluoro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-*a*]pyridine-6-carboxylic acid and 7-[(4-Bromo-2-fluorophenyl)amino]-8-fluoroimidazo[1,2-*a*]pyridine-6-carboxylic acid.

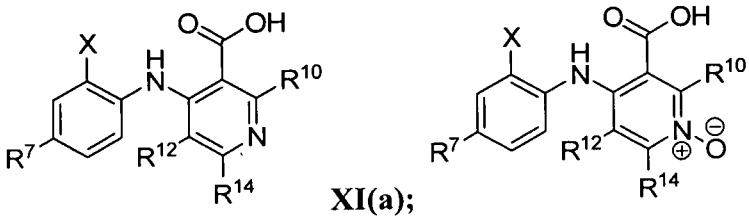
[0282] An intermediate of Formula X(a) and X(b):



X(a); X(b)

wherein R^7, X, R^{10}, R^{12}, and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for Group B can be prepared using procedures known to one of ordinary skill in the art. In particular, wherein R^{10} is hydrogen, halo (specifically chloro), or alkyl (specifically methyl), R^{12} is hydrogen, and R^{14} is hydrogen, halo (specifically bromo), see for example WO 06/045514 which is incorporated by reference herein. To prepare the intermediate of Formula X(b), the nitrogen in the pyridine ring of X(a) can then be oxidized with an agent such as MCPBA or H_2O_2. The following X(a) and X(b) intermediates were prepared using similar methods as disclosed in WO 06/045514: 3-[(2-Fluoro-4-iodophenyl)amino]pyridine-4-carboxylic acid and 3-[(2-Fluoro-4-iodophenyl)amino]pyridine-4-carboxylic acid 1-oxide. The following X(a) intermediates can be prepared using similar methods as disclosed in WO 06/045514: 2-Fluoro-3-[(2-fluoro-4-iodophenyl)amino]pyridine-4-carboxylic acid and 3-[(4-Bromo-2-fluorophenyl)amino]pyridine-4-carboxylic acid.

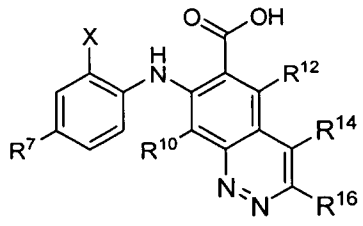
[0283] An intermediate of Formula XI(a):



XI(a); XI(b)

wherein R^7, X, R^{10}, R^{12}, and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for Group B can be prepared using procedures known to one of ordinary skill in the art. In particular, wherein R^{10} is hydrogen, R^{12} is hydrogen or halo (particularly chloro or fluoro), R^{14} is amino or halo (particularly chloro), X is halo (particularly chloro), and R^7 is halo (particularly bromo) see for example US 2005/0054701, US 200549419, and US 2006030610 which are incorporated by reference herein. The intermediate of Formula XI(b) can be prepared by oxidizing the nitrogen in the pyridine ring of XI(a) with an agent such as MCPBA or H_2O_2.

[0284] An intermediate of Formula XII:



XII

wherein R^7, X, R^{10}, R^{12}, R^{14}, and R^{16} are as defined in the compound of Formula I(M) or Formula I(N) for Group B can be prepared using procedures known to one of ordinary skill in the art. In particular, see for example WO 05/051302 which is incorporated by reference herein. The following intermediates can be prepared using similar methods as disclosed in WO 05/051302:

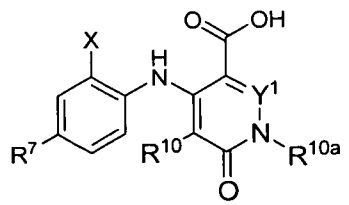
8-Fluoro-7-[(2-fluoro-4-iodophenyl)amino]-4-methylcinnoline-6-carboxylic acid;

7-[(4-Bromo-2-chlorophenyl)amino]-8-fluoro-4-methylcinnoline-6-carboxylic acid;

7-[(4-Bromo-2-fluorophenyl)amino]-8-fluoro-4-methylcinnoline-6-carboxylic acid; and

7-[(4-Bromo-2-fluorophenyl)amino]cinnoline-6-carboxylic acid.

[0285] An intermediate of Formula XIII:



XIII

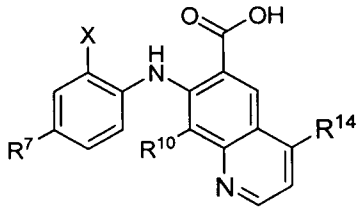
wherein R^7, X, R^{10}, R^{10a}, and Y^1 are as defined in the compound of Formula I(M) or Formula I(N) for Group C can be prepared using procedures known to one of ordinary skill in the art, including for example the procedures in US 05/0256123, Wallace, E. M. *et al. J. Med. Chem.* 2006, 49, 441-4, WO 2005000818, and WO 2005051301 (wherein Y^1 is carbon) which are incorporated by reference herein. 4-[(4-Bromo-2-fluorophenyl)amino]-5-fluoro-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxylic acid was prepared using similar procedures to those disclosed in US 05/0256123 and WO 2005051301. 4-Chloro-1-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylic acid was prepared using similar procedures to those disclosed in US 2005256123.

[0286] The following intermediates can be prepared using the methods disclosed in the above references:

4-[(2-Fluoro-4-iodophenyl)amino]-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxylic acid;

4-[(4-Bromo-2-chlorophenyl)amino]-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxylic acid;
4-[(4-Bromo-2-fluorophenyl)amino]-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxylic acid;
4-[(4-Bromo-2-chlorophenyl)amino]-1-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylic acid;
4-[(4-Bromo-2-chlorophenyl)amino]-5-fluoro-1-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylic acid; and
4-[(4-Bromo-2-fluorophenyl)amino]-1-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylic acid.

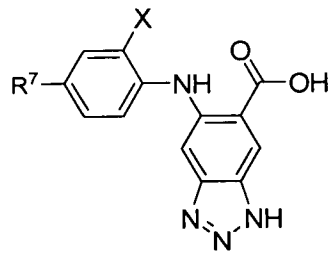
[0287] An intermediate of Formula XIV:



XIV

wherein R^7, X, R^{10}, and R^{14} are as defined in the compound of Formula I(M) or Formula I(N) for Group B can be prepared using procedures known to one of ordinary skill in the art. In particular, see for example WO 05/051302 which is incorporated by reference herein.

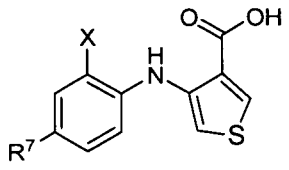
[0288] An intermediate of Formula XVI



XVI

wherein X and R^7 are as defined in the compound of Formula I(M) or Formula I(N) for a Compound of Group B can be prepared using procedures known to one of ordinary skill in the art. In particular, see for example WO 2001005390 and WO 2000042022 for procedures that can be used to prepare the following: 5-[(2-Fluoro-4-iodophenyl)amino]-1*H*-benzotriazole-6-carboxylic acid; 5-[(2-Fluoro-4-iodophenyl)amino]-1-methyl-1*H*-benzotriazole-6-carboxylic acid; and 4-Fluoro-5-[(2-fluoro-4-iodophenyl)amino]-1*H*-benzotriazole-6-carboxylic acid.

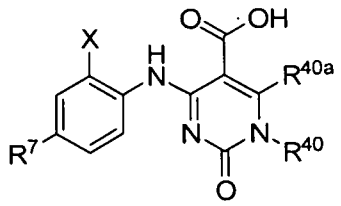
[0289] An intermediate of Formula XVII



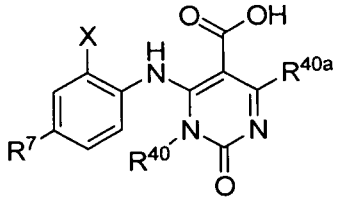
XVII

wherein X and R^7 are as defined in the compound of Formula I(M) or Formula I(N) for a Compound of Group B can be prepared using procedures known to one of ordinary skill in the art. In particular, see Example 29.

[0290] An intermediate of Formula XVIII(a) or XVIII(b)

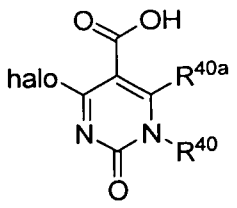


XVIII(a)

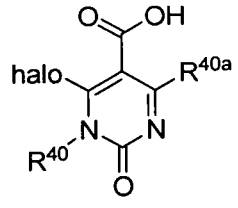


XVIII(b)

wherein X, R^7, R^{40}, and R^{40a} are as defined in the compound of Formula I(M) or Formula I(N) for a Compound of Group D can be prepared using procedures known to one of ordinary skill in the art. In particular, the halo precursors to XVIII(a) and XVIII(b)

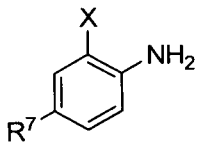


and



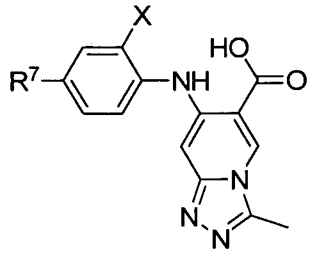
, respectively

can be prepared using procedures similar to those described in Machon and Dlugosz *Acta Poloniae Pharmaceutica* 1983, *40(1),* 1-6 and von Angerer, *Science of Synthesis* 2004, *16,* 379-572 (General Review written in English). The halo precursors are then reacted using



procedures known to one of ordinary skill in the art and the synthetic methods disclosed herein. The following intermediates can be prepared as described above: 6-[(2-fluoro-4-iodophenyl)amino]-2-oxo-1,2-dihydropyrimidine-5-carboxylic acid and 4-[(2-fluoro-4-iodophenyl)amino]-2-oxo-1,2-dihydropyrimidine-5-carboxylic acid.

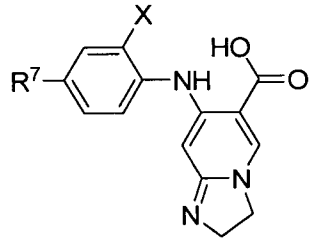
[0291] An intermediate of Formula XIX



XIX

wherein X and R^7 are as defined in the compound of Formula I(M) or Formula I(N) for a Compound of Group C can be prepared using methods known to one of ordinary skill in the art. In particular see US 2005049276.

[0292] An intermediate of Formula XX

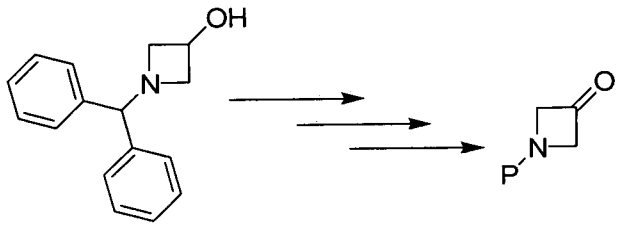


XX

wherein X and R^7 are as defined in the compound of Formula I(M) or Formula I(N) for a Compound of Group C can be prepared using methods known to one of ordinary skill in the art. In particular see US 2005049276.

[0293] The synthesis of azetidines substituted at the 3-position can be conveniently carried out according to Scheme 1:

Scheme 1



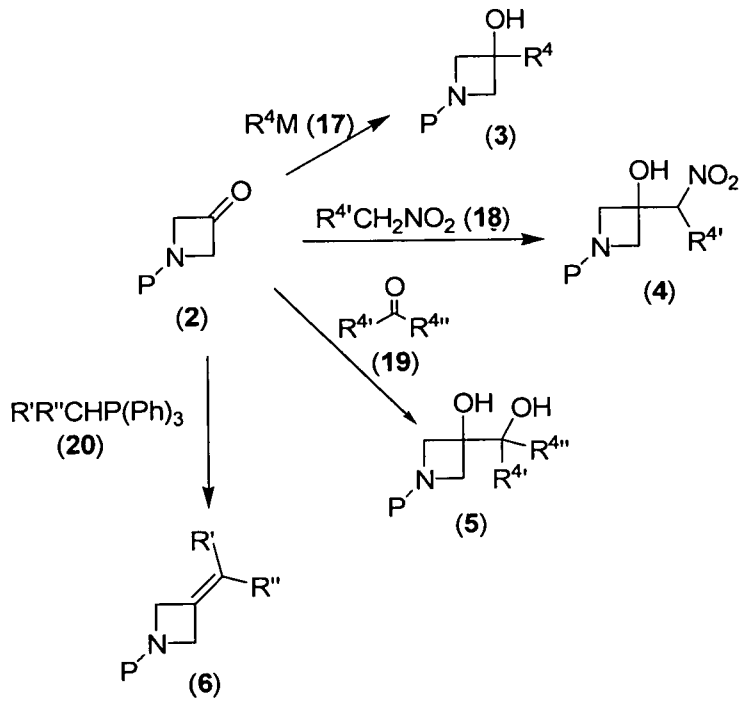
(1) (2)

starting from the *N*-diphenylmethyl protected azetidin-3-ol (**1**), readily prepared by reaction of epichlorohydrin and diphenylmethylamine (Chatterjee, Shym S.; Triggle, D. *J. Chemical Communications (London)* 1968, *2*, 93). Protecting group exchange, from Boc to CBz, on

the azetidine is carried out according to literature protocols (Greene, T.W., Wuts, P.G. Protective Groups in Organic Synthesis, Wiley-Interscience) and subsequent oxidation to the azetidinone (**2**) wherein P is CBz provides a useful intermediate for the preparation of the MEK compounds described herein.

[0294] For example, the ketone intermediates of formula **2** can be broadly functionalized at the 3-position according to Scheme 2.

Scheme 2

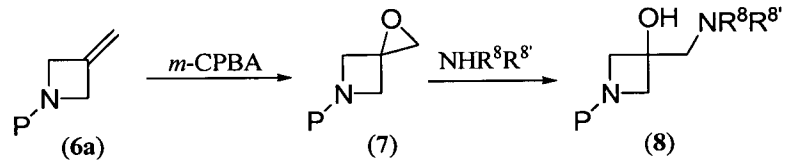


[0295] An intermediate of formula (**3**), wherein R^4 is as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group A, Group B, Group C, or Group D can be prepared by reacting the intermediate **2** with Grignard reagents or other organometallic species of formula **17**, such as organolithiums. Alternatively, the intermediate **2** can be reacted with nitroalkane anions of formula **18** prepared *in-situ* as in the Henry reaction (The Henry reaction, recent examples: Luzzio, F. A. *Tetrahedron* 2001, *57(6),* 915-945) to give (**4**) wherein $R^{4'}$ is hydrogen or alkyl optionally substituted as described for R^4 in the compound of Formula I(M) or Formula I(N) for a compound of Group A, Group B, Group C, or Group D. Alternatively, the intermediate **2** can be reacted with ketone or aldehyde anions of formula **19** in a Claisen-type condensation to give (**5**) wherein $R^{4'}$ is alkyl optionally substituted as described for R^4 in the compound of Formula I(M) or Formula I(N) for a compound of Group A, Group B, Group C, or Group D and $R^{4''}$ is

hydrogen or $R^{4'}$. In addition, **2** can be reacted with Wittig reagents of formula **20** (wherein R' and R" are independently hydrogen, alkyl, alkenyl, aryl, or heteroaryl and the alkyl, alkenyl, aryl, and heteroaryl are optionally substituted as described for R^4 in the compound of Formula I(M) or Formula I(N) for a compound of Group A, Group B, Group C, or Group D) to prepare intermediates of formula **6**, which are also useful as precursors for MEK compounds described.

[0296] According to Scheme 3, intermediates of formula (**6**) wherein wherein (R' and R" are hydrogen and P is a nitrogen-protecting group such as CBz or Boc)

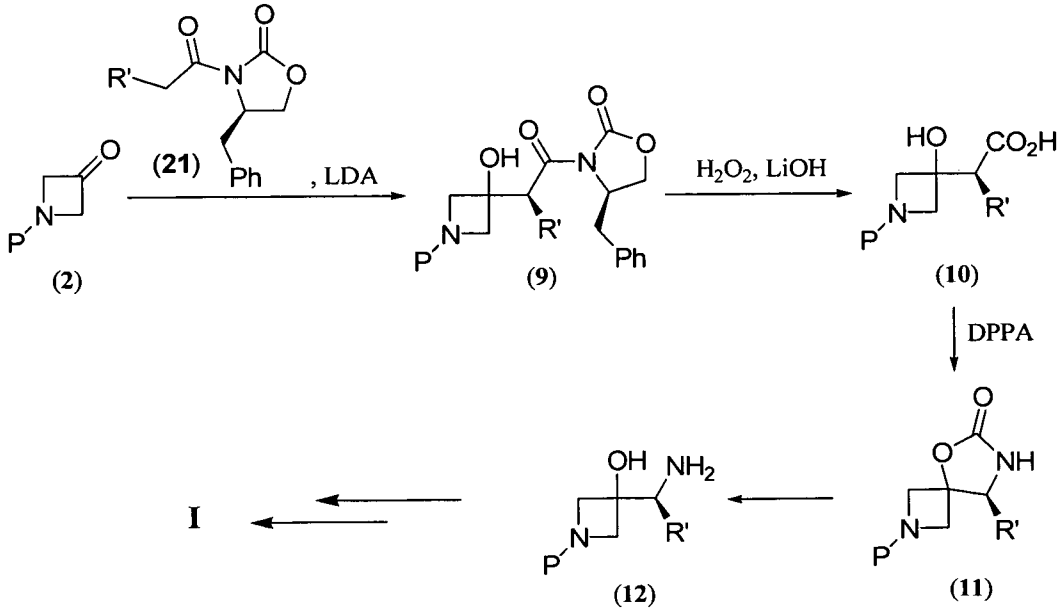
Scheme 3



can be further converted to the corresponding epoxide (**7**) and subsequent reaction with a suitable nitrogen base or other nucleophiles may be carried out to give access to a broad range of azetidin-3-ol derivatives such as (**8**), wherein R^8 and $R^{8'}$ are as defined in the compound of Formula I(M) or Formula I(N).

[0297] In some cases the preparation of optically pure compounds is desired wherein the azetidine contains one or more stereocenters. Numerous techniques for the preparation of optically pure compounds through both resolution techniques and asymmetric synthesis are well known in the art. In one such case, an asymmetric synthesis methodology can be employed wherein an azetidine precursor of formula (**2**) is reacted with an intermediate of formula **21** wherein R' is not hydrogen, as depicted in Scheme 4.

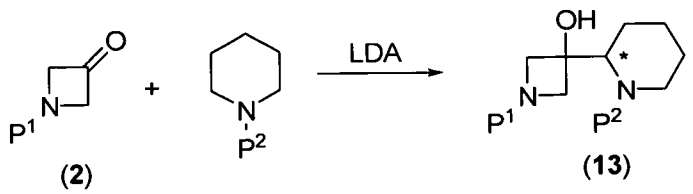
Scheme 4



[0298] One such useful approach makes use of Evans oxazolidinone methodology (Diastereoselective aldol condensation using a chiral oxazolidinone auxiliary. Gage, James R.; Evans, David A. *Organic Syntheses* 1990, *68,* 83-91). The condensation of an azetidinone (**2**) with the a chiral oxazolidinone in the presence of a base such as LDA affords an intermediate oxazolidinone (**9**), wherein P is a nitrogen-protecting group such as CBz or Boc, with diastereoselectivity. Treatment with lithium hydroxide in aqueous hydrogen peroxide gives carboxylic acid (**10**) which can be subject to Curtius rearrangement to provide the chiral oxazolidinone (**11**) then carried forward as required to a useful intermediate (**12**). Further protecting group manipulation and derivatization as required can be employed to prepare compounds of Formula I(M) or I(N).

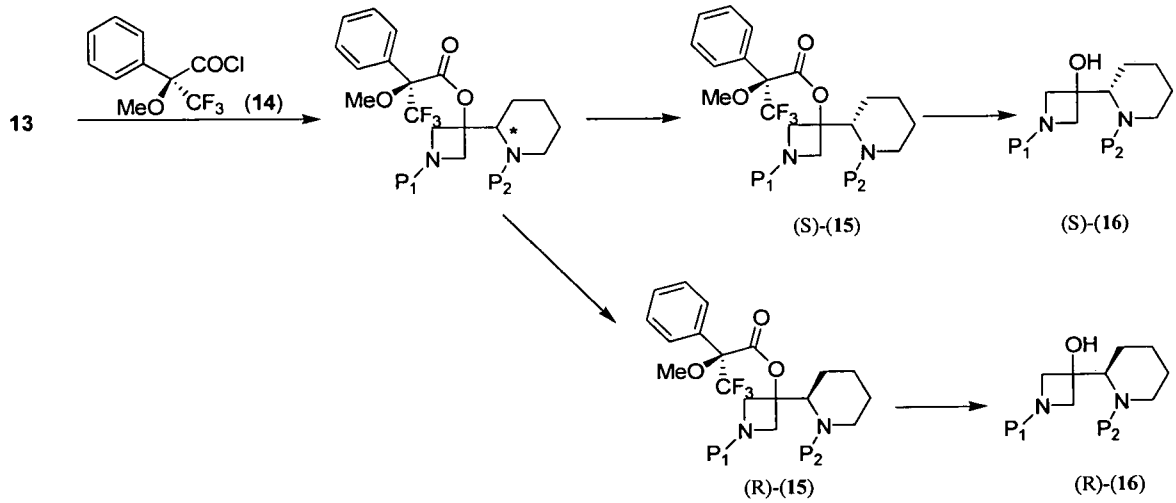
[0299] Alternatively, a racemic mixture of an intermediate of formula (**13**), useful to prepare a compound of Formula I(M) or I(N) wherein R^3 is hydroxy and R^4 is heterocycloalkyl (in particular, wherein R^4 is a N-protected piperidine), can be prepared according to Scheme 5.

Scheme 5



[0300] In the reaction schemes P^1 and P^2 are orthogonal nitrogen-protecting groups. For example, P^1 is Boc and P^2 is CBz or P^1 is CBz and P^2 is Boc. The reaction is carried out *in-situ* by treating **22** to generate the lithated amine and by subsequently treating it with a ketone such as (**2**) according to the method of Peter Beak (Beak, Peter; Lee, Won Koo α-Lithioamine synthetic equivalents: syntheses of diastereoisomers from the Boc-piperidines. Journal of Organic Chemistry 1990, 55(9), 2578-80). The racemate (**13**) thus prepared can be resolved by functionalization, as depicted in Scheme 6, with a chiral acid such as the readily-available Mosher acid (**14**).

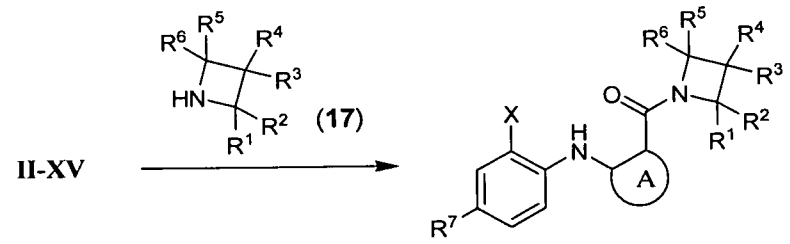
Scheme 6



[0301] The resulting diastereomeric esters (**15**) can be separated by chromatographic means and then carried forward individually as the enantiomerically pure intermediates (R)-(**16**) and (S)-(**16**).

[0302] MEK compounds described herein can be prepared by reacting an intermediate of Formula II, III(a), III(b), IV(a), IV(b), V(a), V(b), VI(a), VI(b), VII(a), VII(b), VIII(a), VIII(b), IX, X(a), X(b), XI(a), XI(b), XII, XIII, XIV, XVI, XVII, XVIII(a), XVIII(b), XIX, or XX with intermediate 17 according to Scheme 7:

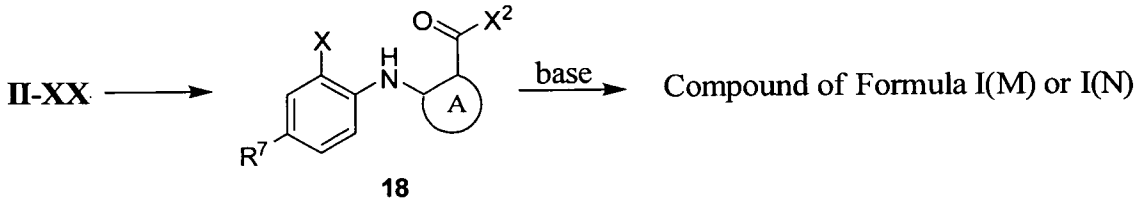
Scheme 7



[0303] The reaction is carried out in a solvent such as DMF, THF, or DCM in the presence of a base such as DIPEA, *N*-methylmorpholine, DMAP, or triethylamine and optionally in the presence of a coupling agent such as PyBOP, HBTU, or EDCI.

Alternatively, an intermediate of Formula II, III(a), III(b), IV(a), IV(b), V(a), V(b), VI(a), VI(b), VII(a), VII(b), VIII(a), VIII(b), IX, X(a), X(b), XI(a), XI(b), XII, XIII, XIV, XVI, XVII, XVIII(a), XVIII(b), XIX, or XX can be converted into an acid halide according to Scheme 8

Scheme 8



18

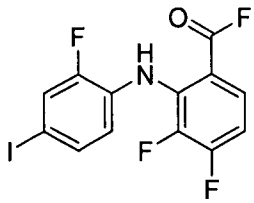
wherein X^2 is halo, such as chloro or fluoro, and all other groups are as defined in the compound of Formula I(M) or Formula I(N) for a compound of Group A, Group B, Group C, or Group D. The reaction is carried out in a solvent such as dioxane, THF, or DCM in the presence of a base such as DIPEA, sodium bicarbonate. The acid halide of formula **18** can then be reacted with an azetidine intermediate of formula **17** to prepare a compound of Formula I(M) or I(N).

SYNTHETIC EXAMPLES FOR MEK COMPOUNDS

[0304] Generally, the compounds listed below were identified by LC-MS, and/or isolated, and characterized by ^{1}H-NMR (most typically 400 MHz). Liquid chromatography-mass spectral (LC-MS) analyses were performed using at least one of: a Hewlett-Packard Series 1100 MSD, an Agilent 1100 Series LC/MSD (available from Agilent Technologies Deutschland GmbH of Waldbronn Germany), or a Waters 8-Channel MUX System (available from Waters Corporation of Milford, Massachusetts). Compounds were identified according to either their observed mass [MH^+] or [MNa^+] ion (positive mode) or [MH^-] ion (negative mode). ^{1}H-NMR data for compounds was taken with a Varian AS400 Spectrometer (400MHz, available from Varian GmbH, Darmstadt, Germany). Starting materials and intermediates used to prepare a MEK compound described herein are either commercially available or can be prepared by one of ordinary skill in the art.

REFERENCE 1

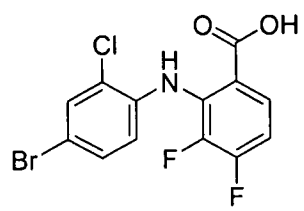
3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino] benzoyl fluoride



[0305] To a stirred mixture of 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino] benzoic acid (12 g, 30.5 mmol), prepared using procedures similar to those described in US 7,019,033, in dichloromethane (70 mL) at 0 °C was added pyridine (2.5 mL, 30.8 mmol) followed by dropwise addition of cyanuric fluoride (2.8 mL, 33.6 mmol). The reaction mixture was stirred at 0 °C for 10 minutes and then warmed to room temperature and stirred for 2 hours. The reaction mixture was diluted with water and extracted with dichloromethane (100 mL). The aqueous layer was extracted once with dichloromethane (50 mL). The combined organic layers were washed with saturated aqueous sodium bicarbonate solution, brine, dried over anhydrous sodium sulfate and concentrated *in vacuo* to give crude product as a brownish solid. Crude product was purified by flash chromatography (plug, 25% ethyl acetate in hexanes) to afford 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino] benzoyl fluoride as a beige solid (11.8 g, 97% yield). ^{1}H NMR (400MHz, CD_3OD): 8.41 (s, 1H), 7.80-7.81 (m, 1H), 7.52 (dd, 1H), 7.43-7.47 (m, 1H), 6.96-7.03 (m, 1H), 6.85-6.92 (m, 1H).

REFERENCE 2

2-[(4-bromo-2-chlorophenyl)amino]-3,4-difluorobenzoic acid



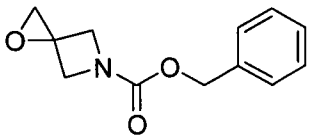
[0306] To a solution of 2,3,4-trifluorobenzoic acid (1 g, 5.68 mmol) and 4-bromo-2-chloroaniline (1.2 g, 5.68 mmol) in acetonitrile (10 mL) was added lithium amide (0.39 g, 17.04 mmol) and the reaction stirred at 60 °C for 1.5 hours. The mixture was cooled to room temperature and then to 0 °C and acidified with aq. hydrochloric acid. The obtained precipitate was collected by filtration and washed with cold water and dried *in vacuo* to

afford 2-[(4-bromo-2-chlorophenyl)amino]-3,4-difluorobenzoic acid (1.92 g, 94% yield) as a beige solid. MS (EI) for $C_{13}H_7BrClF_2NO_2$: 363 (MH^+).

[0307] Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, 2-[(4-iodo-2-fluorophenyl)amino]-3-fluorobenzoic acid was prepared. MS (EI) for $C_{13}H_8F_2INO_2$: 376 (MH^+).

REFERENCE 3

Phenylmethyl 1-oxa-5-azaspiro[2.3]hexane-5-carboxylate



[0308] To a solution of azetidin-3-ol hydrochloride in tetrahydrofuran (90 mL) and water (10 mL) was added triethylamine (15 mL, 0.106 mol) followed by slow addition of benzyl chloroformate (8.0 mL, 0.056 mol) at room temperature. The reaction mixture was stirred at room termperature for 16 hours then partitioned with water and ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate and concentrated. The residue was purified by flash chromatography (SiO_2, 25-50% ethyl acetate in hexanes) to afford phenylmethyl 3-hydroxyazetidine-1-carboxylate (3.56 g, 33% yield) as a clear and colorless oil. ^1H NMR (400 MHz, $CDCl_3$): 7.36-7.31 (m, 5H), 5.09 (s, 2H), 4.64-4.57 (m, 1H), 4.22 (dd, 2H), 3.88 (dd, 2H), 2.61 (d, 1H, J=4.0 Hz). MS (EI) for $C_{11}H_{13}NO_3$: 208 (MH^+).

[0309] To a solution of phenylmethyl 3-hydroxyazetidine-1-carboxylate (3.5 g, 0.0168 mol) in dichloromethane (100 mL) was added Dess-Martin periodinane (10.7 g, 0.0.25 mol) at room temperature and stirred for 5 h. The reaction mixture was quenched with 1:1 ratio of saturated aqueous sodium bicarbonate and 1M sodium thiosulfate (200 mL) and then partitioned with dichloromethane. The organic layer was dried over anhydrous magnesium sulfate and concentrated *in vacuo* to afford phenylmethyl 3-oxoazetidine-1-carboxylate (3.43 g, 99% yield) as a clear and colorless oil without further purification. ^1H NMR (400 MHz, $CDCl_3$): 7.39-7.31 (m, 5H), 5.17 (s, 2H), 4.77 (s, 4H). MS (EI) for $C_{11}H_{11}NO_3$: 205 (M^+).

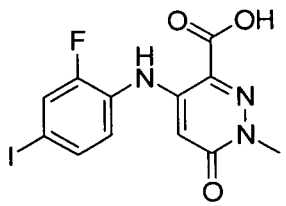
[0310] A suspension of methyltriphenylphosphonium bromide (23.0 g, 0.0649 mol) and potassium *tert*-butoxide (7.3 g, 0.0649 mol) in diethyl ether (140 mL) was stirred at room temperature for 20 min, and then heated to 35 °C for 1 h. To this bright yellow reaction mixture was slowly added a dilute solution of phenylmethyl 3-oxoazetidine-1-carboxylate

(3.33 g, 0.0162 mol) in diethyl ether (50 mL). The reaction mixture was stirred at 35 °C for 12 hours then filtered through a bed of celite and rinsed with ethyl ether. The filtrate was washed with water and brine, dried over anhydrous magnesium sulfate and concentrated. The residue was purified by flash chromatography (SiO_2, 5-10% ethyl acetate in hexanes) to afford phenylmethyl 3-methylideneazetidine-1-carboxylate (2.46 g, 75% yield) as a clear and colorless oil). ^1H NMR (400 MHz, $CDCl_3$): 7.27-7.22 (m, 5H), 5.02 (s, 2H), 4.93-4.90 (m, 2H), 4.48-4.47 (m, 4H). MS (EI) for $C_{12}H_{13}NO_2$: 203 (M^+).

[0311] To a solution of phenylmethyl 3-methylideneazetidine-1-carboxylate (2.46 g, 0.0121 mol) in chloroform (100 mL) was added 3-chloroperoxybenzoic acid (12.5 g, 0.0726 mol) at 0 °C. The reaction mixture was allowed to warm up to room temperature over a period of 12 hours then quenched with 1 M sodium thiosulfate / saturated aqueous sodium bicarbonate (1:1). The layers were separated and the organic layer was dried over anhydrous magnesium sulfate then concentrated. The residue was purified by flash chromatography (5-15% ethyl acetate in hexanes) to afford phenylmethyl 1-oxa-5-azaspiro[2.3]hexane-5-carboxylate (2.2 g, 83% yield) as clear and colorless oil. ^1H NMR (400 MHz, $CDCl_3$): 7.37-7.29 (m, 5H), 5.12 (s, 2H), 4.35-4.26 (m, 4H), 2.85 (s, 2H). MS (EI) for $C_{12}H_{13}NO_3$: 220 (MH^+).

REFERENCE 4

4-(2-fluoro-4-iodophenylamino)-1-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylic acid



[0312] 4-chloro-1-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylic acid was prepared using procedures similar to those disclosed in US 2005256123.

[0313] To a solution of 4-chloro-1-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylic acid (350 mg, 1.855 mmol) and 2-fluoro-4-iodoaniline (1.06 g, 4.453 mmol) in tetrahydrofuran (13.3 mL) was sparged with nitrogen for 5 minutes followed by the slow addition of lithium bis(trimethylsilyl)amide, 1.0 M in THF (7.4 mL). The reaction mixture stirred for an additional 4 hours at room temperature. The mixture was quenched with 1 N HCl and concentrated *in vacuo*. The residue was partitioned between ethyl acetate and 1 N aqueous

HCl. The aqueous layer was extracted (3x) with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous sodium sulfate, filtered and evaporated to afford 4-(2-fluoro-4-iodophenylamino)-1-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylic acid (939 mg, 100% yield). ^{1}H NMR ($CDCl_3$): 7.27 (dd, 1H), 7.21 (d, 1H), 6.54 (t, 1H), 4.84 (broad s, 2H), 2.09 (s, 1H), 1.26 (t, 3H); MS (EI) for $C_{12}H_9N_3O_3FI$: 389 (MH^+).

[0314] A solution of 4-(2-fluoro-4-iodophenylamino)-1-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylic acid (939 mg, 2.413 mmol) in dichloromethane (60 mL) in the presence of dimethylformamide (8.0 mL) was cooled to 0 °C. Malonyl chloride (1.26 mL, 14.48 mmol) was added and stirred at room temperature for 1 hour. The reaction mixture was evaporated and partitioned between ethyl acetate and 1M aqueous ammonium chloride. The aqueous layer was extracted 1x with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to afford 4-(2-fluoro-4-iodophenylamino)-1-methyl-6-oxo-1,6-dihydropyridazine-3-carbonyl chloride. This crude material was taken into the next step without further purification. MS (EI) for $C_{12}H_8N_3O_2ClFI$: 408 (MH^+).

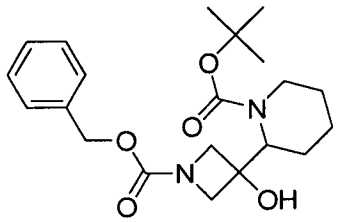
[0315] To a solution of 4-(2-fluoro-4-iodophenylamino)-1-methyl-6-oxo-1,6-dihydropyridazine-3-carbonyl chloride in methanol (15 mL) and benzene (12 mL) was added dropwise trimethylsilyl diazomethane (1 mL) and stirred at room temperature for 15 minutes. The reaction mixture was quenched with acetic acid and evaporated. The residue was partitioned between ethyl acetate and brine. The organic layer was separated, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified on silica gel chromatography column (7:3 hexanes/ethyl acetate) to afford methyl 4-(2-fluoro-4-iodophenylamino)-1-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylate (84.9 mg, 8.7% yield). ^{1}H NMR ($CDCl_3$): 7.49-7.56 (m, 3H), 7.12 (t, 1H), 6.13 (d, 1H), 4.00 (s, 3H), 3.83 (s, 3H); MS (EI) for $C_{13}H_{11}N_3O_3FI$: 404 (MH^+).

[0316] Methyl 4-(2-fluoro-4-iodophenylamino)-1-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylate (84.9 mg, 0.211 mmol) was dissolved in tetrahydrofuran (5 mL), methanol (2.5 mL) and water (2.5 mL). Aqueous 2 M lithium hydroxide (200 µL) was added at room temperature. After 10 minutes, the reaction mixture was heated to 50 °C for 30 minutes and continued to stir at room temperature for 16 hours at which time the solvents were evaporated. The residue was made acidic with 2 M aqueous hydrochloric acid to pH 2 and extracted with ethyl acetate. The organic layer separated, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to provide 4-(2-fluoro-4-iodophenylamino)-1-

methyl-6-oxo-1,6-dihydropyridazine-3-carboxylic acid (54.0 mg, 66% yield). MS (EI) for $C_{12}H_9N_3O_3FI$: 390 (MH^+).

REFERENCE 5

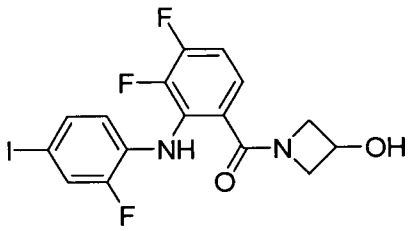
1,1-dimethylethyl 2-(3-hydroxy-1-{[(phenylmethyl)oxy]carbonyl}azetidin-3-yl)piperidine-1-carboxylate



[0317] To a solution of 1,1-dimethylethyl piperidine-1-carboxylate (0.50 g, 2.7 mmol) in anhydrous diethyl ether (9.0 mL) under anhydrous nitrogen gas was added *N,N,N',N'*-tetramethylethane-1,2-diamine (0.41 mL, 2.7 mmol), and the solution was cooled to -78°C. To this solution was added (2-methylpropyl)lithium (2.1 mL, 1.4 M in cyclohexane, 3.0 mmol) in small portions. To this anion solution was added phenylmethyl 3-oxoazetidine-1-carboxylate (1.0 g, 5.4 mmol), prepared using procedures as described in Reference 3, in anhydrous ether (2.0 mL), while maintaining the internal temperature at less than -60°C. The solution was allowed to warm to room temperature and stirred overnight. The reaction was quenched with water, and partitioned between water and diethyl ether. The layers were separated and the aqueous layer was extracted with diethyl ether twice. The combined organic layers were dried (magnesium sulfate), filtered and concentrated *in vacuo*. Chromatography (silica gel, 3:1 hexanes/ethyl acetate) gave 0.13 g (13%) of 1,1-dimethylethyl 2-(3-hydroxy-1-{[(phenylmethyl)oxy]carbonyl}azetidin-3-yl)piperidine-1-carboxylate. ^1H NMR (400 MHz, $CDCl_3$): 7.31 (m, 5H), 5.08 (s, 2H), 4.05 (d, 1H), 4.00 (d, 1H), 3.84 (d, 2H), 3.80 (broad s, 1H), 3.55 (broad s, 1H), 3.10 (broad s, 1H), 1.92 (m, 1H), 1.45-1.62 (m, 6H), 1.43 (s, 9H). MS (EI) for $C_{21}H_{30}N_2O_5$: 335 (M-tBu), 315 (M-OtBu).

EXAMPLE 1

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol



[0318] 3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid (2.1 g, 5.3 mmol), prepared using procedures similar to those in US 7,019,033, was taken into DMF (10 mL) followed by addition of PyBOP (2.6 g, 5.3 mmol) and the mixture was allowed to stir at room temperature over 15 minutes. Azetidin-3-ol hydrochloride (870 mg, 8.0 mmol) and DIPEA (1.85 mL, 11.2 mmol) was then added and the mixture was allowed to stir an additional hour at room temperature. The mixture was then partitioned with ethyl acetate and 0.5 M aqueous sodium hydroxide solution. The organic layer was then washed with water (3x) then brine and dried over anhydrous sodium sulfate. Filtration and concentration followed by silica gel flash chromatography using ethyl acetate: hexanes (5:1) eluent afforded 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol (2.09 g, 87% yield) as a colorless amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$): 8.47 (s, 1H), 7.39 (dd, 1H), 7.32 (d, 1H), 7.13-7.09 (m, 1H), 6.84-6.78 (m, 1H), 6.63-6.57 (m, 1H), 4.74-4.67 (m, 1H), 4.43-4.39 (m, 2H), 4.20-3.96 (br d, 2H), 2.50 (d, 1H).

[0319] Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the compounds in Examples 1(a)-(e) were prepared.

[0320] **EXAMPLE 1(a).** 1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}-carbonyl)azetidin-3-yl]-*N,N*-dimethylpyrrolidin-3-amine. The title compound was prepared by reacting 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid with *N*-methyl-*N*-(2-(pyridin-2-yl)ethyl)azetidin-3-amine. The azetidine intermediate was prepared using procedures similar to those described in Abdel-Magid, et.al., *Tetrahedron Letters* 1990, *31(39),* 5595 starting with *tert*-butyl 3-oxoazetidine-1-carboxylate, which itself was prepared as described in Example 3. The title compound: ^{1}H NMR (400 MHz, d_6-DMSO): 8.56 (s, 1H), 7.58 (m, 1H), 7.38 (d, 1H), 7.31 (m, 1H), 7.16 (m, 1H), 6.67 (m, 1H), 4.16 (m, 1H), 3.97 (m, 2H), 3.77 (m, 1H), 3.26 (br s, 4H), 2.63 (m, 1H), 2.42 (br s, 6H), 1.99 (br s, 1H), 1.74 (br s, 1H). MS (EI) for $C_{22}H_{24}F_3IN_4O$: 545 (MH^+).

[0321] EXAMPLE 1(b). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-methyl-*N*-(2-pyridin-2-ylethyl)azetidin-3-amine. The title compound was prepared by reacting 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid with 1-(azetidin-3-yl)-N,N-dimethylpyrrolidin-3-amine. The azetidine intermediate was prepared using procedures similar to those described in Abdel-Magid, et.al., *Tetrahedron Letters* 1990, *31(39),* 5595 starting with *tert*-butyl 3-oxoazetidine-1-carboxylate, which itself was prepared as described in Example 3. The title compound: ^{1}H NMR(400 MHz, CD_3OD): 8.50 (d, 1H), 7.94 (t, 1H), 7.50-7.30 (m, 5H), 7.07 (q, 1H), 6.66-6.61 (m, 1H), 4.52-4.48 (m, 2H), 4.31(s, 2H), 4.23-4.18 (m, 1H), 3.48- 3.46 (m, 2H), 3.17-3.13 (m, 2H), 2.88 (s, 3H); MS(EI) for $C_{24}H_{22}F_3IN_4O$: 567 (MH^+).

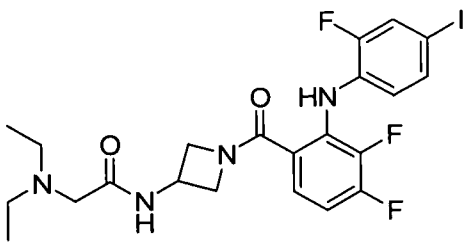
[0322] EXAMPLE 1(c). 6-(Azetidin-1-ylcarbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline: ^{1}H NMR (400 MHz, $CDCl_3$): 8.57 (s, 1H), 7.41-7.38 (dd, 1H), 7.34-7.31 (dt, 1H), 7.13-7.09 (m, 1H), 6.83-6.77 (m, 1H), 6.64-6.58 (m, 1H), 4.27 (b, 2H), 4.18 (b, 2H), 2.38-2.30 (p, 2H); MS (EI) for $C_{16}H_{12}F_3IN_3O$: 433 (MH^+).

[0323] EXAMPLE 1(d). [1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]methanol: ^{1}H NMR (400 MHz, $CDCl_3$): 8.52 (s, 1H), 7.41-7.38 (dd, 1H), 7.34-7.31 (dt, 1H), 7.15-7.11 (m, 1H), 6.83-6.77 (m, 1H), 6.64-6.58 (m, 1H), 4.29-4.20 (m, 2H), 4.09 (b, 1H), 3.93 (b, 1H), 3.82-3.81 (d, 2H), 2.89-2.75 (m, 1H); MS (EI) for $C_{17}H_{14}F_3IN_2O_2$: 463 (MH^+).

[0324] EXAMPLE 1(e). 1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxylic acid: ^{1}H NMR (400 MHz, $CDCl_3$): 7.79 (b, 2H), 7.42-7.38 (dd, 1H), 7.34-7.32 (dt, 1H), 7.15-7.11 (m, 1H), 6.89-6.83 (m, 1H), 6.65-6.60 (m, 1H), 4.46-4.29 (m, 4H), 3.55-3.47 (m, 1H); MS (EI) for $C_{17}H_{12}F_3IN_2O_3$: 477 (MH^+).

EXAMPLE 2

N-[1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N2,N2*-diethylglycinamide



[0325] A solution of 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid (200 mg, 0.51 mmol), prepared using procedures similar to those in US 7,019,033, PyBOP (256 mg, 0.51 mmol), commercially available *tert*-butyl azetidin-3-ylcarbamate (131 mg, 0.77 mmol) and *N,N*-diisopropylethylamine (180 μL, 1.02 mmol) in dimethylformamide (3 mL) was stirred at room temperature for 15 hours. The reaction mixture was partitioned between 5% aqueous lithium chloride and ethyl acetate. The organic portion was washed with 20% aqueous citric acid, saturated aqueous sodium bicarbonate, brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford a brown residue which was purified by silica gel column chromatography eluting with 30% ethyl acetate in hexanes to afford 1,1-dimethylethyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate (225 mg, 80% yield) as a colorless oil. ^{1}H NMR (400 MHz, DMSO): 8.56 (s, 1H), 7.60-7.55 (m, 2H), 7.38 (d, 1H), 7.30-7.26 (m, 1H), 7.20-7.13 (m, 1H), 6.71-6.66 (m, 1H), 4.37-4.20 (m, 2H), 4.18-4.06 (m, 1H), 3.98-3.93 (m, 1H), 3.82-3.75 (m, 1H), 1.37 (s, 9H). MS (EI) $C_{21}H_{21}N_3O_3F_3I$: 548 (MH^+).

[0326] A solution of 1,1-dimethylethyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate (113 mg, 0.20 mmol) and trifluoroacetic acid (500 μL) in dichloromethane (2 mL) was added stirred at room temperature for one hour then was partitioned between saturated aqueous sodium bicarbonate, and dichloromethane. The organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated to afford a colorless residue which was purified by column chromatography eluting with 10% methanol in dichloromethane to afford 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine (85 mg, 95% yield) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$): 8.53 (s, 1H), 7.39 (d, 1H), 7.32 (d, 1H), 7.13-7.09 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.57 (m, 1H), 4.46-4.39 (m, 2H), 3.98-3.75(br m, 4H); MS (EI) for $C_{16}H_{13}F_3IN_3O$: 448 (MH^+).

[0327] A solution of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine (100 mg, 0.22 mmol), PyBOP (131 mg, 0.25 mmol), *N,N*-diisopropylethylamine (80 μL, 0.44 mol) and bromoacetic acid (35 mg, 0.25 mmol) in dimethylformamide (1 mL) was stirred at room temperature for 15 hours. The reaction mixture was concentrated *in vacuo* and the resultant residue was purified by column chromatography eluting with 80% ethyl acetate in hexanes to afford 2-bromo-*N*-[1-({3,4-

difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]acetamide (102 mg, 82% yield) as a white foam. MS (EI) for $C_{18}H_{14}BrF_3IN_3O_2$: 568.

[0328] A solution of 2-bromo-*N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]acetamide (30 mg, 0.05 mmol) and *N,N*-diethylamine (100 μL, excess) in dichloromethane (2 mL) was stirred at room temperature for 15 hours. The reaction mixture was concentrated *in vacuo* and purified by preparative reverse phase HPLC (CH_3CN/H_2O with 0.1% TFA). Isolated product was concentrated *in vacuo* to afford *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N2,N2*-diethylglycinamide trifluoroacetate salt (13.0 mg, 38% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): 9.36 (br s, 1H), 9.25 (d, 1H), 8.60 (s, 1H), 7.60 (d, 1H), 7.40 (d, 1H), 7.33-7.27 (m, 1H), 7.22-7.15 (m, 1H), 6.73-6.66 (m, 1H), 4.54-4.40 (m, 2H), 4.25-4.20 (m, 1H), 4.04-3.82 (m, 4H), 3.17-3.12 (m, 4H), 1.18-1.15 (m, 6H); MS (EI) $C_{22}H_{24}F_3IN_4O_2$: 561 (MH^+).

[0329] Using the same or analogous synthetic techniques and/or substituting with alternative reagents, the compounds in Examples 2(a)-(n) were prepared.

[0330] **EXAMPLE 2(a).** 1,1-Dimethylethyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate: ^{1}H NMR (400 MHz, $CDCl_3$): 8.52 (br s, 1H), 7.40 (dd, 1H), 7.33 (dt, 1H), 7.13-7.07 (m, 1H), 6.80 (ddd, 1H), 6.61 (ddd, 1H), 5.01-4.88 (br, 1H), 4.55-4.37 (br, 4H), 4.05 (br d, 1H), 1.43 (s, 9H); MS (EI) for $C_{21}H_{21}F_3IN_3O_3S$: 548 (MH^+).

[0331] **EXAMPLE 2(b).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine trifluoroacetate salt: ^{1}H NMR (400 MHz, $CDCl_3$): 8.53 (s, 1H), 7.39 (d, 1H), 7.32 (d, 1H), 7.13-7.09 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.57 (m, 1H), 4.46-4.39 (m, 2H), 3.98-3.75(br m, 4H); MS (EI) for $C_{16}H_{13}F_3IN_3O$: 448 (MH^+).

[0332] **EXAMPLE 2(c).** *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-methylpropanamide: ^{1}H NMR (400 MHz, DMSO): 8.60 (s, 1H), 8.38 (d, 1H), 7.59 (d, 1H), 7.38 (d, 1H), 7.32-7.28 (m, 1H), 7.18-7.13 (m, 1H), 6.72-6.66 (m, 1H), 4.45-4.35 (m, 1H), 4.18-3.77 (m, 4H), 2.36-2.28 (m, 1H), 0.99 (d, 6H); MS (EI) $C_{20}H_{19}F_3IN_3O_2$: 518 (MH^+).

[0333] **EXAMPLE 2(d).** *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]formamide: ^{1}H NMR (400 MHz, DMSO):

8.69 (d, 1H), 8.58 (s, 1H), 8.02 (s, 1H), 7.59 (d, 1H), 7.39 (d, 1H), 7.31-7.27 (m, 1H), 7.19-7.13 (m, 1H), 6.70-6.66 (m, 1H), 4.55-4.46 (m, 1H), 4.42-4.36 (m, 1H), 4.20-4.16 (m, 1H), 4.01-3.97 (m, 1H), 3.82-3.79 (m, 1H); MS (EI) $C_{17}H_{13}F_3IN_3O_2$: 476 (MH^+).

[0334] EXAMPLE 2(e). *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-3,4-dihydroxybutanamide: ^{1}H NMR (400 MHz, DMSO): 8.60 (s, 1H), 8.47 (d, 1H), 7.59 (d, 1H), 7.39 (d, 1H), 7.31-7.28 (m, 1H), 7.20-7.14 (m, 1H), 6.72-6.66 (m, 1H), 4.45-4.35 (m, 2H), 4.18-4.14 (m, 1H), 4.00-3.92 (m, 1H), 3.84-3.78 (m, 2H), 3.31-3.18 (m, 2H), 2.38-2.18 (m, 1H), 2.09-2.03 (m, 1H); MS (EI) $C_{20}H_{19}F_3IN_3O_4$: 550 (MH^+).

[0335] EXAMPLE 2(f). methyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate: ^{1}H NMR (400 MHz, DMSO): 8.58 (s, 1H), 7.84 (d, 1H), 7.59 (d, 1H), 7.39 (d, 1H), 7.35-7.27 (m, 1H), 7.20-7.13 (m, 1H), 6.71-6.66 (m, 1H), 4.38-4.25 (m, 2H), 4.17-4.12 (m, 1H), 4.00-3.97 (m, 1H), 3.83-3.78 (m, 1H), 3.53 (s, 3H); MS (EI) $C_{18}H_{15}F_3IN_3O_3$: 506 (MH^+).

[0336] EXAMPLE 2(g). *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-(4-methylpiperazin-1-yl)acetamide trifluoroacetate salt: ^{1}H NMR (400 MHz, DMSO): 8.64 (s, 1H), 8.54 (d, 1H), 7.60 (d, 1H), 7.39 (d, 1H), 7.32-7.29 (m, 1H), 7.21-7.15 (m, 1H), 6.72-6.66 (m, 1H), 4.54-4.28 (m, 2H), 4.19-4.15 (m, 1H), 4.06-4.00 (m, 1H), 3.91-3.84 (m, 1H), 3.44-3.24 (m, 2H), 3.16-2.92 (m, 6H), 2.78 (s, 3H), 2.62-2.50 (m, 2H); MS (EI) $C_{23}H_{25}F_3IN_5O_2$: 588 (MH^+).

[0337] EXAMPLE 2(h). *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N,N*-bis(2-hydroxyethyl)glycinamide trifluoroacetate salt: ^{1}H NMR (400 MHz, DMSO): 9.19 (d, 1H), 7.60 (d, 1H), 7.41 (d, 1H), 7.31-7.27 (m, 1H), 7.21-7.15 (m, 1H), 6.73-6.66 (m, 1H), 4.51-4.40 (m, 2H), 4.23-4.18 (m, 1H), 4.05-3.98 (m, 3H), 3.86-3.82 (m, 1H), 3.75-3.69 (m, 3H), 3.32 (br s, 4H) $C_{22}H_{24}F_3IN_4O_4$: 593 (MH^+).

[0338] EXAMPLE 2(i). *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-piperidin-1-ylacetamide trifluoroacetate salt: ^{1}H NMR (400 MHz, DMSO): 9.20 (d, 1H), 7.60 (d, 1H), 7.41 (d, 1H), 7.31-7.27 (m, 1H), 7.21-7.15 (m, 1H), 6.73-6.66 (m, 1H), 4.52-4.40 (m, 2H), 4.24-4.18 (m, 1H), 4.05-4.00 (m, 1H), 3.87-3.80 (m, 3H), 3.40-3.32 (m, 2H), 3.00-2.91 (m, 2H), 1.82-1.66 (m, 6H); MS (EI) $C_{23}H_{24}F_3IN_4O_2$: 573 (MH^+).

[0339] EXAMPLE 2(j). *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-N3-(2-hydroxyethyl)-N3-methyl-beta-alaninamide hydrochloride: ^{1}H NMR (400 MHz, DMSO): 9.36 (br s, 1H), 8.86 (d, 1H), 8.60 (s, 1H), 7.59 (d, 1H), 7.39 (d, 1H), 7.32-7.26 (m, 1H), 7.21-7.14 (m, 1H), 6.72-6.66 (m, 1H), 5.35-5.33 (m, 1H), 4.48-4.37 (m, 2H), 4.20-4.15 (m, 1H), 4.02-3.96 (m, 1H), 3.84-3.79 (m, 1H), 3.74-3.68 (m, 2H), 3.42-3.06 (m, 4H), 2.75 (s, 3H), 2.65-2.60 (m, 2H); MS (EI) $C_{22}H_{24}F_3IN_4O_3$: 577 (MH^+).

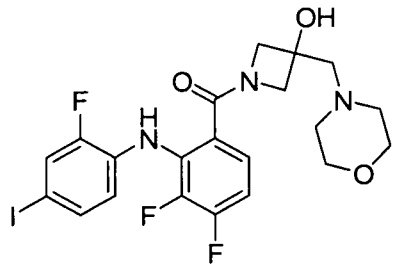
[0340] EXAMPLE 2(k). *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-N3,N3-bis(2-hydroxyethyl)-beta-alaninamide hydrochloride: ^{1}H NMR (400 MHz, DMSO): 9.39 (br s, 1H), 8.91 (d, 1H), 8.61 (s, 1H), 7.59 (d, 1H), 7.39 (d, 1H), 7.31-7.27 (m, 1H), 7.21-7.14 (m, 1H), 6.72-6.66 (m, 1H), 5.31 (br s, 2H), 4.46-4.36 (m, 2H), 4.20-4.15 (m, 1H), 4.02-3.97 (m, 1H), 3.85-3.72 (m, 5H), 3.30-3.17 (m, 4H), 2.68-2.63 (m, 2H); MS (EI) $C_{23}H_{26}F_3IN_4O_4$: 607 (MH^+).

[0341] EXAMPLE 2(m). *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-N2-methylglycinamide trifluoroacetate salt: ^{1}H NMR (400 MHz, DMSO): 9.09 (d, 1H), 8.69 (br s, 2H), 8.60 (s, 1H), 7.60 (d, 1H), 7.39 (d, 1H), 7.31-7.27 (m, 1H), 7.22-7.15 (m, 1H), 6.73-6.66 (m, 1H), 4.54-4.41 (m, 2H), 4.25-4.19 (m, 1H), 3.99-3.96 (m, 1H), 3.84-3.78 (m, 1H), 3.72-3.67 (m, 2H), 2.58-2.54 (m, 3H); MS (EI) $C_{19}H_{18}F_3IN_4O_2$: 519 (MH^+).

[0342] EXAMPLE 2(n). *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]glycinamide trifluoroacetate salt: ^{1}H NMR (400 MHz, DMSO): 8.59 (s, 1H), 8.46 (br s, 1H), 7.59 (d, 1H), 7.39 (d, 1H), 7.32-7.28 (m, 1H), 7.20-7.13 (m, 1H), 6.72-6.66 (m, 1H), 4.49 (br s, 1H), 4.40-4.35 (m, 1H), 4.18-4.13 (m, 1H), 4.05-4.01 (m, 1H), 3.86-3.81 (m, 1H), 3.07 (s, 2H); MS (EI) $C_{18}H_{16}F_3IN_4O_2$: 505 (MH^+).

EXAMPLE 3

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(morpholin-4-ylmethyl)azetidin-3-ol



[0343] A mixture of 3-azetidinol hydrochloride (10 g, 91 mmol), di-*tert*-butyl dicarbonate (18.8 g, 86.3 mmol) and sodium bicarbonate (15.3 g, 182 mmol) in dioxane:water (400 mL, 1:1) was stirred at room temperature for 15 hours. The organic portion was removed *in vacuo* and the aqueous portion was extracted with ethyl acetate three times. The combined organic portion was washed with 5% aqueous HCl, water, brine, dried over sodium sulfate, filtered and concentrated *in-vacuo* to afford 12.8 g, 74 mmol (81%) of 1,1-dimethylethyl 3-hydroxyazetidine-1-carboxylate as a colorless oil without further purification. ^{1}H NMR (400 MHz, DMSO): 5.62 (d, 1H), 4.40-4.33 (m, 1H), 4.02-3.95 (m, 2H), 3.62-3.54 (m, 2H), 1.37 (s, 9H). GC/MS for $C_8H_{15}NO_3$: 173.

[0344] A solution of oxalyl chloride (545 μL, 6.36 mmol) in dichloromethane (25 mL) was cooled to -78 °C. While maintaining an internal temperature of -78 °C, the dropwise addition of DMSO (903 μL, 12.7 mmol) followed by 1,1-dimethylethyl 3-hydroxyazetidine-1-carboxylate (1 g, 5.78 mmol in 30 mL of dichloromethane) and finally triethylamine (3.25 mL, 23.1 mmol in 20 mL of dichloromethane) was performed. The mixture was allowed to warm to room temperature and was stirred for 15 hours. The reaction mixture was diluted with water and partitioned and the organic portion was washed twice with water. The combined aqueous portion was extracted once with dichloromethane. The combined organic portion was washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford a yellow oil which was purified by column chromatography. Eluting with 30% ethyl acetate in hexanes, isolated product was concentrated *in vacuo* to afford 893 mg, 5.20 mmol (90%) of 1,1-dimethylethyl 3-oxoazetidine-1-carboxylate as a colorless oil, which solidified upon standing. ^{1}H NMR (400 MHz, DMSO): 4.67 (s, 4H), 1.42 (s, 9H). GC/MS for $C_8H_{13}NO_3$: 171.

[0345] A mixture of potassium *tert*-butoxide (15.5 g, 137 mmol) and methyltriphenylphosphine bromide (49 g, 137 mmol) in diethyl ether (300 mL) was stirred at room temperature for 1 hour, followed by the addition of 1,1-dimethylethyl 3-oxoazetidine-1-carboxylate (10 g, 58 mmol in 100 mL diethyl ether). The mixture was stirred at 35 °C for 2 hours and then allowed to cool to room temperature. The mixture was filtered through a pad of celite, washing with diethyl ether. The filtrate was partitioned with water and washed twice with water, brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to give an orange oil which was purified by column chromatography. Eluting with 10% ethyl acetate in hexanes, isolated product was concentrated *in vacuo* to afford 9.80 g, 58 mmol (100%) of 1,1-dimethylethyl 3-methylideneazetidine-1-carboxylate as a colorless oil. ^{1}H NMR (400 MHz, DMSO): 5.05-4.85 (m, 2H), 4.95-4.63 (m, 4H), 1.45 (s, 9H). GC-MS for $C_9H_{15}NO_2$: 169.

[0346] To a solution of 1,1-dimethylethyl 3-methylideneazetidine-1-carboxylate (2.96 g, 17.5 mmol) in chloroform (180 mL) was added 3-chloroperoxybenzoic acid (77%, 13.9 g, 62.0 mmol), and the resulting mixture was stirred at room temperature for 2 days. The reaction mixture was quenched with a 1:1 mixture (150 mL) of 10% sodium thiosulfate and saturated sodium bicarbonate solutions. The organic portion was isolated, dried over sodium sulfate, filtered and concentrated to give an oily residue which was then purified by flash chromatography (15-50% ethyl acetate-hexanes) to give 1,1-dimethylethyl 1-oxa-5-azaspiro[2.3]hexane-5-carboxylate (1.65g, 51%), GC-MS for $C_9H_{15}NO_3$: 185.

[0347] 1,1-Dimethylethyl 1-oxa-5-azaspiro[2.3]hexane-5-carboxylate (51 mg, 0.28 mmol) was taken into THF (1 mL) followed by addition of morpholine (123 μL, 1.4 mmol) and the mixture was stirred for one hour at room temperature. The solution was then concentrated and the residue partitioned with ethyl acetate and water. The organic layer was washed once with water then brine and the organic layer dried over anhydrous sodium sulfate. Filtration and concentration gave a colorless oil that was purified by silica gel flash chromatography using ethyl acetate to 10% methanol in dichloromethane as eluents. The combined pure fractions were concentrated and the residue treated with neat TFA (1 mL) for 5 minutes then concentrated. The residue was taken into methanol (2 mL) and basified to pH > 10 by addition of Biorad AG-1X hydroxide form resin. Filtration and concentration afforded 3-(morpholin-4-ylmethyl)azetidin-3-ol (11.6 mg, 24% yield) as a colorless oil. ^{1}H NMR (400

MHz, CD_3OD): 3.69-3.66 (m, 4H), 3.55 (d, 2H), 3.49 (d, 2H), 2.66 (s, 2H), 2.57-2.55 (m, 4H).

[0348] 3-(Morpholin-4-ylmethyl)azetidin-3-ol (11.6 mg, 0.07 mmol) was taken into DMF (1 mL) followed by addition of DIPEA (35 μL, 0.21 mmol) and 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoyl fluoride (28 mg, 0.07 mmol), prepared using procedures similar to those described in Reference 1, and the mixture was stirred for 30 minutes at room temperature. The solution was then concentrated *in vacuo* and the residue purified by preparative reverse phase HPLC. Lyophillization of the combined fractions gave 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(morpholin-4-ylmethyl)azetidin-3-ol trifluoroacetate salt (6.3 mg) as a colorless amorphous solid. ^1H NMR (400 MHz, CD_3OD): 7.48 (d, 1H), 7.36 (d, 1H), 7.33-7.29 (m, 1H), 7.08-7.02 (m, 1H), 6.65-6.60 (m, 1H), 4.39 (br d, 1H), 4.24-4.18 (br, 2H), 4.08-3.96 (br m, 3H), 3.80 (br s, 2H), 3.51 (d, 2H), 3.40 (br s, 2H), 3.24 (br s, 2H).

[0349] Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the following compounds were prepared.

[0350] **EXAMPLE 3(a).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(pyrrolidin-1-ylmethyl)azetidin-3-ol: MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 532 (MH^+).

[0351] **EXAMPLE 3(b).** 1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}piperidin-4-ol: MS (EI) for $C_{22}H_{23}F_3IN_3O_3$: 562 (MH^+).

[0352] **EXAMPLE 3(c).** 3-{[bis(2-hydroxyethyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: MS (EI) for $C_{21}H_{23}F_3IN_3O_4$: 566 (MH^+).

[0353] **EXAMPLE 3(d).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(4-methylpiperazin-1-yl)methyl]azetidin-3-ol: MS (EI) for $C_{22}H_{24}F_3IN_4O_2$: 561 (MH^+).

[0354] **EXAMPLE 3(e).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(4-methyl-1,4-diazepan-1-yl)methyl]azetidin-3-ol: MS (EI) for $C_{23}H_{26}F_3IN_4O_2$: 575 (MH^+).

[0355] **EXAMPLE 3(f).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[methyl(1-methylpyrrolidin-3-yl)amino]methyl}azetidin-3-ol: MS (EI) for $C_{23}H_{26}F_3IN_4O_2$: 575 (MH^+).

[0356] **EXAMPLE 3(g).** 3-(1,4'-bipiperidin-1'-ylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: MS (EI) for $C_{27}H_{32}F_3IN_3O_2$: 629 (MH^+).

[0357] **EXAMPLE 3(h).** 3-({4-[2-(diethylamino)ethyl]piperazin-1-yl}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: MS (EI) for $C_{27}H_{35}F_3IN_3O_2$: 647 (MH^+).

[0358] **EXAMPLE 3(i).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxyethyl)(methyl)amino]methyl}azetidin-3-ol: MS (EI) for $C_{20}H_{21}F_3IN_3O_3$: 536 (MH^+).

[0359] **EXAMPLE 3(j).** 3-(azetidin-1-ylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: MS (EI) for $C_{20}H_{19}F_3IN_3O_2$: 518 (MH^+).

[0360] **EXAMPLE 3(k).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-methylethyl)amino]methyl}azetidin-3-ol: MS (EI) for $C_{20}H_{21}F_3IN_3O_2$: 520 (MH^+).

[0361] **EXAMPLE 3(m).** 3-(aminomethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: MS (EI) for $C_{17}H_{15}F_3IN_3O_2$: 478 (MH^+).

[0362] **EXAMPLE 3(n).** *N*-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}acetamide: MS (EI) for $C_{19}H_{17}F_3IN_3O_3$: 520 (MH^+).

[0363] **EXAMPLE 3(o).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,1-dimethylethyl)amino]methyl}azetidin-3-ol: MS (EI) for $C_{21}H_{23}F_3IN_3O_4$: 534 (MH^+).

[0364] **EXAMPLE 3(q).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(hydroxyamino)methyl]azetidin-3-ol: ^1H NMR (400 MHz, d_4-MeOH): 7.45 (2d, 1H), 7.35 (m, 1H), 7.28 (m, 1H), 7.03 (m, 1H), 6.63 (m, 1H), 4.32 (d, 1H), 4.05 (dd, 2H), 3.85 (d, 1H), 3.00 (s, 2H); MS (EI) for $C_{17}H_{15}F_3IN_3O_3$: 494 (MH^+).

[0365] **EXAMPLE 3(r).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(methyloxy)amino]methyl}azetidin-3-ol: ^1H NMR (400 MHz, d_4-MeOH): 7.45 (2d, 1H), 7.35 (m, 1H), 7.27 (m, 1H), 7.04 (m, 1H), 6.62 (m,

1H), 4.26 (d, 1H), 4.08 (d, 1H), 4.00 (d, 1H), 3.84 (d, 1H), 3.30 (s, 3H), 3.00 (d, 2H); MS (EI) for $C_{18}H_{17}F_3IN_3O_3$: 508 (MH^+).

[0366] EXAMPLE 3(s). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(ethyloxy)amino]methyl}azetidin-3-ol: ^{1}H NMR (400 MHz, d_4-MeOH): 7.45 (2d, 1H), 7.34 (m, 1H), 7.26 (m, 1H), 7.03 (m, 1H), 6.63 (m, 1H), 4.26 (d, 1H), 4.12 (d, 1H), 4.00 (d, 1H), 3.84 (d, 1H), 3.61 (dd, 2H), 3.00 (s, 2H), 1.06 (t, 3H); MS (EI) for $C_{19}H_{19}F_3IN_3O_3$: 522 (MH^+).

[0367] EXAMPLE 3(t). 1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}guanidine acetate salt: ^{1}H NMR (400 MHz, d_4-MeOH): 7.46 (2d, 1H), 7.36 (m, 1H), 7.30 (m, 1H), 7.04 (m, 1H), 6.62 (m, 1H), 4.18 (d, 1H), 4.08 (d, 1H), 4.02 (d, 1H), 3.88 (1*H*), 3.40 (s, 2H); MS (EI) for $C_{18}H_{17}F_3IN_5O_2$: 520 (MH^+).

[0368] EXAMPLE 3(u). *N*-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}benzenecarboximidamide hydrochloride: ^{1}H NMR (400 MHz, d_4-MeOH): 7.70 (d, 3H), 7.58 (m, 2H), 7.46 (dd, 1H), 7.36 (m, 1H), 7.31 (m, 1H), 7.04 (m, 1H), 6.62 (m, 1H), 4.28 (m, 1H), 4.15 (m, 2H), 3.96 (m, 1H), 3.78 (s, 2H); MS (EI) for $C_{24}H_{20}F_3IN_4O_2$: 581 (MH^+).

[0369] EXAMPLE 3(v). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(pyrimidin-2-ylamino)methyl]azetidin-3-ol hydrochloride: ^{1}H NMR (400 MHz, d_4-MeOH): 8.48 (s, 2H), 7.46 (2d, 1H), 7.36 (m, 1H), 7.28 (m, 1H), 7.04 (m, 1H), 6.85 (t, 1H), 6.61 (m, 1H), 4.24 (d, 1H), 4.06 (t, 2H), 3.87 (d, 1H), 3.75 (d, 2H); MS (EI) for $C_{21}H_{17}F_3IN_5O_2$: 556 (MH^+).

[0370] EXAMPLE 3(w). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(pyridin-2-ylamino)methyl]azetidin-3-ol hydrochloride: ^{1}H NMR (400 MHz, d_4-MeOH): 7.87 (dd, 1H), 7.85 (dd, 1H), 7.46 (2d, 1H), 7.36 (m, 2H), 7.06 (m, 2H), 6.89 (m, 1H), 6.61 (m, 1H), 4.53 (d, 2H), 4.46 (m, 1H), 4.28 (m, 1H), 4.16 (m, 1H), 3.96 (m, 1H); MS (EI) for $C_{22}H_{18}F_3IN_4O_2$: 555 (MH^+).

[0371] EXAMPLE 3(x). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(ethylamino)methyl]azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 8.61 (s, 2H), 7.59 (d, 1H), 7.40 (d, 1H), 7.36-7.33 (m, 1H), 7.23-7.18 (m, 1H), 6.71 (s, 2H), 4.31-4.26 (m, 1H), 4.13-4.05 (m, 2H), 3.88-3.84 (m, 1H), 3.21 (br m, 2H), 2.97-2.90 (m, 2H), 1.19 (t, 3H). MS (EI) for $C_{19}H_{19}F_3IN_3O_2$: 506 (MH^+).

[0372] EXAMPLE 3(y). 3-[(cyclopropylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 8.99 (br s, 2H), 8.60 (s, 1H), 7.58 (d, 1H), 7.39 (d, 1H), 7.36-7.33 (m, 1H), 7.23-7.16 (m, 1H), 6.72 (s, 2H), 4.34-4.29 (m, 1H), 4.14-4.04 (m, 2H), 3.88-3.84 (m, 1H), 2.70-2.64 (m, 1H), 0.89 (br s, 2H), 0.74-0.69 (br s, 2H). MS (EI) for $C_{20}H_{19}F_3IN_3O_2$: 518 (MH^+).

[0373] EXAMPLE 3(z). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2,2,2-trifluoroethyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 8.60 (s, 1H), 7.58 (d, 1H), 7.38 (d, 1H), 7.35-7.30 (m, 1H), 7.22-7.17 (m, 1H), 6.72-6.67 (m, 1H), 4.25-4.19 (m, 1H), 4.07-3.98 (m, 2H), 3.86-3.77 (m, 2H), 3.19-3.09 (m, 2H). MS (EI) for $C_{19}H_{16}F_6IN_3O_2$: 560 (MH^+).

[0374] EXAMPLE 3(aa). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-1,2,3-triazol-1-ylmethyl)azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 8.55 (s, 1H), 8.04 (s, 1H), 7.66 (s, 1H), 7.58 (d, 1H), 7.39 (d, 1H), 7.34-7.29 (m, 1H), 7.22-7.15 (m, 1H), 6.72-6.66 (m, 1H), 6.29 (s, 1H), 4.64 (s, 2H), 4.29-4.25 (m, 1H), 4.13-4.09 (m, 1H), 4.00-3.96 (m, 1H), 3.77-3.73 (m, 1H), 3.16 (d, 1H). MS (EI) for $C_{19}H_{15}F_3IN_5O_2$: 530 (MH^+).

[0375] EXAMPLE 3(bb). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2,2-dimethylpropyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 8.61 (s, 1H), 8.30 (s, 2H), 7.59 (d, 1H), 7.39 (d, 1H), 7.36-7.17 (m, 4H), 6.77-6.66 (m, 4H), 4.35-4.30 (m, 1H), 4.16-4.08 (m, 2H), 3.92-3.87 (m, 1H), 3.31-3.27 (m, 2H), 2.78-2.74 (m, 2H), 1.76 (s, 4H), 0.99 (s, 9H). MS (EI) for $C_{22}H_{25}F_3IN_3O_2$: 548 (MH^+).

[0376] EXAMPLE 3(cc). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(4-methylphenyl)ethyl]amino}methyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, $CDCl_3$): 8.48 (s, 1H), 7.39 (dd, 1H), 7.31-7.34 (m, 1H), 7.08 (dd, 5H), 6.77-6.83 (m, 1H), 6.58-6.63 (m, 1H), 4.20 (br s, 1H), 4.01 (d, 1H), 2.87 (t, 4H), 2.75 (t, 4H), 2.5 (br s, 2H), 2.33 (s, 3H), 2.08 (s, 2H). MS (EI) for $C_{26}H_{25}F_3IN_3O_2$: 594 (M-H).

[0377] EXAMPLE 3(dd). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2,3-dihydro-1*H*-inden-2-ylamino)methyl]azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, $CDCl_3$): 8.48 (s, 1H), 7.40 (dd, 1H), 7.32-7.34 (m, 1H), 7.15-7.22 (m, 4H), 7.10-7.14 (m, 1H), 6.77-6.83 (m, 1H), 6.58-6.64 (m, 1H), 4.22 (br s,

1H), 4.04 (d, 1H), 3.57-3.63 (m, 1H), 3.17 (dd, 2H), 2.94 (s, 2H), 2.75 (dd, 2H), 2.48 (br s, 4H), 2.08 (s, 2H). MS (EI) for $C_{26}H_{23}F_3IN_3O_2$: 592 (M-H).

[0378] EXAMPLE 3(ee). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1S,2S)-2-hydroxycyclopentyl]amino}methyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.46 (dd, 1H), 7.33-7.37 (m, 1H), 7.26-7.31 (m, 1H), 7.00-7.08 (m, 1H), 6.58-6.65 (m, 1H), 4.2 (t, 1H), 3.86-4.06 (m, 4H), 2.92-3.10 (m, 3H), 2.00-2.10 (m, 1H), 1.91-1.97 (m, 3H), 1.66-1.78 (m, 2H), 1.52-1.61 (m, 1H), 1.32-1.44 (m, 1H). MS (EI) for $C_{22}H_{23}F_3IN_3O_3$: 560 (M-H).

[0379] EXAMPLE 3(ff). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,2-dimethylpropyl)amino]methyl}azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.45 (dd, 1H), 7.33-7.37 (m, 1H), 7.26-7.31 (m, 1H), 7.01-7.08 (m, 1H), 6.59-6.64 (m, 1H), 4.14-4.22 (m, 1H), 3.98-4.06 (m, 2H), 3.84-3.90 (m, 1H), 2.86-3.20 (m, 2H), 2.65 (br s, 1H), 1.92 (s, 2H), 1.76-1.86 (m, 1H), 1.06 (d, 3H), 0.91 (dd, 6H). MS (EI) for $C_{22}H_{25}F_3I\ N_3O_2$: 546 (M-H).

[0380] EXAMPLE 3(gg). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-methyl-2-(methyloxy)ethyl]amino}methyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.55 (dd, 1H), 7.33-7.36 (m, 1H), 7.26-7.31 (m, 1H), 7.01-7.09 (m, 1H), 6.59-6.65 (m, 1H), 4.14-4.22 (m, 1H), 3.96-4.06 (m, 2H), 3.85-3.92 (m, 1H), 3.40-3.48 (m, 1H), 3.34 (s, 3H), 2.90-3.15 (m, 3H), 1.94 (s, 3H), 1.11 (d, 3H). MS (EI) for $C_{21}H_{23}F_3IN_3O_3$: 548 (M-H).

[0381] EXAMPLE 3(hh). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-ethylpropyl)amino]methyl}azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.45 (dd, 1H), 7.33-7.36 (m, 1H), 7.26-7.31 (m, 1H), 7.01-7.09 (m, 1H), 6.58-6.65 (m, 1H), 4.15-4.20 (m, 1H), 3.99-4.06 (m, 2H), 3.86-3.91 (m, 1H), 2.94 (s, 2H), 2.55-2.63 (m, 1H), 1.92 (s, 2H), 1.48-1.58 (m, 4H), 0.92 (t, 6H). MS (EI) for $C_{22}H_{25}F_3IN_3O_2$: 546 (M-H).

[0382] EXAMPLE 3(ii). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-imidazol-1-ylmethyl)azetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.67 (br s, 1H), 7.48 (m, 1H), 7.36 (m, 1H), 6.91 (br s, 1H), 6.63 (m, 1H), 4.25 (s, 2H), 4.22 (m, 1H), 4.02 (m, 2H), 3.82 (m, 1H). MS (EI) for $C_{20}H_{16}F_3IN_4O_2$: 529 (MH^+).

[0383] EXAMPLE 3(jj). 3-{[(cyclopropylmethyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.47 (m, 1H), 7.36 (m, 1H), 7.31 (m, 1H), 7.05 (m, 1H), 6.62 (m, 1H), 4.30 (m, 1H), 4.24 (m, 2H), 3.99 (m, 1H), 3.66 (m, 2H), 2.91 (d, 2H), 1.08 (m, 1H), 0.71 (m, 2H), 0.40 (m, 2H). MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 532 (MH^+).

[0384] EXAMPLE 3(kk). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(phenylmethyl)amino]methyl}azetidin-3-ol hydrochloride: ^{1}H NMR (400 MHz, CD_3OD): 7.47 (m, 5H), 7.43 (m, 1H), 7.35 (m, 1H), 7.27 (m, 1H), 7.04 (m, 1H), 6.61 (m, 1H), 4.24 (m, 3H), 4.08 (m, 2H), 3.96 (m, 1H). MS (EI) for $C_{24}H_{21}F_3IN_3O_2$: 568 (MH^+).

[0385] EXAMPLE 3(mm). 3-[(butylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.56 (s, 1H), 7.57 (dd, 1H), 7.36 (d, 1H), 7.31 (t, 1H), 7.17 (q, 1H), 6.67 (dt, 1H), 4.04 (d, 1H), 3.88 (q, 2H), 3.69 (d, 1H), 2.59 (s, 2H), 1.90 (s, 2H), 1.22-1.33 (m, 4H), 0.84 (t, 3H); MS (EI) for $C_{21}H_{23}F_3IN_3O_2$: 534 (MH^+).

[0386] EXAMPLE 3(nn). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1-ethylpyrrolidin-2-yl)methyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.59 (s, 1H), 7.57 (dd, 1H), 7.36 (d, 1H), 7.31 (t, 1H), 7.17 (q, 1H), 6.68 (dt, 1H), 4.02 (t, 1H), 3.89 (q, 2H), 3.69 (d, 1H), 2.98 (s, 1H), 2.67-2.76 (m, 1H), 2.62 (s, 1H), 2.39-2.45 (m, 1H), 2.29 (s, 1H), 1.97-2.13 (m, 2H), 1.69 (s, 1H), 1.54 (s, 3H), 0.97 (t, 3H); MS (EI) for $C_{24}H_{28}F_3IN_4O_2$: 589 (MH^+).

[0387] EXAMPLE 3(oo). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxyethyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.57 (s, 1H), 7.57 (dd, 1H), 7.37 (d, 1H), 7.32 (t, 1H), 7.18 (q, 1H), 6.68 (dt, 1H), 4.06 (d, 1H), 3.87 (d, 2H), 3.70 (d, 1H), 3.42 (t, 2H), 2.65 (s, 2H), 2.56 (dt, 2H). 1.91 (s, 2H); MS (EI) for $C_{19}H_{19}F_3IN_3O_3$: 522 (MH^+).

[0388] EXAMPLE 3(pp). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(dimethylamino)ethyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.58 (s, 1H), 7.57 (dd, 1H), 7.36 (d, 1H), 7.31 (t, 1H), 7.17 (q, 1H), 6.68 (dt, 1H), 4.02 (d, 1H), 3.87 (t, 2H), 3.70 (d, 1H), 2.62 (s, 1H), 2.54 (t, 1H), 2.23 (t, 1H), 2.09 (s, 4H), 7.85 (s, 6H); MS (EI) for $C_{21}H_{24}F_3IN_4O_2$: 549 (MH^+).

[0389] EXAMPLE 3(qq). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(1-methylpyrrolidin-2-yl)ethyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.58 (s, 1H), 7.57 (dt, 1H), 7.36 (d, 1H), 7.31 (t, 1H), 7.17 (q, 1H), 6.68 (dt, 1H), 4.04 (d, 1H), 3.89 (d, 2H), 3.79 (d, 1H), 2.88-2.92 (m, 1H), 2.61 (s, 2H), 2.15 (s, 3H), 1.93-2.04 (m, 2H), 1.75-1.83 (m, 3H), 1.54-1.70 (m, 3H), 1.20-1.37 (m, 2H); MS (EI) for $C_{24}H_{28}F_3IN_4O_2$: 589 (MH^+).

[0390] EXAMPLE 3(rr). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(tetrahydrofuran-2-ylmethyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.58 (s, 1H), 7.57 (dd, 1H), 7.37 (d, 1H), 7.31 (t, 1H), 7.14 (q, 1H), 6.68 (dt, 1H), 5.75 (s, 1H), 4.03 (t, 1H), 3.87 (t, 2H), 3.76 (q, 1H), 3.68 (q, 2H), 3.54-3.58 (m, 1H), 2.63 (s, 2H), 1.91 (s, 2H), 1.71-1.87 (m, 3H), 1.40-1.48 (m, 1H); MS (EI) for $C_{22}H_{23}F_3IN_3O_3$: 562 (MH^+).

[0391] EXAMPLE 3(ss). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-pyrrolidin-1-ylpropyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.58 (s, 1H), 7.57 (dd, 1H), 7.36 (d, 1H), 7.31 (t, 1H), 7.17 (q, 1H), 6.68 (dt, 1H), 4.04 (d, 1H), 3.89 (d, 2H), 3.69 (d, 1H), 2.60 (s, 1H), 2.34-2.37 (m, 4H), 1.86 (s, 8H), 1.64 (s, 2H), 1.46-1.53 (m, 1H); MS (EI) for $C_{24}H_{28}F_3IN_4O_2$: 589 (MH^+).

[0392] EXAMPLE 3(tt). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(methyloxy)ethyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): ^{1}H NMR (400MHz, d_6-DMSO): 8.57 (s, 1H), 7.57 (dd, 1H), 7.37 (d, 1H), 7.31 (t, 1H), 7.17 (q, 1H), 6.68 (dt, 1H), 4.03 (d, 1H), 3.86 (d, 2H), 3.70 (d, 1H), 3.21 (s, 3H), 2.63 (s, 4H), 1.88 (s, 2H); MS (EI) for $C_{20}H_{21}F_3IN_3O_3$: 536 (MH^+).

[0393] EXAMPLE 3(uu). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1-methylpiperidin-4-yl)methyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.58 (s, 1H), 7.57 (d, 1H), 7.37 (d, 1H), 7.31 (t, 1H), 7.17 (q, 1H), 6.68 (t, 1H), 4.03 (d, 1H), 3.89 (t, 2H), 3.69 (d, 1H), 2.68 (d, 2H), 2.57 (s, 1H), 2.34 (d, 2H), 1.88 (s, 4H), 1.73 (t, 2H), 1.57 (d, 2H), 1.23 (s, 1H), 1.05 (q, 2H); MS (EI) for $C_{24}H_{28}F_3IN_4O_3$: 589 (MH^+).

[0394] EXAMPLE 3(vv). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[4-(dimethylamino)butyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 7.57 (dd, 1H), 7.36 (d, 1H), 7.31 (t, 1H), 7.18 (q, 1H), 6.68 (dt, 1H), 4.03 (t, 2H), 3.88 (t, 2H), 3.70 (d, 1H), 3.08 (s, 1H), 2.60 (s, 1H), 2.44-2.47 (m,

2H), 2.28-2.33 (m, 1H), 2.07-2.16 (m, 6H), 1.29-1.35 (m, 4H); MS (EI) for $C_{23}H_{28}F_3IN_4O_2$: 577 (MH^+).

[0395] EXAMPLE 3(ww). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-furan-2-ylethyl)amino]methyl}azetidin-3-ol: ^1H NMR (400MHz, d_6-DMSO): 8.58 (s, 1H), 7.57 (d, 1H), 7.49 (s, 1H), 7.36 (d, 1H), 7.31 (t, 1H), 7.17 (q, 1H), 6.68 (t, 1H), 6.33 (s, 1H), 6.08 (s, 1H), 5.72 (s, 1H), 4.04 (d, 1H), 3.87 (d, 2H), 3.70 (d, 1H), 2.74 (d, 2H), 2.69 (d, 2H), 2.64 (s, 2H); MS (EI) for $C_{23}H_{21}F_3IN_3O_3$: 572 (MH^+).

[0396] EXAMPLE 3(xx). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-ethylbutyl)amino]methyl}azetidin-3-ol: ^1H NMR (400MHz, d_6-DMSO): 8.58 (s, 1H), 7.56 (dd, 1H), 7.36 (d, 1H), 7.31 (t, 1H), 7.17 (q, 1H), 6.67 (dt, 1H), 4.03 (d, 1H), 3.90 (d, 2H), 3.69 (d, 1H), 2.58 (s, 2H), 2.37 (d, 2H), 1.17-1.27 (m, 5H), 0.78 (t, 6H); MS (EI) for $C_{23}H_{27}F_3IN_3O_2$: 562 (MH^+).

[0397] EXAMPLE 3(yy). 1,1-dimethylethyl [3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)propyl]carbamate: ^1H NMR (400MHz, d_6-DMSO): 8.58 (s, 1H), 7.57 (d, 1H), 7.30-7.38 (m, 3H), 7.17 (q, 1H), 6.82 (t, 1H), 6.68 (dt, 1H), 4.07 (d, 1H), 3.89 (d, 2H), 3.70 (d, 1H), 3.36 (s, 2H), 2.93 (q, 2H), 2.61 (s, 2H), 1.46 (t, 2H), 1.36 (s, 9H); MS (EI) for $C_{25}H_{30}F_3IN_4O_4$: 635 (MH^+).

[0398] EXAMPLE 3(zz). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(pyrrolidin-2-ylmethyl)amino]methyl}azetidin-3-ol: ^1H NMR (400MHz, d_6-DMSO): 8.53 (s, 1H), 7.58 (dd, 1H), 7.37 (d, 1H), 7.33 (d, 1H), 7.18 (q, 1H), 6.67 (dt, 1H), 6.25 (s, 1H), 4.07 (d, 1H), 3.96 (q, 2H), 3.78 (s, 3H), 3.34 (s, 6H), 1.73 (s, 1H), 1.35-1.39 (m, 1H); MS (EI) for $C_{22}H_{24}F_3IN_4O_2$: 561 (MH^+).

[0399] EXAMPLE 3(aaa). 1,1-dimethylethyl 4-[({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)methyl]piperidine-1-carboxylate: ^1H NMR (400MHz, d_6-DMSO): 8.56 (s, 1H), 7.56 (dd, 1H), 7.36 (d, 1H), 7.30 (t, 1H), 7.17 (q, 1H), 6.68 (dt, 1H), 4.03 (d, 1H), 3.88 (t, 4H), 3.69 (d, 1H), 2.58 (s, 2H), 2.35 (d, 2H), 1.60 (d, 2H), 1.47 (s, 1H), 1.39 (s, 10H), 0.90 (q, 2H); MS (EI) for $C_{28}H_{34}F_3IN_4O_4$: 675 (MH^+).

[0400] EXAMPLE 3(bbb). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(2-hydroxyphenyl)methyl]amino}methyl)azetidin-3-ol: ^1H NMR (400MHz, d_6-DMSO): 8.56 (s, 1H), 7.54 (dd, 1H), 7.35 (d, 1H), 7.30 (t, 1H),

7.17 (q, 1H), 7.05 (t, 2H), 6.64-6.72 (m, 3H), 4.07 (d, 1H), 3.90 (t, 2H), 3.78 (s, 2H), 3.72 (d, 1H), 2.65 (s, 2H); MS (EI) for $C_{24}H_{21}F_3IN_3O_3$: 584 (MH^+).

[0401] EXAMPLE 3(ccc). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(3-hydroxyphenyl)methyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.58 (s, 1H), 7.56 (d, 1H), 7.35 (d, 1H), 7.29 (t, 1H), 7.16 (q, 1H), 7.06 (t, 1H), 6.64-6.72 (m, 3H), 6.60 (dd, 1H), 4.07 (d, 1H), 3.88 (t, 2H), 3.69 (d, 1H), 3.60 (s, 2H), 2.58 (d, 2H); MS (EI) for $C_{24}H_{21}F_3IN_3O_3$: 584 (MH^+).

[0402] EXAMPLE 3(ddd). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(4-hydroxyphenyl)methyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.57 (s, 1H), 7.55 (dd, 1H), 7.35 (d, 1H), 7.27 (t, 1H), 7.16 (q, 1H), 7.06 (d, 2H), 6.64-6.70 (m, 3H), 4.04 (d, 1H), 3.85 (t, 2H), 3.68 (d, 1H), 3.55 (s, 2H), 2.56 (d, 2H); MS (EI) for $C_{24}H_{21}F_3IN_3O_3$: 584 (MH^+).

[0403] EXAMPLE 3(eee). 3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)-5-(hydroxymethyl)cyclopentane-1,2-diol: ^{1}H NMR (400MHz, d_6-DMSO): 8.60 (broad s, 1H), 7.57 (dd, 1H), 7.37 (d, 1H), 7.32 (t, 1H), 7.16 (q, 1H), 6.68 (t, 1H), 4.06 (q, 2H), 3.86 (t, 3H), 3.72 (dd, 1H), 3.60 (t, 1H), 3.36-3.43 (m, 2H), 3.30 (dd, 1H), 2.80 (q, 1H), 2.62-2.72 (m, 2H), 1.88-1.95 (m, 1H), 0.82-0.90 (m, 1H); MS (EI) for $C_{23}H_{25}F_3IN_3O_5$: 608 (MH^+).

[0404] EXAMPLE 3(fff). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(piperidin-4-ylmethyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.59 (broad s, 1H), 7.57 (dd, 1H), 7.37 (d, 1H), 7.30 (t, 1H), 7.17 (q, 1H), 6.68 (dt, 1H), 4.03 (d, 1H), 3.87 (d, 2H), 3.69 (d, 1H), 3.01 (d, 2H), 2.59 (s, 2H), 2.43-2.56 (m, 1H), 2.35 (d, 2H), 1.65 (d, 2H), 1.47 (s, 1H), 1.07 (q, 2H); MS (EI) for $C_{23}H_{26}F_3IN_4O_2$: 575 (MH^+).

[0405] EXAMPLE 3(ggg). 3-{[(3-aminopropyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 7.57 (dd, 1H), 7.37 (d, 1H), 7.31 (t, 1H), 7.17 (q, 1H),, 6.68 (dt, 1H), 4.05 (d, 1H), 3.88 (d, 2H), 3.69 (d, 1H), 2.61 (t, 3H), 2.53-2.56 (m, 1H), 1.49 (t, 1.49); MS (EI) for $C_{23}H_{26}F_3IN_4O_2$: 535 (MH^+).

[0406] EXAMPLE 3(hhh). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[({[2-(4-methylpiperazin-1-yl)phenyl]methyl}amino)methyl]azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.59 (broad s, 1H), 7.55 (dd, 1H), 7.34 (t, 2H), 7.28 (d, 1H), 7.13-7.20 (m, 1H), 7.05 (d, 1H), 6.99 (t, 1H),

6.66 (dt, 1H), 4.03 (d, 1H), 3.90 (t, 2H), 3.71 (d, 3H), 2.83 (s, 5H), 2.60 (s, 2H), 2.42 (s, 3H), 2.20 (s, 3H); MS (EI) for $C_{29}H_{31}F_3IN_5O_2$: 666 (MH^+).

[0407] EXAMPLE 3(iii). 3-[(1*H*-benzimidazol-2-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^1H NMR (400MHz, $CDCl_3$): 8.04 (s, 2H), 7.28-7.35 (m, 2H), 7.23-7.26 (m, 2H), 7.09-7.12 (m, 2H), 6.80 (q, 1H), 6.57-6.63 (m, 1H), 5.28 (broad s, 2H), 4.38 (s, 3H), 4.25 (s, 1H), 4.21 (d, 2H); MS (EI) for $C_{24}H_{19}F_3IN_5O_2$: 594 (MH^+).

[0408] EXAMPLE 3(jjj). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1*H*-imidazol-2-ylamino)methyl]azetidin-3-ol: ^1H NMR (400MHz, d_6-DMSO): 12.12 (s, 1H), 8.68 (s, 1H), 7.57-7.61 (m, 3H), 7.36-7.41 (m, 2H), 7.19 (q, 1H), 6.99 (s, 1H), 6.91 (s, 1H), 6.71 (dt, 1H), 6.45 (s, 1H), 4.28 (d, 1H), 4.06 (d, 1H), 4.03 (d, 1H), 3.82 (d, 2H); MS (EI) for $C_{24}H_{17}F_3IN_5O_2$: 544 (MH^+).

[0409] EXAMPLE 3(kkk). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{2-[(2,2,3,3,3-pentafluoropropyl)amino]ethyl}azetidin-3-ol: ^1H NMR (400 MHz, d_6-DMSO): 8.58 (br s, 1H), 7.56 (dd, 1H), 7.37 (dd, 1H), 7.34-7.28 (m, 1H), 7.22-7.13 (m, 1H), 6.68 (ddd, 1H), 5.82 (br s, 1H), 4.06 (d, 1H), 3.91 (t, 2H), 3.70 (d, 1H), 3.40-3.25 (m, 2H), 2.76 (d, 2H), 2.40-2.31 (m, 1H); MS (EI) for $C_{20}H_{16}F_8IN_3O_2$: 610 (MH^+).

[0410] EXAMPLE 3(mmm). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{2-[(3,3,3-trifluoropropyl)amino]ethyl}azetidin-3-ol: ^1H NMR (400 MHz, d_6-DMSO): 8.58 (br s, 1H), 7.57 (dd, 1H), 7.37 (dd, 1H), 7.34-7.28 (m, 1H), 7.22-7.13 (m, 1H), 6.68 (ddd, 1H), 5.76 (br s, 1H), 4.05 (d, 1H), 3.88 (d, 2H), 3.70 (d, 1H), 2.71 (t, 2H), 2.63 (s, 2H), 2.41-2.26 (m, 2H); MS (EI) for $C_{20}H_{18}F_6IN_3O_2$: 574 (MH^+).

[0411] EXAMPLE 3(nnn). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2,3-dihydro-1*H*-inden-1-ylamino)methyl]azetidin-3-ol acetate salt: ^1H NMR (400 MHz, DMSO): 8.61-8.56 (m, 1H), 7.55 (d, 1H), 7.37-7.07 (m, 8H), 6.71-6.64 (m, 1H), 4.16-4.05 (m, 2H), 3.98-3.85 (m, 2H), 3.72-3.68 (m, 1H), 2.90-2.82 (m, 1H), 2.74-2.64 (m, 2H), 1.91 (s, 3H), 1.73-1.63 (m, 1H); MS (EI) for $C_{26}H_{23}F_3IN_3O_2$: 594 (MH^+).

[0412] EXAMPLE 3(ooo). 3-[(cyclooctylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^1H NMR (400 MHz, DMSO): 8.56 (s, 1H), 7.55 (d, 1H), 7.20-7.14 (m, 2H), 6.70-6.66 (m, 1H), 4.03-3.98 (m, 1H), 3.92-3.86 (m, 2H), 3.72-3.67 (m, 1H), 2.60 (s, 2H), 1.90 (s, 3H), 1.64-1.22 (m, 15H); MS (EI) for $C_{25}H_{29}F_3IN_3O_2$: 588 (MH^+).

[0413] EXAMPLE 3(ppp). 3-[(cycloheptylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, DMSO): 8.55 (s, 1H), 7.55 (d, 1H), 7.36-7.28 (m, 2H), 7.21-7.14 (m, 1H), 6.70-6.66 (m, 1H), 4.04-4.00 (m, 1H), 3.92-3.85 (m, 2H), 3.71-3.66 (m, 1H), 2.60 (s, 2H), 1.90 (s, 3H), 1.70-1.13 (m, 13H); MS (EI) for $C_{24}H_{27}F_3IN_3O_2$: 574 (MH^+).

[0414] EXAMPLE 3(qqq). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-pyridin-3-ylethyl)amino]methyl}azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, DMSO): 8.58 (s, 1H), 8.42-8.37 (m, 2H), 7.62-7.54 (m, 2H), 7.38-7.27 (m, 3H), 7.21-7.14 (m, 1H), 6.71-6.66 (m, 1H), 4.06-4.02 (m, 1H), 3.90-3.86 (m, 2H), 3.72-3.68 (m, 1H), 2.80-2.64 (m, 6H), 1.90 (s, 3H); MS (EI) for $C_{24}H_{22}F_3IN_4O_2$: 583 (MH^+).

[0415] EXAMPLE 3(rrr). *N*-cyclohexyl-N2-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-2-methylalaninamide acetate salt: ^{1}H NMR (400 MHz, DMSO): 8.66 (br s 1H), 8.55 (s, 1H), 7.93-7.90 (m, 1H), 7.58 (d, 1H), 7.40-7.31 (m, 2H), 7.24-7.17 (m, 1H), 6.71-6.66 (m, 1H), 6.60 (br s, 1H), 4.28-4.23 (m, 1H), 4.14-4.02 (m, 2H), 3.89-3.83 (m, 1H), 3.12 (br s, 2H), 1.90 (s, 3H), 1.74-1.42 (m, 11H), 1.31-1.02 (m, 6H); MS (EI) for $C_{27}H_{32}F_3IN_4O_3$: 645 (MH^+).

[0416] EXAMPLE 3(sss). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(tetrahydro-2H-pyran-4-ylmethyl)amino]methyl}azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, DMSO): 8.56 (s, 1H), 7.56 (d, 1H), 7.38-7.27 (m, 2H), 7.20-7.14 (m, 1H), 6.71-6.66 (m, 1H), 4.05-4.01 (m, 1H), 3.91-3.78 (m, 4H), 3.71-3.67 (m, 1H), 3.25-3.18 (m, 2H), 2.60 (s, 2H), 2.36 (d, 2H), 1.90 (s, 3H), 1.57-1.50 (m, 3H), 1.13-1.02 (m, 2H); MS (EI) for $C_{23}H_{25}F_3IN_3O_3$: 576 (MH^+).

[0417] EXAMPLE 3(ttt). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(dimethylamino)-1-methylethyl]amino}methyl)azetidin-3-ol trifluoroacetate salt: ^{1}H NMR (400 MHz, DMSO): 8.59-8.54 (m, 1H), 7.56 (d, 1H), 7.38-7.28 (m, 2H), 7.21-7.13 (m, 1H), 6.71-6.63 (m, 1H), 4.04-3.95 (m, 1H), 3.88-3.78 (m, 2H), 3.73-3.68 (m, 1H), 2.70-2.50 (m, 3H), 2.08 (s, 6H), 1.88 (s, 2H), 0.85-0.82 (m, 3H); MS (EI) for $C_{22}H_{26}F_3IN_4O_2$: 563 (MH^+).

[0418] EXAMPLE 3(uuu). *N*-cyclopropyl-1-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino) cyclopentanecarboxamide trifluoroacetate salt: ^{1}H NMR (400 MHz, DMSO): 8.80 (br s, 1H), 8.58 (s, 1H), 8.04 (s, 1H), 7.59 (d, 1H), 7.40-7.31 (m, 2H), 7.25-7.16 (m, 1H), 6.74-6.58 (m,

2H), 4.26-3.82 (m, 4H), 3.10 (br s, 2H), 2.69-2.64 (m, 1H), 2.11-1.88 (m, 4H), 1.82-1.61 (m, 4H), 0.67-0.62 (m, 2H), 0.52-0.48 (m, 2H); MS (EI) for $C_{26}H_{28}F_3IN_4O_3$: 629 (MH^+).

[0419] EXAMPLE 3(vvv). N2-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-*N*-ethyl-2-methylalaninamide acetate salt: ^{1}H NMR (400 MHz, DMSO): 8.60 (s, 1H), 7.60-7.72 (m, 1H), 7.56 (d, 1H), 7.38-7.30 (m, 2H), 7.22-7.14 (m, 1H), 6.69-6.63 (m, 1H), 4.07-4.04 (m, 1H), 3.95-3.90 (m, 2H), 3.72-3.68 (m, 1H), 3.05-3.01 (m, 2H), 2.47 (br s, 2H), 1.90 (s, 3H), 1.09 (s, 6H), 0.94 (t, 3H); MS (EI) for $C_{23}H_{26}F_3IN_4O_3$: 591 (MH^+).

[0420] EXAMPLE 3(www). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2-methylhydrazino)methyl]azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, DMSO): 8.54 (s, 1H), 7.57 (d, 1H), 7.38-7.30 (m, 2H), 7.19-7.12 (m, 1H), 6.69-6.63 (m, 1H), 4.04-4.01 (m, 1H), 3.92-3.84 (m, 2H), 3.68-3.63 (m, 1H), 2.55 (s, 2H), 2.39 (s, 3H), 1.90 (s, 3H); MS (EI) for $C_{18}H_{18}F_3IN_4O_2$: 507 (MH^+).

[0421] EXAMPLE 3(xxx). 3-[(azetidin-3-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, DMSO): 7.57 (d, 1H), 7.39-7.30 (m, 2H), 7.20-7.13 (m, 1H), 6.70-6.65 (m, 1H), 4.10-4.04 (m, 1H), 3.90-3.83 (m, 2H), 3.78-3.67 (m, 3H), 3.61-3.53 (m, 1H), 3.48-3.42 (m, 2H), 2.61-2.54 (m, 2H), 1.90 (s, 3H); MS (EI) for $C_{20}H_{20}F_3IN_4O_2$: 533 (MH^+).

[0422] EXAMPLE 3(yyy). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1,3-thiazol-2-ylamino)methyl]azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, DMSO): 8.60 (s, 1H), 7.57 (d, 1H), 7.38-7.28 (m, 2H), 7.20-7.13 (m, 1H), 6.75 (d, 1H), 6.70-6.64 (m, 1H), 5.93 (d, 1H), 4.26-4.22 (m, 1H), 4.11-4.08 (m, 1H), 4.00-3.88 (m, 3H), 3.74-3.70 (m, 1H), 1.90 (s, 3H); MS (EI) for $C_{20}H_{16}F_3IN_4O_2S$: 561 (MH^+).

[0423] EXAMPLE 3(zzz). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(methyloxy)phenyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400 MHz, DMSO): 8.57 (s, 1H), 7.56 (d, 1H), 7.38-7.30 (m, 2H), 7.20-7.12 (m, 1H), 6.95-6.91 (m, 1H), 6.70-6.66 (m, 1H), 6.21-6.17 (m, 2H), 6.14-6.10 (m, 1H), 5.94 (s, 1H), 5.49-5.44 (m, 1H), 4.14-4.10 (m, 1H), 3.98-3.93 (m, 2H), 3.78-3.75 (m, 1H), 3.65 (s, 3H), 3.21 (d, 2H); MS (EI) for $C_{24}H_{21}F_3IN_3O_3$: 584 (MH^+).

[0424] EXAMPLE 3(ab). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[4-(methyloxy)phenyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400 MHz, DMSO): 8.56 (s, 1H), 7.58 (d, 1H), 7.39-7.30 (d, 2H), 7.20-7.13 (m, 1H), 6.71-6.66 (m, 3H),

6.55 (d, 2H), 5.93 (s, 1H), 5.00-4.95 (m, 1H), 4.14-4.08 (m, 1H), 3.98-3.92 (m, 2H), 3.79-3.74 (m, 1H), 3.63 (s, 3H), 3.13 (d, 2H); MS (EI) for $C_{24}H_{21}F_3IN_3O_3$: 584 (MH^+).

[0425] EXAMPLE 3(ac). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(ethyloxy)ethyl]amino}methyl)azetidin-3-ol: ^1H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.36-7.33 (d, 1H), 7.31-7.26 (m, 1H), 7.08-7.00 (q, 1H), 6.65-6.58 (t, 1H), 4.24-4.16 (d, 1H), 4.08-3.98 (t, 2H), 3.92-3.85 (d, 1H), 3.60-3.55 (t, 2H), 3.54-3.47 (q, 2H), 3.01-2.96 (s, 2H), 2.94-2.89 (t, 2H), 1.20-1.15 (t, 3H); MS (EI) for $C_{21}H_{23}F_3IN_3O_3$: 550 (MH^+).

[0426] EXAMPLE 3(ad). 3-({[2,2-bis(methyloxy)ethyl]amino}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^1H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.37-7.32 (d, 1H), 7.30-7.24 (m, 1H), 7.08-7.00 (q, 1H), 6.65-6.57 (t, 1H), 4.48-4.42 (t, 1H), 4.20-4.11 (d, 1H), 4.02-3.93 (t, 2H), 3.86-3.80 (d, 1H), 3.38-3.34 (s, 6H), 2.84-2.80 (s, 2H), 2.75-2.70 (d, 2H),1.93-1.87 (s, 3H); MS (EI) for $C_{21}H_{23}F_3IN_3O_4$: 566 (MH^+).

[0427] EXAMPLE 3(ae). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-hydroxypropyl)amino]methyl}azetidin-3-ol acetate salt: ^1H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.38-7.33 (d, 1H), 7.32-7.26 (m, 1H), 7.09-7.00 (q, 1H), 6.66-6.58 (t, 1H), 4.31-4.23 (d, 1H), 4.16-4.05 (t, 2H), 3.99-3.89 (d, 1H), 3.70-3.64 (t, 2H), 3.26-3.22 (s, 2H), 3.11-3.04 (t, 2H), 1.93-1.89 (s, 3H), 1.89-1.82 (t, 3H); MS (EI) for $C_{20}H_{21}F_3IN_3O_3$: 536 (MH^+).

[0428] EXAMPLE 3(af). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-pyridin-4-ylethyl)amino]methyl}azetidin-3-ol acetate salt: ^1H NMR (400 MHz, CD_3OD): 8.36-8.32 (d, 2H), 7.38-7.33 (d, 1H), 7.26-7.14 (m, 3H), 7.00-6.91 (q, 1H), 4.12-4.04 (d, 1H), 3.96-3.88 (t, 2H), 3.80-3.73 (d, 2H), 2.92-2.74 (m, 6H), 1.87-1.84 (s, 3H); MS (EI) for $C_{24}H_{22}F_3IN_4O_2$: 583 (MH^+).

[0429] EXAMPLE 3(ag). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-(phenylmethyl)pyrrolidin-3-yl]amino}methyl)azetidin-3-ol acetate salt: ^1H NMR (400 MHz, CD_3OD): 7.47-7.24 (m, 8H), 7.08-7.00 (q, 1H), 6.64-6.57 (t, 1H), 4.19-4.11 (d, 1H), 4.05-3.81 (m, 5H), 3.52-3.44 (m, 1H), 3.09-2.99 (m, 2H), 2.91-2.76 (m, 3H), 1.93-1.91 (s, 3H), 1.82-1.71 (m, 1H); MS (EI) for $C_{28}H_{28}F_3IN_4O_2$: 637 (MH^+).

[0430] EXAMPLE 3(ah). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(2-thienyl)ethyl]amino}methyl)azetidin-3-ol acetate salt: ^1H NMR (400

MHz, CD_3OD): 7.47-7.42 (d, 1H), 7.36-7.31 (d, 1H), 7.30-7.24 (m, 1H), 7.21-7.17 (d, 1H), 7.08-7.00 (q, 1H), 6.93-6.89 (t, 1H), 6.86-6.83 (d, 1H), 6.64-6.57 (t, 1H), 4.18-4.11 (d, 1H), 4.01-3.93 (t, 2H), 3.85-3.78 (d, 1H), 3.04-2.97 (t, 2H), 2.92-2.87 (t, 2H), 2.82-2.78 (s, 2H), 1.92-1.87 (s, 3H); MS (EI) for $C_{23}H_{21}F_3IN_3O_2S$: 588 (MH^+).

[0431] EXAMPLE 3(ai). 3-[({2-[bis(1-methylethyl)amino]ethyl}amino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^1H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.36-7.33 (d, 1H), 7.31-7.26 (m, 1H), 7.08-7.00 (q, 1H), 6.65-6.58 (t, 1H), 4.18-4.13 (d, 1H), 4.06-3.98 (t, 2H), 3.88-3.82 (d, 2H), 3.57-3.47 (q, 2H), 3.05-2.99 (t, 2H), 2.92-2.85 (t, 4H), 1.92-1.88 (s, 3H), 1.28-1.22 (d, 12H); MS (EI) for $C_{25}H_{32}F_3IN_4O_2$: 605 (MH^+).

[0432] EXAMPLE 3(aj). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(phenyloxy)ethyl]amino}methyl)azetidin-3-ol acetate salt: ^1H NMR (400 MHz, CD_3OD): 7.36-7.31 (d, 1H), 7.26-7.22 (d, 1H), 7.20-7.13 (m, 3H), 6.97-6.89 (t, 1H), 6.86-6.80 (m, 3H), 6.54-6.47 (t, 1H), 4.13-4.07 (d, 1H), 4.01-3.96 (t, 2H), 3.79-3.74 (d, 1H), 2.97-2.91 (t, 2H), 2.84-2.79 (s, 2H), 1.84-1.81 (s, 3H); MS (EI) for $C_{25}H_{23}F_3IN_3O_3$: 598 (MH^+).

[0433] EXAMPLE 3(ak). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxypropyl)amino]methyl}azetidin-3-ol acetate salt: ^1H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.36-7.33 (d, 1H), 7.31-7.26 (m, 1H), 7.08-7.00 (q, 1H), 6.65-6.58 (t, 1H), 4.27-4.19 (d, 1H), 4.10-4.00 (m, 2H), 3.15-3.00 (t, 2H), 3.57-3.47 (q, 2H), 3.15-3.00 (t, 2H), 2.87-2.81 (d, 1H), 2.72-2.64 (t, 1H), 1.94-1.91 (s, 3H), 1.19-1.15 (d, 3H); MS (EI) for $C_{20}H_{21}F_3IN_3O_3$: 536 (MH^+).

[0434] EXAMPLE 3(am). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[({2-[(1-methylethyl)oxy]ethyl}amino)methyl]azetidin-3-ol acetate salt: ^1H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.36-7.33 (d, 1H), 7.31-7.26 (m, 1H), 7.08-7.00 (q, 1H), 6.65-6.58 (t, 1H), 4.21-4.13 (d, 1H), 4.04-3.95 (t, 2H), 3.88-3.82 (d, 1H), 3.64-3.51 (m, 3H), 2.89-2.84 (s, 2H), 2.83-2.77 (t, 2H), 1.91-1.89 (s, 3H), 1.15-1.12 (d, 6H); MS (EI) for $C_{22}H_{25}F_3IN_3O_3$: 564 (MH^+).

[0435] EXAMPLE 3(an). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-ethylpiperidin-3-yl)amino]methyl}azetidin-3-ol acetate salt: ^1H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.36-7.33 (d, 1H), 7.31-7.26 (m, 1H), 7.08-7.00 (q, 1H), 6.65-6.58 (t, 1H), 4.17-4.10 (d, 1H), 4.04-3.95 (t, 2H), 3.88-3.82

(d, 1H), 3.24-3.06 (m, 2H), 2.95-2.75 (m, 6H), 2.76-2.46 (m, 2H), 1.93-1.90 (s, 3H), 1.74-1.62 (m, 1H), 1.44-1.31 (m, 1H), 1.28-1.20 (t, 3H); MS (EI) for $C_{24}H_{28}F_3IN_4O_2$: 589 (MH^+).

[0436] EXAMPLE 3(ao). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]amino}methyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.36-7.33 (d, 1H), 7.31-7.26 (m, 1H), 7.08-7.00 (q, 1H), 6.65-6.58 (t, 1H), 4.20-4.13 (d, 1H), 4.00-3.90 (t, 2H), 3.83-3.75 (d, 1H), 2.84-2.78 (s, 2H), 2.53-2.48 (s, 2H), 1.93-1.87 (s, 3H); MS (EI) for $C_{21}H_{19}F_3IN_5O_3$: 574 (MH^+).

[0437] EXAMPLE 3(ap). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{[(1-methylbutyl)amino]methyl}azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.38-7.33 (d, 1H), 7.32-7.27 (m, 1H), 7.09-7.01 (q, 1H), 6.65-6.58 (t, 1H), 4.25-4.19 (d, 1H), 4.12-4.02 (t, 2H), 3.96-3.90 (d, 1H), 3.16-2.96 (m, 3H), 1.91-1.89 (s, 3H), 1.68-1.57 (m, 1H), 1.49-1.29 (m, 3H), 1.23-1.18 (d, 3H), 0.99-0.92 (t, 3H); MS (EI) for $C_{22}H_{25}F_3IN_3O_2$: 548 (MH^+).

[0438] EXAMPLE 3(aq). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{[(1-methylpropyl)amino]methyl}azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.37-7.33 (d, 1H), 7.32-7.26 (m, 1H), 7.09-7.01 (q, 1H), 6.65-6.58 (t, 1H), 4.27-4.20 (d, 1H), 4.14-4.03 (t, 2H), 3.98-3.92 (d, 1H), 3.20-3.16 (s, 2H), 3.07-2.97 (m, 1H), 1.91-1.89 (s, 3H), 1.80-1.70 (m, 1H), 1.54-1.41 (m, 1H), 1.26-1.22 (d, 3H), 1.00-0.94 (t, 3H); MS (EI) for $C_{21}H_{23}F_3IN_3O_2$: 534 (MH^+).

[0439] EXAMPLE 3(ar). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{[(2-methylbutyl)amino]methyl}azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.37-7.33 (d, 1H), 7.32-7.26 (m, 1H), 7.09-7.01 (q, 1H), 6.65-6.58 (t, 1H), 4.26-4.19 (d, 1H), 4.10-4.01 (t, 2H), 3.94-3.87 (d, 1H), 3.05-2.99 (s, 2H), 2.77-2.70 (m, 1H), 2.61-2.54 (m, 1H), 1.91-1.89 (s, 3H), 1.73-1.61 (m, 1H), 1.49-1.39 (m, 1H), 1.24-1.12 (m, 1H), 0.94-0.84 (m, 6H); MS (EI) for $C_{22}H_{25}F_3IN_3O2$: 548 (MH^+).

[0440] EXAMPLE 3(as). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-[(pentylamino)methyl]azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.37-7.33 (d, 1H), 7.32-7.26 (m, 1H), 7.09-7.01 (q, 1H), 6.65-6.58 (t, 1H), 4.29-4.23 (d, 1H), 4.15-4.05 (t, 2H), 3.98-3.90 (d, 1H), 3.21-3.18 (s, 2H), 2.93-2.86 (m, 2H), 1.91-1.89 (s, 3H), 1.70-1.60 (m, 2H), 1.42-1.29 (m, 4H), 0.97-0.90 (t, 3H); MS (EI) for $C_{22}H_{25}F_3IN_3O_2$: 548 (MH^+).

[0441] EXAMPLE 3(at). 3-[(cyclohexylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.38-7.34 (d, 1H), 7.33-7.27 (m, 1H), 7.09-7.01 (q, 1H), 6.65-6.58 (t, 1H), 4.25-4.19 (d, 1H), 4.14-4.03 (t, 2H), 3.98-3.90 (d, 1H), 3.21-3.18 (s, 2H), 2.93-2.86 (m, 1H), 2.07-2.00 (d, 2H), 1.92-1.90 (s, 3H), 1.89-1.82 (d, 2H), 1.73-1.66 (d, 1H), 1.42-1.14 (m, 5H); MS (EI) for $C_{23}H_{25}F_3IN_3O_2$: 560 (MH^+).

[0442] EXAMPLE 3(au). 3-[(azepan-3-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.37-7.33 (d, 1H), 7.32-7.26 (m, 1H), 7.09-7.01 (q, 1H), 6.65-6.58 (t, 1H), 4.19-4.13 (d, 1H), 4.05-3.95 (t, 2H), 3.90-3.81 (d, 1H), 3.37-3.34 (s, 2H), 3.22-3.03 (m, 2H), 2.91-2.64 (m, 3H), 1.93-1.89 (s, 3H), 1.88-1.52 (m, 6H); MS (EI) for $C_{23}H_{26}F_3IN_4O_2$: 575 (MH^+).

[0443] EXAMPLE 3(av). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(2,3-dihydro-1*H*-indol-3-yl)ethyl]amino}methyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.58-7.54 (d, 1H), 7.48-7.43 (d, 1H), 7.36-7.33 (d, 1H), 7.31-7.26 (m, 1H), 7.14-6.99 (m, 4H), 6.65-6.58 (t, 1H), 4.25-4.19 (d, 1H), 4.10-4.02 (t, 2H), 3.95-3.88 (d, 1H), 3.23-3.03 (m, 9H), 1.94-1.92 (s, 3H); MS (EI) for $C_{27}H_{26}F_3IN_4O_2$: 623 (MH^+).

[0444] EXAMPLE 3(aw). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1,3,5-triazin-2-ylamino)methyl]azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 8.48-8.46 (s, 1H), 8.36-8.34 (s, 1H), 7.48-7.43 (d, 1H), 7.37-7.33 (d, 1H), 7.28-7.22 (m, 1H), 7.06-6.98 (q, 1H), 6.65-6.58 (t, 1H), 4.24-4.18 (d, 1H), 4.10-3.96 (t, 2H), 3.84-3.78 (d, 1H), 3.69-3.67 (s, 2H), 1.99-1.97 (s, 3H); MS (EI) for $C_{20}H_{16}F_3IN_6O_2$: 557 (MH^+).

[0445] EXAMPLE 3(ax). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(4-hydroxycyclohexyl)amino]methyl}azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.37-7.33 (d, 1H), 7.32-7.26 (m, 1H), 7.09-7.01 (q, 1H), 6.65-6.58 (t, 1H), 4.22-4.15 (d, 1H), 4.08-3.99 (t, 2H), 3.93-3.87 (d, 1H), 3.56-3.47 (m, 1H), 3.05-3.02 (s, 2H), 2.76-2.68 (m, 1H), 2.03-1.96 (m, 4H), 1.93-1.89 (s, 3H), 1.35-1.23 (m, 4H); MS (EI) for $C_{23}H_{25}F_3IN_3O_3$: 576 (MH^+).

[0446] EXAMPLE 3(ay). 3-[(cyclopent-3-en-1-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.37-7.33 (d, 1H), 7.32-7.26 (m, 1H), 7.09-7.01 (q, 1H), 6.65-6.58 (t, 1H), 5.70-5.65 (s, 2H), 4.20-4.14 (d, 1H), 4.03-3.95 (t, 2H), 3.90-3.81 (d, 1H), 3.58-

3.50 (m, 1H), 2.90-2.86 (s, 2H), 2.68-2.58 (m, 2H), 2.26-2.16 (m, 2H), 1.93-1.89 (s, 3H); MS (EI) for $C_{22}H_{21}F_3IN_3O_2$: 544 (MH^+).

[0447] EXAMPLE 3(az). *N*-[4-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)phenyl]acetamide acetate salt: ^1H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.37-7.33 (d, 1H), 7.27-7.20 (m, 3H), 7.09-7.01 (q, 1H), 6.65-6.55 (m, 3H), 4.22-4.16 (d, 1H), 4.08-3.98 (t, 2H), 3.88-3.82 (d, 1H), 3.28-3.24 (s, 2H), 2.08-2.05 (s, 3H), 2.91-2.64 (m, 3H), 1.93-1.89 (s, 3H); MS (EI) for $C_{25}H_{22}F_3IN_4O_3$: 611 (MH^+).

[0448] EXAMPLE 3(ba). *N*-[3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)phenyl]acetamide acetate salt: ^1H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.36-7.33 (d, 1H), 7.27-7.20 (m, 1H), 7.04-6.96 (m, 3H), 6.72-6.68 (d, 1H), 6.65-6.58 (t, 1H), 6.40-6.35 (d, 1H), 4.24-4.18 (d, 1H), 4.08-3.98 (t, 2H), 3.87-3.81 (d, 1H), 3.28-3.25 (s, 2H), 2.10-2.07 (s, 3H), 1.97-1.95 (s, 3H); MS (EI) for $C_{25}H_{22}F_3IN_4O_3$: 611 (MH^+).

[0449] EXAMPLE 3(bc). (1R,2S)-4-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)cyclopentane-1,2-diol acetate salt: ^1H NMR (400 MHz, DMSO): 8.58-8.54 (s, 1H), 7.61-7.53 (d, 1H), 7.39-7.28 (m, 2H), 7.21-7.13 (m, 1H), 6.71-6.63 (t, 1H), 5.58-5.64 (s, 1H), 5.63-5.58 (s, 1H), 4.06-4.01 (d, 1H), 3.90-3.84 (t, 2H), 3.72-3.66 (d, 1H), 3.31-3.26 (m, 3H), 2.61-2.57 (s, 2H), 2.46-2.36 (m, 2H), 2.02-1.93 (dd, 2H), 1.91-1.88 (s, 3H); MS (EI) for $C_{22}H_{23}F_3IN_3O_4$: 578 (MH^+).

[0450] EXAMPLE 3(bd). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-(hydroxymethyl)cyclohexyl]amino}methyl)azetidin-3-ol acetate salt: ^1H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.37-7.33 (d, 1H), 7.32-7.26 (m, 1H), 7.09-7.01 (q, 1H), 6.65-6.58 (t, 1H), 4.22-4.15 (d, 1H), 4.08-3.99 (t, 2H), 3.89-3.83 (d, 1H), 3.49-3.45 (s, 2H), 2.86-2.80 (s, 2H), 1.91-1.89 (s, 3H), 1.67-1.34 (m, 10H); MS (EI) for $C_{24}H_{27}F_3IN_3O_3$: 590 (MH^+).

[0451] EXAMPLE 3(be). 3-{[(3-chlorophenyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^1H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.37-7.33 (d, 1H), 7.32-7.26 (m, 1H), 7.08-6.98 (m, 2H), 6.65-6.55 (m, 3H), 6.53-6.44 (d, 1H), 4.22-4.15 (d, 1H), 4.06-3.98 (t, 2H), 3.88-3.82 (d, 1H), 3.27-3.24 (s, 2H), 1.91-1.89 (s, 3H); MS (EI) for $C_{23}H_{18}ClF_3IN_3O_2$: 588 (MH^+).

[0452] EXAMPLE 3(bf). 3-{[(4-chlorophenyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.45-7.40 (d, 1H), 7.35-7.30 (d, 1H), 7.28-7.22 (m, 1H), 7.06-6.97 (m, 3H), 6.62-6.54 (m, 3H), 6.53-6.44 (d, 1H), 4.22-4.15 (d, 1H), 4.06-3.98 (t, 2H), 3.88-3.82 (d, 1H), 3.26-3.22 (s, 2H), 1.96-1.94 (s, 3H); MS (EI) for $C_{23}H_{18}ClF_3IN_3O_2$: 588 (MH^+).

[0453] EXAMPLE 3(bg). 3-[(5-amino-3-methyl-1*H*-pyrazol-1-yl)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.38-7.33 (d, 1H), 7.28-7.24 (d, 1H), 7.21-7.15 (m, 1H), 6.98-6.90 (q, 1H), 6.56-6.49 (t, 1H), 5.16-5.14 (s, 1H), 4.36-4.30 (d, 1H), 4.22-4.16 (d, 1H), 3.99-3.97 (s, 1H), 3.95-3.90 (d, 1H), 3.77-3.71 (d, 1H), 1.96-1.92 (s, 3H), 1.85-1.82 (s, 3H); MS (EI) for $C_{21}H_{19}F_3IN_5O_2$: 558 (MH^+).

[0454] EXAMPLE 3(bh). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(5-methyl-1*H*-pyrazol-3-yl)amino]methyl}azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.38-7.33 (d, 1H), 7.28-7.24 (d, 1H), 7.21-7.15 (m, 1H), 6.98-6.90 (q, 1H), 6.56-6.49 (t, 1H), 5.22-5.19 (s, 1H), 4.15-4.08 (d, 1H), 4.02-3.88 (m, 2H), 3.75-3.68 (d, 1H), 3.20-3.18 (s, 2H), 2.07-2.05 (s, 3H), 1.85-1.82 (s, 3H); MS (EI) for $C_{21}H_{19}F_3IN_5O_2$: 558 (MH^+).

[0455] EXAMPLE 3(bi). 3-[(diethylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 8.54 (s, 1H), 7.58-7.55 (dd, 1H), 7.38-7.35 (dt, 1H), 7.33-7.31 (m, 1H), 7.22-7.15 (m, 1H), 6.69-6.64 (m, 1H), 5.56 (b, 1H), 4.06-4.04 (d, 1H), 3.90-3.88 (m, 2H), 3.72-3.69 (d 1H), 2.51-2.49 (m, 6H), 0.86-0.83 (t, 6H); MS (EI) for $C_{21}H_{23}F_3IN_3O_2$: 534 (MH^+).

[0456] EXAMPLE 3(bj). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(dimethylamino)methyl]azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 8.56 (s, 1H), 7.59-7.56 (dd, 1H), 7.38-7.36 (dt, 1H), 7.34-7.33 (m, 1H), 7.21-7.14 (m, 1H), 6.71-6.65 (m, 1H), 5.55 (b, 1H), 4.07-4.05 (d, 1H), 3.89-3.84 (t, 2H), 3.74-3.719 (d, 1H), 2.46 (m, 2H), 2.19 (br s, 6H); MS (EI) for $C_{19}H_{19}F_3IN_3O_2$: 506 (MH^+).

[0457] EXAMPLE 3(bk). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxy-1,1-dimethylethyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400MHz, $CDCl_3$): 8.40 (s, 1H), 7.38 (dd, 1H), 7.33-7.30 (m, 1H), 7.12 (m, 1H), 6.85-6.79 (m, 1H), 6.63-6.57 (m, 1H), 4.22-4.11(br m, 4H), 3.55 (s, 2H), 3.15 (s, 2H), 1.32 (s, 6H); MS (EI) for $C_{21}H_{23}F_3IN_3O_3$: 550 (MH^+).

[0458] EXAMPLE 3(bm). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-[(prop-2-en-1-ylamino)methyl]azetidin-3-ol): ^{1}H NMR (400MHz, $CDCl_3$): 8.47 (s, 1H), 7.40 (dd, 1H), 7.34-7.31 (m, 1H), 7.12 (m, 1H), 6.83-6.77 (m, 1H), 6.64-6.59 (m, 1H), 6.64-6.59 (m, 1H), 5.88-5.78 (m, 1H), 5.00-5.12 (m, 2H), 4.13 (br m, 4H), 3.26 (d, 2H), 2.88 (d, 2H), 2.02 (s, 1H); MS (EI) for $C_{21}H_{19}F_3IN_3O_2$: 518 (MH^+).

[0459] EXAMPLE 3(bn). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[2-(tetrahydro-2H-pyran-4-yl)ethyl]amino}methyl)azetidin-3-ol): ^{1}H NMR (400MHz, $CDCl_3$): 8.45 (s, 1H), 7.39 (dd, 1H), 7.34-7.31 (m, 1H), 7.14-7.10 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.58 (m, 1H), 4.26-4.04 (m, 4H), 3.95 (dd, 2H), 3.35 (t, 2H), 2.92 (d, 2H), 2.67 (m, 2H), 1.40-1.25 (m, 8H); MS (EI) for $C_{24}H_{27}F_3IN_3O_3$: 590 (MH^+).

[0460] EXAMPLE 3(bo). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{[(1,1-dimethylprop-2-yn-1-yl)amino]methyl}azetidin-3-ol): ^{1}H NMR (400MHz, $CDCl_3$): 8.46 (s, 1H), 7.39 (dd, 1H), 7.33-7.30 (m, 1H), 7.15-7.11 (m, 1H), 6.84-6.77 (m, 1H), 6.64-6.58 (m, 1H), 4.20 (br, 1H), 4.07 (br, 1H), 2.92 (s, 2H), 1.58 (m, 4H), 0.92 (dd, 6h); MS (EI) for $C_{22}H_{21}F_3IN_3O_2$: 572 (MH^+).

[0461] EXAMPLE 3(bp). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[2-(1*H*-imidazol-4-yl)ethyl]amino}methyl)azetidin-3-ol): ^{1}H NMR (400MHz, $CDCl_3$):

8.44 (s, 1H), 7.33-7.14 (m, 3H), 7.00 (m, 1H), 6.67 (dd, 1H), 6.59 (s, 1H), 6.44 (m, 1H), 3.93 (d, 2H), 2.75 (m, 2H), 2.60 (m, 1H), 2.42 (m, 1H) 2.02 (AcOH; s, 3H), 1.86 (m, 4H); MS (EI) for $C_{22}H_{21}F_3IN_5O_2$: 572 (MH^+).

[0462] EXAMPLE 3(bq). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[3-(ethyloxy)propyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, $CDCl_3$):

8.49 (s, 1H), 7.39 (dd, 1H), 7.34-7.31 (m, 1H), 7.14-7.10 (m, 1H), 6.83-6.76 (m, 1H), 6.64-6.58 (m, 1H), 4.26-4.03 (br m, 4H), 3.53-3.44 (m, 4H), 2.92-2.73 (m, 4H), 1.72 (m, 2H) 1.18 (t, 3H); MS (EI) for $C_{22}H_{23}F_3IN_3O_3$: 564 (MH^+).

[0463] EXAMPLE 3(br). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{[(3,3-dimethylbutyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400MHz, $CDCl_3$): 8.46 (s, 1H), 7.39 (dd, 1H), 7.34-7.31 (m, 1H), 7.14-7.10 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.58 (m, 1H), 4.18 (br, 3H), 3.15 (s, 2H), 2.71 (m, 2H) 2.05 (AcOH; s, 3H), 1.43 (m, 2H), 0.90 (s, 9H); MS (EI) for $C_{23}H_{27}F_3IN_3O_2$: 562 (MH^+).

[0464] EXAMPLE 3(bs). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{[(3-methylbutyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400MHz, $CDCl_3$): 8.46 (s, 1H), 7.39 (dd, 1H), 7.34-7.30 (m, 1H), 7.14-7.11 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.59 (m, 1H), 4.27-3.61 (br m, 6H), 2.98 (m, 2H), 2.72 (t, 2H) 2.05 (AcOH; s, 3H), 1.61 (m,1H), 1.43 (m, 2H), 0.90 (d, 6H); MS (EI) for $C_{22}H_{25}F_3IN_3O_2$: 547 (MH^+).

[0465] EXAMPLE 3(bt). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[3-(dimethylamino)propyl]amino}methyl)azetidin-3-ol: MS (EI) for $C_{22}H_{26}F_3IN_4O_2$: 563 (MH^+).

[0466] EXAMPLE 3(bu). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[3-(1*H*-imidazol-1-yl)propyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, $CDCl_3$):

8.46 (s, 1H), 7.53 (s, 1H), 7.40 (dd, 1H), 7.34-7.30 (m, 1H), 7.14-7.09 (m, 1H), 7.05 (s, 1H), 6.89 (s, 1H), 6.84-6.77 (m, 1H), 6.63-6.59 (m, 1H), 4.24-4.00 (br m, 6H), 2.84 (m, 2H), 2.61 (m, 2H), 1.94 (m, 2H); MS (EI) for $C_{23}H_{21}F_3IN_5O_2$: 586 (MH^+).

[0467] EXAMPLE 3(bv). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[2-(methylthio)ethyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, $CDCl_3$):

8.49 (s, 1H), 7.39 (dd, 1H), 7.34-7.31 (m, 1H), 7.14-7.11 (m, 1H), 6.83-6.77 (m, 1H), 6.63-6.59 (m, 1H), 4.26-4.03 (br m, 4H), 2.88 (s, 2H), 2.82 (t, 2H), 2.62 (t, 2H), 2.08 (s, 3H); MS (EI) for $C_{23}H_{21}F_3IN_3O_2S$: 552 (MH^+).

[0468] EXAMPLE 3(bw). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{[(1,1,3,3-tetramethylbutyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400MHz, $CDCl_3$):

8.49 (s, 1H), 7.38 (dd, 1H), 7.34-7.30 (m, 1H), 7.14-7.11 (m, 1H), 6.83-6.77 (m, 1H), 6.64-6.59 (m, 1H), 4.25-4.01 (br m, 4H), 2.82 (s, 2H), 1.45 (s, 2H), 1.15 (s, 6H), 0.90 (s, 9H); MS (EI) for $C_{25}H_{31}F_3IN_3O_2$: 590 (MH^+).

[0469] EXAMPLE 3(bx). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{[(1,1-dimethylpropyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400MHz, $CDCl_3$):

8.50 (s, 1H), 7.39 (dd, 1H), 7.35-7.30 (m, 1H), 7.15-7.11 (m, 1H), 6.83-6.77 (m, 1H), 6.65-6.59 (m, 1H), 4.27-4.01 (br m, 4H), 2.82 (s, 2H), 1.46 (s, 2H), 1.08 (s, 6H), 0.89 (s, 3H); MS (EI) for $C_{22}H_{21}F_3IN_4O_3$: 548 (MH^+).

[0470] EXAMPLE 3(by). 3-{[(3-amino-2-hydroxypropyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: MS (EI) for $C_{23}H_{22}F_3IN_4O_3$: 551 (MH^+).

[0471] EXAMPLE 3(bz). 1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}pyrrolidin-3-ol: MS (EI) for $C_{21}H_{21}F_3IN_3O_3$: 548 (MH^+).

[0472] EXAMPLE 3(ca). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({(2S)-2-[(methyloxy)methyl]pyrrolidin-1-yl}methyl)azetidin-3-ol: MS (EI) for $C_{23}H_{25}F_3IN_3O_3$: 576 (MH^+).

[0473] EXAMPLE 3(cb). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxyphenyl)amino]methyl}azetidin-3-ol: ^1H NMR (400MHz, $CDCl_3$): 8.46 (s, 1H), 7.41 (dd, 1H), 7.35-7.30 (m, 1H), 7.15-7.11 (m, 1H), 6.89-5.98 (m, 6H), 4.92 (s, 1H), 4.28-4.05 (br m, 4H), 3.44 (s, 2H); MS (EI) for $C_{23}H_{19}F_3IN_3O_3$: 570 (MH^+).

[0474] EXAMPLE 3(cd). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(4-hydroxyphenyl)amino]methyl}azetidin-3-ol: ^1H NMR (400MHz, $CDCl_3$): 8.46 (s, 1H), 7.78 (s, 1H), 7.40-7.05 (m, 4H), 6.72 (m, 1H), 6.62 (d, 1H), 6.50 (m, 1H), 6.42 (d, 1H) 4.04-3.98 (m, 4H), 3.18 (s, 2H); MS (EI) for $C_{23}H_{19}F_3IN_3O_3$: 570 (MH^+).

[0475] EXAMPLE 3(ce). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-hydroxyphenyl)amino]methyl}azetidin-3-ol: ^1H NMR (400MHz, $CDCl_3$): 8.52 (s, 1H), 8.22 (s, 1H), 7.39 (dd, 1H), 7.34-7.31 (m, 1H), 7.14-7.11 (m, 1H), 6.85 (dd, 1H), 6.84-6.77 (m, 1H), 6.63-6.59 (m, 1H), 6.15 (d, 1H) 6.09-6.01 (m, 3H), 4.16-3.95 (br m, 4H), 3.22 (d, 2H) 2.15 (AcOH; s, 3H); MS (EI) for $C_{23}H_{19}F_3IN_3O_3$: 570 (MH^+).

[0476] EXAMPLE 3(cf). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(phenyloxy)methyl]azetidin-3-ol: MS (EI) for $C_{23}H_{18}F_3IN_2O_3$: 555 (MH^+).

[0477] EXAMPLE 3(cg). 3-({[1-({3, 4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)propane-1,2-diol: MS (EI) for $C_{20}H_{21}F_3IN_3O_4$: 552 (MH^+).

[0478] EXAMPLE 3(ch). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(phenylthio)methyl]azetidin-3-ol: ^1H NMR (400MHz, $CDCl_3$): 8.46 (s, 1H), 7.45-7.23 (m, 5H), 7.14-7.05 (m, 1H), 6.78 (dd, 1H), 6.60 (m, 1H), 4.14-3.92 (br m, 4H), 3.33 (s, 2H); MS (EI) for $C_{23}H_{18}F_3IN_2O_2$: 571 (MH^+).

[0479] EXAMPLE 3(ci). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{[(4-hydroxybutyl)amino]methyl}azetidin-3-ol): ^{1}H NMR (400MHz, $CDCl_3$): 8.43 (s, 1H), 7.38 (dd, 1H), 7.34-7.30 (m, 1H), 7.14-7.10 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.58 (m, 1H), 4.26-4.04 (m, 4H), 3.61 (m, 2H), 2.96 (s, 2H), 2.73 (s, 2H); MS (EI) for $C_{21}H_{23}F_3IN_3O_3$: 550 (MH^+).

[0480] EXAMPLE 3(cj). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{[(2-hydroxyethyl)oxy]methyl}azetidin-3-ol: ^{1}H NMR (400MHz, $CDCl_3$): 8.51 (s, 1H), 7.39 (dd, 1H), 7.35-7.31 (m, 1H), 7.14-7.11 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.59 (m, 1H), 4.21-4.05 (br m, 4H), 3.77 (m, 2H), 3.66 (m, 2H); MS (EI) for $C_{19}H_{18}F_3IN_2O_4$: 523 (MH^+).

[0481] EXAMPLE 3(ck). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[(1S,2S)-2-hydroxycyclohexyl]amino}methyl)azetidin-3-ol): MS (EI) for $C_{23}H_{25}F_3IN_3O_3$: 576 (MH^+).

[0482] EXAMPLE 3(cm). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{[(1,1-dimethyl-2-pyrrolidin-1-ylethyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400MHz, $CDCl_3$):

8.49 (s, 1H), 7.39 (dd, 1H), 7.34-7.29 (m, 1H), 7.14-7.11 (m, 1H), 6.83-6.77 (m, 1H), 6.64-6.59 (m, 1H), 4.25-4.07 (br m, 4H), 2.88 (d, 2H), 2.62 (m, 4H), 2.58 (m, 2H), 1.78 (m, 4H), 2.05 (AcOH; s, 3H); MS (EI) for $C_{25}H_{30}F_3IN_4O_2$: 603 (MH^+).

[0483] EXAMPLE 3(cn). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[(1-methyl-1*H*-imidazol-4-yl)methyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, $CDCl_3$): 8.50 (s, 1H), 7.41-7.11 (m, 3H), 7.12 (m, 1H), 6.85-6.79 (m, 2H), 4.12-3.98 (br m, 4H), 3.78 (s, 2H), 3.66 (s, 3H), 2.95 (s, 2H), 2.08 (AcOH; s, 4H) ,2.05 (AcOH; s, 3H); MS (EI) for $C_{22}H_{21}F_3IN_5O_2$: 572 (MH^+).

[0484] EXAMPLE 3(co). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[(1-methyl-1*H*-imidazol-5-yl)methyl]amino}methyl)azetidin-3-ol: ^{1}H NMR (400MHz, $CDCl_3$): 8.45 (s, 1H), 7.47 (s, 1H), 7.39 (dd, 1H), 7.33-7.30 (m, 1H), 7.15-7.10 (m, 1H), 6.91 (s, 1H), 6.87-6.77 (m, 1H), 6.63-6.58 (m, 1H), 4.18-4.02 (m, 4H), 3.3.80 (s, 2H), 3.62 (s, 3H), 2.90 (s, 1H), 2.05 (AcOH; s, 3H); MS (EI) for $C_{22}H_{21}F_3IN_5O_2$: 572 (MH^+).

[0485] EXAMPLE 3(cp). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[(2S)-2-(methyloxy)cyclopentyl]amino}methyl)azetidin-3-ol): MS (EI) for $C_{23}H_{25}F_3IN_3O_3$: 576 (MH^+).

[0486] EXAMPLE 3(cq). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[(1R)-2-hydroxycyclohexyl]amino}methyl)azetidin-3-ol): MS (EI) for $C_{23}H_{25}F_3IN_3O_3$: 576 (MH^+).

[0487] EXAMPLE 3(cr). *N*-[3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl} amino)phenyl]methanesulfonamide: ^1H NMR (400MHz, $CDCl_3$): 7.33 (dd, 1H), 7.22 (m, 1H), 7.08 (dd, 1H), 6.83-6.77 (m, 1H), 6.03-5.98 (m, 2H), 6.64-6.59 (m, 1H), 4.08-3.77 (br m, 5H), 2.88 (s, 3H); MS (EI) for $C_{24}H_{22}F_3IN_4O_4S$: 647 (MH^+).

[0488] EXAMPLE 3(cs). 3-{[(4-aminophenyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^1H NMR (400MHz, $CDCl_3$): 8.44 (s, 1H), 7.39 (dd, 1H), 7.34-7.30 (m, 1H), 7.14-7.10 (m, 1H), 6.84-6.77 (m, 1H), 6.64-6.53 (m, 5H), 4.22-4.04 (br m, 4H), 3.34 (s, 2H); MS (EI) for $C_{23}H_{20}F_3IN_4O_2$: 569 (MH^+).

[0489] EXAMPLE 3(ct). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{[(2-hydroxy-2-methylcyclopentyl)amino]methyl}azetidin-3-ol: MS (EI) for $C_{23}H_{25}F_3IN_3O_3$: 576 (MH^+).

[0490] EXAMPLE 3(cu). 3-[(cyclopentylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^1H NMR (400 MHz, CD_3OD): 7.44 (dd, 1H), 7.36-7.31 (m, 1H), 7.30-7.24 (m, 1H), 7.09-6.99 (m, 1H), 6.64-6.57 (m, 1H), 4.17-4.10 (m,1H), 4.01-3.91 (m, 2H), 3.87-3.79 (m, 1H), 3.07-2.97 (m, 1H), 2.75 (s, 2H), 1.92-1.79 (m, 2H), 1.75-1.62 (m, 2H), 1.61-1.47 (m, 2H), 1.37-1.22 (m, 2H). MS (EI) for $C_{22}H_{23}F_3IN_3O_2$: 546 (MH^+)

[0491] EXAMPLE 3(cv). 3-{[(cyclohexylmethyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate (salt): ^1H NMR (400 MHz, CD_3OD): 7.46 (dd, 1H), 7.39-7.32 (m, 1H), 7.31-7.25 (m, 1H), 7.11-6.99 (m, 1H), 6.67-6.57 (m, 1H), 4.27-4.15 (m, 1H), 4.12-3.97 (m, 2H), 3.96-3.85 (m, 1H), 3 (s,2H), 2.62 (d, 2H), 1.90 (s, 3H), 1.82-1.45 (m, 6H), 1.40-1.07 (m, 3H), 1.04-0.80 (m, 2H). MS (EI) for $C_{24}H_{27}F_3IN_3O_2$: 574 (MH^+).

[0492] EXAMPLE 3(cw). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-[(propylamino)methyl]azetidin-3-ol: ^1H NMR (400 MHz, d_6-DMSO): δ 8.56 (s, 1H), 7.57 (dd, 1H), 7.37 (dd, 1H), 7.32 (m, 1H), 7.18 (m, 1H), 6.67 (m, 1H), 4.03 (d, 1H), 3.89 (m, 2H), 3.69 (d, 1H), 2.59 (s, 2H), 2.42 (t, 2H), 1.90 (s, 3H), 1.32 (m, 2H), 0.81 (t, 3H); MS (EI) for $C_{20}H_{21}F_3IN_3O_2$: 520 (MH^+).

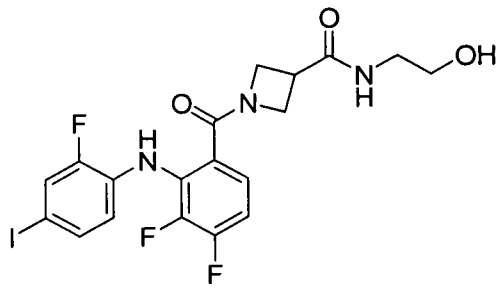
[0493] **EXAMPLE 3(cx).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-methylpropyl)amino]methyl}azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): δ 8.56 (s, 1H), 7.56 (dd, 1H), 7.36 (dd, 1H), 7.31 (m, 1H), 7.18 (m, 1H), 6.67 (m, 1H), 4.02 (d, 1H), 3.89 (m, 2H), 3.70 (d, 1H), 2.57 (s, 2H), 2.27 (d, 2H), 1.91 (s, 3H), 1.55 (m, 1H), 0.79 (d, 6H); MS (EI) for $C_{21}H_{23}F_3IN_3O_2$: 534 (MH^+).

[0494] **EXAMPLE 3(cy).** methyl (2xi)-2-deoxy-2-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)-beta-D-arabino-hexopyranoside: ^{1}H NMR (400 MHz, d_4-methanol, ~3:1 mixture of anomers): δ 7.46 (d, 1H), 7.34 (d, 1H), 7.28 (m, 1H), 7.04 (q, 1H), 6.62 (m, 1H), 4.19-5.92 (m, 4H), 3.87-3.78 (m, 2H), 3.68 (m, 1H), 3.56-3.18 (m, 5H), 2.99-2.82 (m, 3H), 2.56 (m, 0.25H), 2.29 (m, 0.75H) MS (EI) for $C_{24}H_{27}F_3IN_3O_7$: 652 (M-H).

[0495] **EXAMPLE 3(cz).** 3-({[3-(diethylamino)propyl]amino}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.38-7.33 (d, 1H), 7.32-7.26 (m, 1H), 7.09-7.00 (q, 1H), 6.66-6.58 (t, 1H), 4.24-4.16 (d, 1H), 4.11-3.99 (t, 2H), 3.92-3.85 (d, 1H), 3.10-3.02 (m, 8H), 2.99-2.96 (s, 2H), 2.92-2.87 (t, 2H), 1.93-1.87 (s, 3H), 1.27-1.20 (t, 6H); MS (EI) for $C_{24}H_{30}F_3IN_4O_2$: 591 (MH^+).

EXAMPLE 4

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2-hydroxyethyl)azetidine-3-carboxamide



[0496] To a solution of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxylic acid (15 mg, 0.03 mmol), prepared using procedures similar to those in Example 1, in *N,N*-dimethylformamide (2.00 mL) was added HBTU (38 mg, 0.10 mmol). The mixture was stirred for 15 minutes at room temperature followed by the addition of 2-aminoethanol (3.6 μL, 0.06 mmol) and *N*-methylmorpholine (110 μL, 1.00 mmol). The mixture was allowed to stir at room

temperature for 3 d, then diluted the mixture with chloroform (20 mL), and washed with water (30 mL). The aqueous phase was back extracted with chloroform (10 mL). The combined organic phases were dried over sodium sulfate, filtered and the filtrate concentrated *in vacuo*. The residue was purified by high pressure liquid chromatography to afford the title compound (9.20 mg, 58%) as the trifluoroacetic acid salt: ^{1}H NMR (400MHz, $CDCl_3$): 8.54 (s, 1H), 7.41-7.37 (m, 1H), 7.34-7.31 (m, 1H), 7.18-7.14 (m, 1H), 6.85-6.77 (m, 1H), 6.64-6.58 (m, 1H), 4.66 (br, 1H), 4.40-4.24 (br, 3H), 3.83-3.23 (br m, 7H), 1.18 (t, 3H); MS (EI) for $C_{19}H_{17}F_3IN_3O_3$: 542 (MNa^+).

[0497] Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the following compounds of the invention were prepared:

[0498] **EXAMPLE 4(a):** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(3,4-dihydroxybutyl)azetidine-3-carboxamide: ^{1}H NMR (400 MHz, $CDCl_3$): 8.55 (s, 1H), 7.40 (dd, 1H), 7.31-7.35 (m, 1H), 7.14-7.18 (m, 1H), 6.78-6.84 (m, 1H), 6.59-6.65 (m, 1H), 6.14 (br s, 1H), 4.50-4.60 (m, 1H), 4.20-4.40 (m, 3H), 3.60-3.80 (m, 3H), 3.40-3.52 (m, 2H), 3.20-3.32 (m, 2H), 1.96 (br s, 1H), 1.18-1.28 (m, 2H). MS (EI) for $C_{21}H_{21}F_3IN_3O_4$: 562 (M-H).

[0499] **EXAMPLE 4(b):** *N*-butyl-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxamide: ^{1}H NMR (400MHz, $CDCl_3$): 8.53 (s, 1H), 7.39 (dd, 1H), 7.33-7.31 (m, 1H), 7.17-7.13 (m, 1H), 6.83-6.77 (m, 1H), 6.64-6.58 (m, 1H), 5.50 (m, 1H), 4.57 (br, 1H), 4.29 (br m, 3H), 3.27 (m, 3H), 1.49 (m, 1H), 1.33 (m, 2H), 0.92 (t, 3H); MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 532 (MH^+), 554 (MNa^+).
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-prop-2-en-1-ylazetidine-3-carboxamide: ^{1}H NMR (400MHz, $CDCl_3$): 8.54 (s, 1H), 7.39 (dd, 1H), 7.34-7.31 (m, 1H), 7.17.7.12 (m, 1H), 6.83-6.77 (m, 1H), 6.64-6.58 (m, 1H), 5.88-5.77 (m, 1H), 5.57 (br, 1H), 5.21-5.16 (m, 2H), 4.59 (br, 1H), 4.30 (br m, 3H), 3.9 (tt, 2H), 3.32-3.25 (m, 1H)); MS (EI) for $C_{20}H_{17}F_3IN_3O_2$: 516 (MH^+), 538 (MNa^+).

[0500] **EXAMPLE 4(c):** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-ethylazetidine-3-carboxamide: ^{1}H NMR (400MHz, $CDCl_3$): 8.54 (s, 1H), 7.38 (dd, 1H), 7.33-7.30 (m, 1H),7.17-7.12 (m, 1H), 6.83-6.77 (m, 1H), 6.63-6.57 (m, 1H), 5.55 (br s, 1H), 4.57 (br s, 1H), 4.28 (br m, 1H), 3..36-3.29 (m, 2H), 3.27- 3..20 (m, 1H), 1.15 (t, 3H); MS (EI) for $C_{19}H_{17}F_3IN_3O_2$: 504 (MH^+), 526 (MNa^+).

[0501] **EXAMPLE 4(d):** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2-hydroxyethyl)azetidine-3-carboxamide: ^{1}H NMR

(400MHz, $CDCl_3$): 8.50 (s, 1H), 7.39 (dd, 1H), 7.33-7.30 (m, 1H),7.16-7.12 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.57 (m, 1H), 4.57 (br, 1H), 4.28 (br, 3H), 3.73 (t, 2H), 3.49-3.44 (m, 2H), 3.33-3.27 (m, 1H), 2.18 (br, 1H); MS (EI) for $C_{19}H_{17}F_3IN_3O_3$: 542 (MNa^+).

[0502] EXAMPLE 4(e): 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2-piperidin-1-ylethyl)azetidine-3-carboxamide: ^1H NMR (400MHz, $CDCl_3$): 11.28 (s, 1H), 8.55 (s, 1H), 7.38 (dd, 1H), 7.33-7.30 (m, 1H), 7.15-7.10 (m, 1H), 6.82-6.76 (m, 1H), 6.63-6.58 (m, 1H), 4.42 (b, 1H), 4.26 (br m, 3H), 3.68 (br s, 2H), 3.58 (br d, 2H), 3.36 (br m, 1H)3.17 (br s, 1H), 2.63 (m, 4H), 1.92 (m, 5 H); MS (EI) for $C_{24}H_{26}F_3IN_4O_2$: 587 (MH^+).

[0503] EXAMPLE 4(f): 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-phenylazetidine-3-carboxamide: ^1H NMR (400MHz, $CDCl_3$): 8.52 (s, 1H), 7.50 (d, 1H), 7.41-7.27 (m, 4H), 7.16 (m, 2H), 6.85-6.78 (m, 1H), 6.65-6.59 (m, 1H), 4.37 (br, 3H), 3.43 (m, 1H); MS (EI) for $C_{23}H_{17}F_3IN_3O_2$: 574 (MNa^+).

[0504] EXAMPLE 4(g): *N*-[2-(diethylamino)ethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxamide: ^1H NMR (400MHz, $CDCl_3$): 11.43 (s, 1H), 8.90 (s, 1H), 8.55 (s, 1H), 7.39 (dd, 1H), 7.33-7.30 (m, 1H), 7.15-7.10 (m, 1H), 6.87-6.77 (m, 1H), 6.63-6.58 (m, 1H), 4.44-4.22 (m, 4H), 3.65 (m, 2H), 3.38 (m, 1H), 3.19-3.13 (m, 5H), 1.33(t, 6H); MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 575 (MH^+).

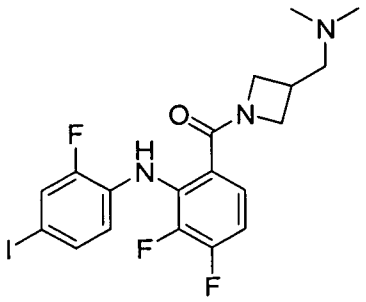
[0505] EXAMPLE 4(h): 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-[(2,3-dihydroxypropyl)oxy]azetidine-3-carboxamide: MS (EI) for $C_{20}H_{19}F_3IN_3O_5$: 566 (MH^+).

[0506] EXAMPLE 4(i): 1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2,3-dihydroxypropyl)azetidine-3-carboxamide: ^1H NMR (400 MHz, $CDCl_3$): 8.40 (br s, 1H), 7.35 (dd, 1H), 7.30 (br d, 1H), 7.16-7.09 (m, 1H), 6.89-6.76 (m, 2H), 6.58 (ddd, 1H), 4.58-4.40 (br, 1H), 4.27 (br t, 2H), 4.22-4.14 (br, 1H), 4.08-3.12 (m, 5H), 2.18-1.82 (br, 2H); MS (EI) for $C_{20}H_{19}F_3IN_3O_4$: 550 (MH^+).

[0507] EXAMPLE 4(j): 1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-hydroxyazetidine-3-carboxamide: ^1H NMR (400 MHz, $CDCl_3$): 8.23-8.10 (b, 1H), 7.35-7.28 (m, 2H), 7.14-7.07 (m, 1H), 6.86-6.80 (m, 1H), 6.60-6.54 (m, 1H), 4.52-4.38 (b, 1H), 4.32-4.08 (m, 3H), 3.30-3.21 (m, 1H); MS (EI) for $C_{17}H_{13}F_3IN_3O_3$: 492 (MH^+).

EXAMPLE 5

6-({3-[dimethylamino)methyl]azetidin-1-yl}carbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline



[0508] A mixture of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxylic acid (196 mg, 0.41 mmol), prepared using procedures similar to those in Example 1, triethylamine (58 μL, 0.41 mmol), PyBOP (213 mg, 0.41 mmol) and sodium borohydride (48 mg, 1.24 mmol) in tetrahydrofuran (2 mL) was stirred at room temperature for 15 hours. The reaction mixture was concentrated *in vacuo* and the resultant residue was partitioned between 20% aqueous citric acid and ethyl acetate. The organic portion was washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford a colorless residue that was purified by column chromatography. Eluting with 60% ethyl acetate in hexanes, isolated product was concentrated *in vacuo* to afford 48 mg, 0.11 mmol (25%) of [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]methanol as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): 7.44 (d, 1H), 7.34 (d, 1H), 7.28-7.23 (m, 1H), 7.04-6.97 (m, 1H), 4.26-4.18 (m, 1H), 4.02-3.94 (m, 2H), 3.78-3.72 (m, 1H), 3.03 (d, 2H), 3.34 (s, 1H), 2.80-2.71 (m, 1H). MS (EI) for $C_{17}H_{14}F_3IN_2O$: 463 (MH^+).

[0509] A solution of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]methanol (48 mg, 0.11 mmol), 1,4-diazabicyclo[2.2.2]octane (18 mg, 0.16 mmol) and methanesulfonyl chloride (10 μL, 0.13 mmol) in tetrahydrofuran (2 mL) was stirred at room temperature for 15 minutes. The mixture was then partitioned between water and ethyl acetate. The organic portion was washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford a colorless residue which was purified by column chromatography. Eluting with 70% ethyl acetate in hexanes, isolated product was concentrated *in vacuo* to afford 28 mg, 0.05 mmol (47%) of [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]methyl methanesulfonate as a colorless residue which was immediately dissolved in ethylene glycol dimethyl ether (2 mL). To the

solution was added dimethylamine (excess) and the solution was stirred in a seal tube at 50 °C for 15 hours. The reaction mixture was concentrated *in vacuo*, and the resultant residue was purified by preparative reverse phase HPLC. Isolated product was concentrated *in vacuo* to afford 12 mg, 0.02 mmol (40%) of 6-({3-[dimethylamino)methyl]azetidin-1-yl}carbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline acetate salt as a white solid. ^{1}H NMR (400 MHz, DMSO): 8.54 (br s, 1H), 7.58 (d, 1H), 7.37 (d, 1H), 7.33-7.28 (m, 1H), 7.18-7.12 (m, 1H), 6.70-6.64 (m, 1H), 4.18-4.12 (m, 1H), 3.99-3.76 (m, 1H), 3.52-3.47 (m, 1H), 2.52-2.48 (m, 1H), 2.39 (d, 2H), 1.85 (s, 6H); MS (EI) for $C_{19}H_{19}F_3IN_3O$: 490 (MH^+).

[0510] Using the same or analogous synthetic techniques and/or substituting with alternative reagents, the following MEK compounds were prepared:

[0511] **EXAMPLE 5(a):** 2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)-6-[(3-{[(1-methylethyl)amino]methyl}azetidin-1-yl)carbonyl]aniline: ^{1}H NMR (400 MHz, $CDCl_3$): 8.54 (s, 1H), 7.40 (dd, 1H), 7.31-7.33 (m, 1H), 7.11-7.15 (m, 1H), 6.76-6.82 (m, 1H), 6.58-6.64 (m, 1H), 4.23-4.30 (m, 2H), 3.90-4.00 (m, 1H), 3.76-3.84 (m, 1H), 2.69-2.85 (m, 4H), 1.05 (d, 6H). MS (EI) for $C_{20}H_{21}F_3IN_3O$: 502 (M-H).

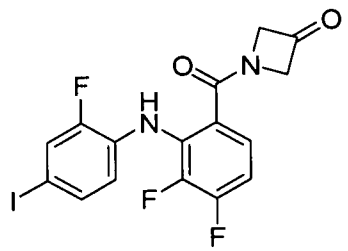
[0512] **EXAMPLE 5(b):** 2-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-2-yl]methyl}amino)ethanol: MS (EI) for $C_{19}H_{19}F_3IN_3O_2$: 506 (MH^+).

[0513] **EXAMPLE 5(c):** *N*-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-2-yl]methyl}ethane-1,2-diamine: MS (EI) for $C_{19}H_{20}F_3IN_4O$: 505 (MH^+).

[0514] **EXAMPLE 5(d):** 6-({3-[dimethylamino)methyl]azetidin-1-yl}carbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline acetate salt: ^{1}H NMR (400 MHz, DMSO): 8.54 (br s, 1H), 7.58 (d, 1H), 7.37 (d, 1H), 7.33-7.28 (m, 1H), 7.18-7.12 (m, 1H), 6.70-6.64 (m, 1H), 4.18-4.12 (m, 1H), 3.99-3.76 (m, 1H), 3.52-3.47 (m, 1H), 2.52-2.48 (m, 1H), 2.39 (d, 2H), 1.85 (s, 6H); MS (EI) for $C_{19}H_{19}F_3IN_3O$: 490 (MH^+).

EXAMPLE 6

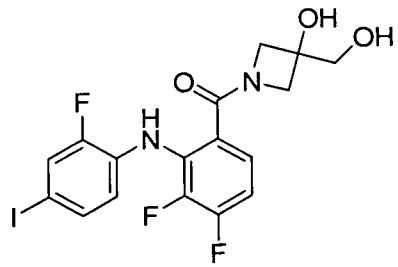
1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one



[0515] 1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol (132 mg, 0.295 mmol)ures similar to those in Example 1, was dissolved in dichloromethane (8 mL) and cooled to 0 °C. Dess-Martin periodinane (187 mg, 0.441 mmol) was added and the mixture was stirred at ambient for 2 h. The mixture was quenched with saturated sodium bicarbonate solution: 10% sodium thiosulfate solution (1:1; 6 mL) and diluted with ethyl acetate. The organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 40-50% ethyl acetate in hexanes) gave 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one (122 mg, 0.273 mmol, 93% yield): ^{1}H NMR (400 MHz, $CDCl_3$): 8.43 (br s, 1H), 7.44-7.38 (m, 1H), 7.36-7.32 (m, 1H), 7.27-7.20 (m, 1H), 6.86 (ddd, 1H), 6.64 (ddd, 1H), 4.94-4.93 (m, 4H); MS (EI) for $C_{16}H_{10}F_3IN_2O_2$: 447 (MH^+).

EXAMPLE 7

1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(hydroxymethyl)azetidin-3-ol



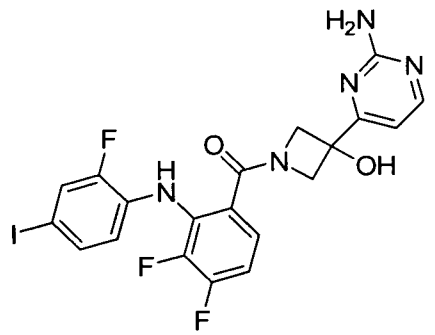
[0516] Methyl triphenylphosphonium bromide (508 mg, 1.42 mmol) was treated with potassium *tert*-butoxide (159 mg, 1.42mmol) in tetrahydrofuran (5 mL) at 0 °C for 10 minutes. 1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one (270 mg, 0.605 mmol), prepared using procedures similar to those described in Example 6, was dissolved in tetrahydrofuran (2 mL) and was added to the mixture. The mixture was stirred at ambient for 15 h and then the mixture was filtered and the filtrate was partitioned between ethyl acetate and water. The aqueous portion was extracted with ethyl acetate. The combined organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 20% ethyl acetate in hexanes) gave 2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)-6-[(3-methylideneazetidin-1-yl)carbonyl]aniline (57 mg, 0.128 mmol, 21% yield): ^{1}H NMR (400 MHz, $CDCl_3$): 8.56 (br

s, 1H), 7.39 (dd, 1H), 7.35-7.30 (m, 1H), 7.18-7.12 (m, 1H), 6.86-6.76 (m, 1H), 6.62 (ddd, 1H), 5.14-5.00 (br, 2H), 4.74 (br d, 4H); MS (EI) for $C_{17}H_{12}F_3IN_2O$: 445 (MH^+).

[0517] 2,3-Difluoro-*N*-(2-fluoro-4-iodophenyl)-6-[(3-methylideneazetidin-1-yl)carbonyl]aniline (56 mg, 0.126 mmol) and 4-methylmorpholine *N*-oxide (44 mg, 0.376 mmol) were dissolved in acetone / water (4:1; 10 mL) and osmium tetroxide (4 wt.% in water; 0.7 mL) was added. The solution was stirred at ambient for 4 h, then was quenched with saturated sodium bisulfite (2 mL) and concentrated *in vacuo*. The residue was partitioned between ethyl acetate and water. The organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 80% ethyl acetate in hexanes) and then reverse phase HPLC gave 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(hydroxymethyl)-azetidin-3-ol (17 mg, 0.036 mmol, 28% yield): ^1H NMR (400 MHz, $CDCl_3$): 8.43 (br s, 1H), 7.40 (dd, 1H), 7.35-7.31 (m, 1H), 7.16-7.10 (m, 1H), 6.81 (ddd, 1H), 6.61 (ddd, 1H), 4.25-4.00 (m, 4H), 3.78 (s, 2H); MS (EI) for $C_{17}H_{14}F_3IN_2O_3$: 479 (MH^+).

EXAMPLE 8

3-(2-aminopyrimidin-4-yl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol



[0518] To a solution of 4-iodo-2-(methylthio)pyrimidine (2.00 g, 7.92 mmol) in tetrahydrofuran (4.00 ml) was added isopropylmagnesium chloride (815 mg, 7.92 mmol). The mixture was allowed to stir for 1 h at 0 °C, followed by the addition of 1,1-dimethylethyl 3-oxoazetidiene-1-carboxylate (1.64 g, 9.60 mmol), prepared using procedures similar to those described in Example 3. The reaction mixture was then allowed to warm to room temperature and stirred for 6h. The mixture was quenched with 1 N hydrochloric acid (10 mL) and extracted with ethyl acetate. The organic layer was separated, dried over anhydrous sodium sulfate, filtered and the filtrate concentrated *in vacuo*. The residue was purified by

column chromatography (SiO_2, hexanes/ethyl acetate) to afford 1,1-dimethylethyl 3-hydroxy-3-[2-(methylthio)pyrimidin-4-yl]azetidine-1-carboxylate (380 mg, 16%) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$): 8.62-8.59 (d, 1H), 7.36-7.33 (d, 1H), 5.14-5.11 (s, 1H), 4.29-4.24 (d, 2H), 4.13-4.08 (d, 2H), 2.61-2.58 (s, 3H), 1.50-1.47 (s, 9H); MS (EI) for $C_{13}H_{19}N_3O_3S$: 298 (MH^+).

[0519] A solution of 1,1-dimethylethyl 3-hydroxy-3-[2-(methylthio)pyrimidin-4-yl]azetidine-1-carboxylate (480 mg, 1.62 mmol), and 3-chloroperoxybenzoic (558 mg, 3.23 mmol) acid in dichloromethane (25 mL) was stirred at room temperature for 22 h. The reaction mixture was quenched with a saturated solution of sodium thiosulfate and the pH adjusted to 7 with sodium carbonate. The organic layer was separated, dried over anhydrous sodium sulfate, filtered and the filtrate concentrated *in vacuo*. The resulting crude 1,1-dimethylethyl 3-hydroxy-3-[2-(methylsulfonyl)pyrimidin-4-yl]azetidine-1-carboxylate (524 mg, 98%) was used without further purification. ^1H NMR (400 MHz, $CDCl_3$): 9.01-8.97 (d, 1H), 7.96-7.93 (d, 1H), 4.57-4.53 (s, 1H), 4.31-4.27 (d, 2H), 4.23-4.18 (d, 2H), 3.42-3.39 (s, 3H), 1.50-1.47 (s, 9H); MS (EI) for $C_{13}H_{19}N_3O_5S$: 330 (MH^+).

[0520] A solution of 1,1-dimethylethyl 3-hydroxy-3-[2-(methylsulfonyl)pyrimidin-4-yl]azetidine-1-carboxylate (215 mg, 0.652 mmol), and aqueous ammonia (7 mL, 28% solution) in dioxane (15 mL) within a sealed steel bomb cylinder was heated at 80°C for 4h. The mixture was cooled to room temperature and the solvent was evaporated. The residue was dissolved in dichloromethane and a solution of saturated sodium carbonate. The organic layer was separated, dried over anhydrous sodium sulfate, filtered and the filtrate concentrated *in vacuo*. The resulting crude 1,1-dimethylethyl 3-(2-aminopyrimidin-4-yl)-3-hydroxyazetidine-1-carboxylate (140 mg, 100%) was used without further purification. ^1H NMR (400 MHz, $CDCl_3$): 8.38-8.35 (d, 1H), 6.97-6.94 (d, 1H), 5.30-5.28 (s, 2H), 4.23-4.18 (d, 2H), 4.08-4.04 (d, 2H), 1.48-1.45 (s, 9H).

[0521] To a solution of 1,1-dimethylethyl 3-(2-aminopyrimidin-4-yl)-3-hydroxyazetidine-1-carboxylate (140 mg, 0.524 mmol) in dichloromethane (10 ml) was added trifluoroacetic acid (3 ml). The reaction mixture was stirred for 2h at room temperature. The mixture was concentrated *in vacuo*. The resulting crude 3-(2-aminopyrimidin-4-yl)azetidin-3-ol (87 mg, 100%) was used without further purification.

[0522] A solution of 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid (201 mg, 0.512 mmol), prepared using procedures similar to those described in US 7,019,033, 3-(2-aminopyrimidin-4-yl)azetidin-3-ol (87 mg, 0.52 mmol), benzotriazol-1-yl-oxy-

tris(pyrrolidino)phosphonium hexafluorophosphate (293 mg, 0.563 mmol) and *N,N*-diisopropylethylamine (270 uL, 2.82 mmol) in *N,N*-dimethylformamide (2 mL) was stirred at room temperature for 20h. The mixture was partitioned between ethyl acetate and saturated sodium bicarbonate. The organic layer was separated and washed with brine, dried over sodium sulfate, filtered and the filtrate concentrated *in vacuo*. The residue was purified by reverse phase HPLC to afford the title compound 3-(2-aminopyrimidin-4-yl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol (22 mg, 7%). ^{1}H NMR (400 MHz, CD_3OD): 8.23-8.20 (d, 1H), 7.48-7.43 (d, 1H), 7.35-7.32 (m, 2H), 7.09-7.00 (m, 1H), 6.88-6.84 (d, 1H), 6.70-6.63 (t, 1H), 4.59-4.54 (d, 1H), 4.45-4.40 (d, 1H), 4.23-4.18 (d, 1H), 3.04-3.99 (t, 1H); MS (EI) for $C_{20}H_{15}F_3IN_5O_2$: 542 (MH^+).

[0523] Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the following MEK compounds were prepared:

[0524] **EXAMPLE 8(a):** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-pyridin-2-ylazetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 8.47 (m, 1H), 7.80 (m, 1H), 7.65 (d, 1H), 7.44 (m, 1H), 7.33 (m, 3H), 7.04 (m, 1H), 6.65 (m, 1H), 4.61 (d, 1H), 4.44 (d, 1H), 4.29 (d, 1H), 4.12 (d, 1H). MS (EI) for $C_{21}H_{15}F_3IN_3O_2$: 526 (MH^+).

[0525] **EXAMPLE 8(b):** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-imidazol-2-yl)azetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.42 (m, 1H), 7.37 (m, 1H), 7.32 (m, 1H), 7.02 (m, 3H), 6.63 (m, 1H), 4.65 (d, 1H), 4.42 (d, 1H), 4.33 (d, 1H), 4.16 (d, 1H). MS (EI) for $C_{19}H_{14}F_3IN_4O_2$: 515 (MH^+).

[0526] **EXAMPLE 8(c):** 3-(1*H*-benzimidazol-2-yl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.55 (br s, 2H), 7.42 (m, 2H), 7.33 (m, 1H), 7.23 (m, 2H), 7.04 (m, 1H), 6.65 (m, 1H), 4.76 (d, 1H), 4.57 (d, 1H), 4.43 (d, 1H), 4.25 (d, 1H). MS (EI) for $C_{23}H_{16}F_3IN_4O_2$: 565 (MH^+).

[0527] **EXAMPLE 8(d):** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(5-methyl-1*H*-imidazol-2-yl)azetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.41 (m, 1H), 7.36 (m, 1H), 7.31 (m, 1H), 7.02 (m, 1H), 6.67 (br s, 1H), 6.63 (m, 1H), 4.63 (d, 1H), 4.39 (d, 1H), 4.30 (d, 1H), 4.13 (d, 1H), 2.18 (s, 3H). MS (EI) for $C_{20}H_{16}F_3IN_4O_2$: 529 (MH^+).

[0528] **EXAMPLE 8(e):** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}-carbonyl)-3-prop-2-en-1-ylazetidin-3-ol: ^{1}H NMR (400 MHz, $CDCl_3$): 8.47 (br s, 1H), 7.40 (dd, 1H), 7.35-7.31 (m, 1H), 7.15-7.10 (m, 1H), 6.81 (ddd, 1H), 6.62 (ddd, 1H), 5.84-5.72

(m, 1H), 5.27-5.20 (m, 2H), 4.22-3.94 (m, 4H), 2.52 (d, 2H), 2.25 (s, 1H); MS (EI) for $C_{19}H_{16}F_3IN_2O_2$: 489 (MH^+).

[0529] EXAMPLE 8(f): 3-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}-carbonyl)-3-hydroxyazetidin-3-yl]propane-1,2-diol: ^{1}H NMR (400 MHz, $CDCl_3$): 8.43 (br s, 1H), 7.39 (dd, 1H), 7.35-7.30 (m, 1H), 7.16-7.10 (m, 1H), 6.82 (ddd, 1H), 6.61 (ddd, 1H), 4.31-3.91 (m, 5H), 3.68 (br d, 1H), 3.54-3.49 (m, 1H), 2.01-1.80 (m, 2H); MS (EI) for $C_{19}H_{18}F_3IN_2O_4$: 523 (MH^+).

[0530] EXAMPLE 8(g): 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-ethenylazetidin-3-ol: ^{1}H NMR (400 MHz, $CDCl_3$): 8.48 (br s, 1H), 7.40 (dd, 1H), 7.35-7.31 (m, 1H), 7.17-7.11 (m, 1H), 6.81 (ddd, 1H), 6.62 (ddd, 1H), 6.15 (dd, 1H), 5.39 (d, 1H), 5.28 (d, 1H), 4.30-4.10 (m, 4H); MS (EI) for $C_{18}H_{14}F_3IN_2O_2$: 475 (MH^+).

[0531] EXAMPLE 8(h): 1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-hydroxyazetidin-3-yl]ethane-1,2-diol hydrochloride: ^{1}H NMR (400 MHz, d_6-DMSO): 8.66 (d, 1H), 7.58 (dd, 1H), 7.38 (d, 1H), 7.33-7.27 (m, 1H), 7.17 (q, 1H), 6.74-6.65 (m, 1H), 4.50-3.58 (br, 3H), 4.29 (dd, 1H), 4.14 (dd, 1H), 3.87 (t, 1H), 3.66 (t, 1H), 3.56-3.32 (m, 3H); MS (EI) for $C_{18}H_{16}F_3IN_2O_4$: 509 (MH^+).

[0532] EXAMPLE 8(i): 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-ethylazetidin-3-ol: ^{1}H NMR (400 MHz, $CDCl_3$): 8.23 (br s, 1H), 7.40 (d, 1H), 7.33 (d, 1H), 7.15-7.10 (m, 1H), 6.85-6.79 (m, 1H), 6.64-6.58 (m, 1H), 4.14-3.94 (m, 4H), 1.78 (q, 2H), 0.96 (t, 3H); MS (EI) for $C_{18}H_{16}F_3IN_2O_2$: 477 (MH^+).

[0533] EXAMPLE 8(j): 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-methylazetidin-3-ol: ^{1}H NMR (400 MHz, $CDCl_3$): 8.31 (br s, 1H), 7.40 (d, 1H), 7.33 (d, 1H), 7.15-7.11 (m, 1H), 6.85-6.78 (m, 1H), 6.65-6.59 (m, 1H), 4.24-4.04 (m, 4H), 1.55 (s, 3H); MS (EI) for $C_{17}H_{14}F_3IN_2O_2$: 463 (MH^+).

[0534] EXAMPLE 8(k): 3-(2-aminopyrimidin-4-yl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 8.22-8.20 (d, 1H), 7.48-7.43 (d, 1H), 7.38-7.30 (m, 1H), 7.09-7.01 (q, 1H), 6.88-6.84 (d, 1H), 6.70-6.61 (t, 1H), 4.59-4.54 (d, 1H), 4.44-4.39 (d, 1H), 4.23-4.19 (d, 1H), 4.05-3.99 (d, 1H), 3.90-3.81 (d, 1H), 1.99-1.97 (s, 3H); MS (EI) for $C_{20}H_{15}F_3I\,N_5O_2$: 542 (MH^+).

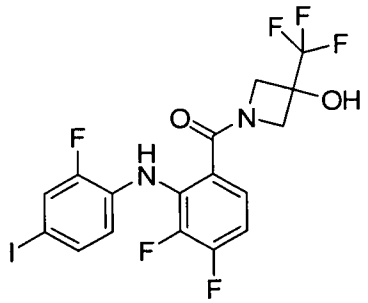
[0535] EXAMPLE 8(m): 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-(1*H*-pyrrol-2-yl)azetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.37 (dd, 1H), 7.31-7.23 (m, 2H), 7.07-6.97 (m, 1H), 6.73-6.68 (m, 1H), 6.65-6.56 (m, 1H), 6.06-5.98 (m,

2H), 4.49-4.40 (m,1H), 4.32-4.18 (m, 2H), 4.15-88-4.07 (m, 1H). MS (EI) for $C_{20}H_{15}F_3IN_3O_2$: 514 (MH^+)

[0536] EXAMPLE 8(n): 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-(1-methyl-1*H*-imidazol-2-yl)azetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.34 (dd, 1H), 7.31-7.25 (m, 1H), 7.23-7.18 (m, 1H), 7.11-7.09 (m, 1H), 7.06-6.97 (m, 1H), 6.89-6.86 (m, 1H), 6.62-6.55 (m, 1H), 4.88-4.80 (m, 1H), 4.52-4.44 (m,1H), 4.38-4.30 (m, 1H), 4.21-4.12 (m, 1H), 3.68 (s, 3H). MS (EI) for $C_{20}H_{16}F_3IN_4O_2$: 529 (MH^+).

EXAMPLE 9

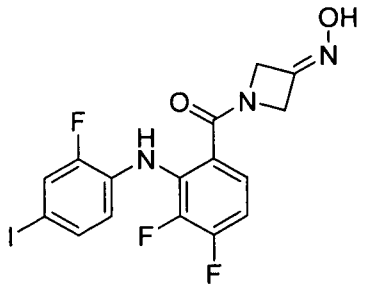
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(trifluoromethyl)azetidin-3-ol



[0537] 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one (25 mg, 0.056 mmol), prepared using procedures described in Example 6, was taken into DMF (0.5 mL) followed by addition of (trifluoromethyl)trimethylsilane (40 μL, 0.28 mmol) and cesium carbonate (22 mg, 0.067mmol) and the mixture was stirred for one hour at room temperature. The mixture was partitioned with ethyl ether and water and the organic phase washed three times with additional water then brine and dried over anhydrous sodium sulfate. Filtration and concentration followed by silica gel flash chromatography of the residue using hexanes:ethyl acetate 3:2 as eluent afforded 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(trifluoromethyl)azetidin-3-ol (19.8 mg, 69% yield) as a colorless crystalline solid. ^{1}H-NMR (400 MHz, $CDCl_3$): 8.31-8.26 (br, 1H), 7.40 (d, 1H), 7.33 (d, 1H), 7.13-7.10 (m, 1H), 6.86-6.80 (m, 1H), 6.65-6.60 (m, 1H), 4.42 (br s, 2H), 4.18 (br s, 2H). MS (EI) for $C_{17}H_{11}F_6IN_2O_2$: 517 (MH^+).

EXAMPLE 10

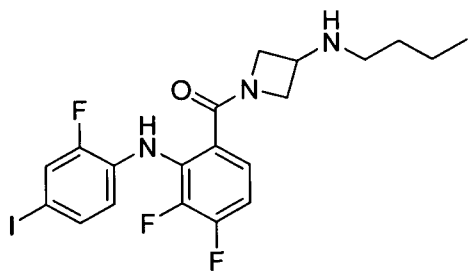
1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one oxime



[0538] To a solution of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)azetidin-3-one (100 mg, 0.22 mmol), prepared using procedures similar to those described in Example 6, in dioxane (1.0 mL) was added hydroxylamine (0.10 mL, 50% solution in water, 1.5 mmol), and the resulting solution was heated at 60 °C for 18 h. The mixture was cooled to room temperature and the crude product was purified by reverse phase HPLC to afford 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one oxime (56 mg, 54% yield): ^{1}HNMR (400MHz, $CDCl_3$), 8.43 (br s), 7.43-7.39 (m, 2H), 7.35-7.32 (dd,1H), 7.19-7.15 (m, 1H), 6.87-6.81 (m,1H), 6.65-6.59 (m, 1H), 4.89 (br s, 2H), 4.85 (br s, 2H); MS (EI) for $C_{16}H_{11}F_3IN_3O_2$: 462 (MH^+).

Example 11

***N*-butyl-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine**

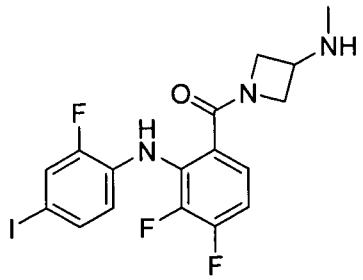


[0539] To a solution of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)azetidin-3-amine (0.09 M in acetonitrile, 500 μL, 0.045 mmol), prepared using procedures similar to those described in Example 2, was added triethylamine (20 μL, 0.135 mmol) and *n*-butylbromide (6.14 μL, 0.054 mmol) followed by additional acetonitrile (1.0 mL). The reaction mixture was stirred at room temperature for 16 h, at which time it was purified directly by reverse phase HPLC to afford the title compound (8.4 mg). ^{1}H NMR (400 MHz, $CDCl_3$): 8.50 (s, 1H), 7.39 (dd, 1H), 7.32 (dd, 1H), 7.13-7.09 (m, 1H), 6.84-6.77

(m, 1H), 6.63-6.57 (m, 1H), 4.35 (br s, 2H), 4.00 (br s, 1H), 3.87 (br s, 1H), 3.74-3.68 (m, 1H), 3.20 (br s, 3.5H), 2.56 (t, 2H), 2.03 (s, 2H), 1.50-1.42 (m, 2H), 1.39-1.29 (m, 2H), 0.91 (t, 3H). MS (EI) for $C_{20}H_{21}F_3IN_3O$: 504 (MH^+).

EXAMPLE 12

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-methylazetidin-3-amine



[0540] To a solution of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)azetidin-3-amine (0.10 M in acetonitrile, 1.0 mL, 0.09 mmol), prepared using procedures similar to those described in Example 2, in 1:1 ratio of methanol and tetrahydrofuran (2.0 mL) was added formaldehyde (37%wt, 6.7 μL, 0.09 mmol) followed by sodium cyanoborohydride (11.0 mg, 0.18 mmol). The reaction mixture was stirred at room temperature for 16 h, at which time it was quenched with saturated aqueous ammonium chloride. The solution was then purified directly by reverse phase HPLC to afford the title compound (14.9 mg). ^1H NMR (400 MHz, $CDCl_3$): 8.13 (br s, 1H), 7.35 (d, 1H), 7.30 (d, 1H), 7.09-7.04 (m, 1H), 6.84-6.78 (m, 1H), 6.60-6.54 (m, 1H), 4.46-4.33 (br m, 4H), 3.93 (br m, 1H), 2.64 (s, 3H). MS (EI) for $C_{17}H_{15}F_3IN_3O$: 462 (MH^+).

[0541] Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the following MEK compounds were prepared:

[0542] **EXAMPLE 12(a).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-*N*-methylazetidin-3-amine: ^1H NMR (400 MHz, $CDCl_3$): 8.13 (br s, 1H), 7.35 (d, 1H), 7.30 (d, 1H), 7.09-7.04 (m, 1H), 6.84-6.78 (m, 1H), 6.60-6.54 (m, 1H), 4.46-4.33 (br m, 4H), 3.93 (br m, 1H), 2.64 (s, 3H). MS (EI) for $C_{17}H_{15}F_3IN_3O$: 462 (MH^+).

[0543] **EXAMPLE 12(b).** 2-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)azetidin-3-yl]amino}ethanol: ^1H NMR (400 MHz, $CDCl_3$): 8.20 (s, 1H), 7.36 (d, 1H), 7.30 (d, 1H), 7.13-7.09 (m, 1H), 6.85-6.79 (m, 1H), 6.61-6.55 (m, 1H), 4.43 (br m, 3H),

3.98 (br m, 1H), 3.87 (br m, 1H), 3.02 (br m, 1H), 1.24-1.20 (m, 1H). MS (EI) for $C_{18}H_{17}F_3IN_3O_2$: 492 (MH^+).

[0544] EXAMPLE 12(c). *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)azetidin-3-yl]propane-1,3-diamine: ^{1}H NMR (400 MHz, $CDCl_3$): 8.51 (s, 1H), 7.39 (d, 1H), 7.32 (d, 1H), 7.14-7.10 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.57 (m, 1H), 4.33 (br s, 2H), 3.99 (br s, 1H), 3.84 (br s, 1H), 3.71-3.64 (m, 1H), 2.91 (t, 2H), 2.70-2.66 (m, 2H), 2.01 (s, 4H), 1.76-1.69 (m, 2H). MS (EI) for $C_{19}H_{20}F_3IN_4O$: 505 (MH^+).

[0545] EXAMPLE 12(d). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-*N*-ethylazetidin-3-amine: ^{1}H NMR (400 MHz, $CDCl_3$): 8.47 (s, 1H), 7.38 (d, 1H), 7.31 (d, 1H), 7.13-7.09 (m, 1H), 6.83-6.77 (m, 1H), 6.62-6.57 (m, 1H), 4.49 (br s, 3H), 4.36 (br s, 2H), 4.08 (br s, 1H), 3.94 (br s, 1H), 3.77-3.72 (m, 1H), 2.69-2.63 (m, 2H), 1.99 (s, 2H), 1.14 (t, 3H). MS (EI) for $C_{18}H_{17}F_3IN_3O$: 476 (MH^+).

[0546] EXAMPLE 12(e). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-*N*-(2-methylpropyl)azetidin-3-amine: ^{1}H NMR (400 MHz, $CDCl_3$): 8.50 (s, 1H), 7.38 (d, 1H), 7.31 (d, 1H), 7.14-7.09 (m, 1H), 6.83-6.76 (m, 1H), 6.63-6.57 (m, 1H), 4.34 (br s, 2H), 4.00 (br s, 1H), 3.86 (br s, 1H), 3.71-3.66 (m, 1H), 3.42 (br s, 2H), 2.36 (d, 2H), 2.00 (s, 1H), 1.75-1.65 (m, 1H), 0.91 (d, 6H). MS (EI) for $C_{20}H_{21}F_3IN_3O$: 504 (MH^+).

[0547] EXAMPLE 12(f). *N*-(cyclopropylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine: ^{1}H NMR (400 MHz, $CDCl_3$): 8.48 (s, 1H), 7.39 (d, 1H), 7.32 (d, 1H), 7.13-7.09 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.57 (m, 1H), 5.78 (s, 3H), 4.36 (br s, 2H), 4.10 (br s, 1H), 3.94 (br s, 1H), 3.81-3.75 (m, 1H), 2.49 (d, 2H), 2.01 (s, 4H), 0.94-0.86 (m, 1H), 0.53 (d, 2H), 0.13 (d, 2H). MS (EI) for $C_{20}H_{19}F_3IN_3O$: 502 (MH^+).

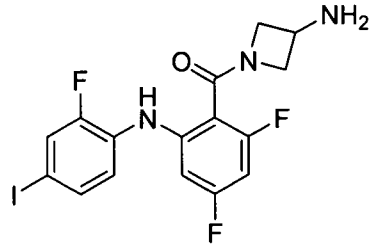
[0548] EXAMPLE 12(g). *N*-(cyclohexylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine: ^{1}H NMR (400 MHz, $CDCl_3$): 8.48 (s, 1H), 7.38 (dd, 1H), 7.31 (d, 1H), 7.13-7.08 (m, 1H), 6.83-6.77 (m, 1H), 6.63-6.57 (m, 1H), 4.55 (br s, 2H), 4.33 (br m, 2H), 4.02 (br s, 1H) 3.87 (br s, 1H), 3.71-3.65 (m, 1H), 2.38 (d, 2H), 1.74-1.68 (m, 4H), 1.46-1.36 (m, 1H), 1.27-1.12 (m, 3H), 0.94-0.84 (m, 2H). MS (EI) for $C_{23}H_{25}F_3IN_3O$: 544 (MH^+).

[0549] EXAMPLE 12(h). *N*-(cyclopentylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine: ^{1}H NMR (400 MHz, $CDCl_3$): 8.32 (s, 1H), 7.37 (d, 1H), 7.31 (d, 1H), 7.11-7.07 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.57 (m, 1H),

4.44-4.37 (m, 3H), 4.02-3.96 (m, 1H), 2.84 (d, 2H), 2.54 (br s, 5H), 2.20-2.12 (m, 1H), 1.88-1.81 (m, 2H), 1.68-1.54 (m, 4H), 1.24-1.15 (m, 2H). MS (EI) for $C_{22}H_{23}F_3IN_3O$: 530 (MH^+).

EXAMPLE 13

1-({2,4-difluoro-6-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine



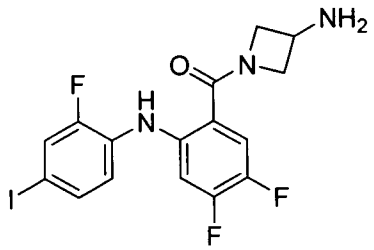
[0550] 2,4,6-Trifluorobenzoic acid (643 mg, 3.65 mmol) and 2-fluoro-4-iodoaniline (1.0 g, 4.22 mmol) were taken into acetonitrile (30 mL) followed by addition of lithium amide (290 mg, 12.7 mmol) and the mixture was heated to 60 °C under a nitrogen atmosphere for one hour. On cooling to room temperature the mixture was added to 1 N aqueous hydrochloric acid (100 mL) and the precipitate formed was collected by filtration and washed once with water then hexanes and dried *in vacuo* to give 2,4-difluoro-6-[(2-fluoro-4-iodophenyl)amino]benzoic acid (849 mg, 59% yield) as a tan solid. ^{1}H-NMR (400 MHz, D_6-DMSO): 13.72 (br s, 1H), 9.46 (s, 1H), 7.75 (d, 1H), 7.56 (d, 1H) 7.28 (tr, 1H), 6.73-6.67 (m, 1H), 6.53 (d, 1H).

[0551] 2,4-Difluoro-6-[(2-fluoro-4-iodophenyl)amino]benzoic acid (100 mg, 0.25 mmol) was taken into DMF (1 mL) followed by addition of PyBOP (137 mg, 0.26 mmol) and the mixture was stirred for 15 minutes then NMM (60 μL, 0.5 mmol) and commercially available 1,1-dimethylethyl azetidin-3-ylcarbamate (43 mg, 0.25 mmol) were subsequently added. The mixture was allowed to stir for 12 hours at room temperature then partitioned with ethyl acetate and water. The organic phase was washed three times with additional water then brine and dried over anhydrous sodium sulfate. Filtration and concentration followed by silica gel flash chromatography of the residue using hexanes:ethyl acetate 3:1 as eluent afforded 1,1-dimethylethyl [1-({2,4-difluoro-6-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)azetidin-3-yl]carbamate (125 mg) as a colorless oil. The oil was taken into trifluoroacetic acid (1 mL) and allowed to stand at room temperature for 5 minutes then concentrated *in vacuo*. The residue was portioned with ethyl acetate and saturated aqueous sodium bicarbonate and the organic phase washed with brine then dried over anhydrous sodium sulfate. The organic solution was filtered and concentrated then the

residue taken into methanol (1 mL) followed by addition of 4 N HCl in dioxane until the solution was acidic. The solution was concentrated and the residue triturated with ethyl ether to give a thick precipitate. The solid was collected by filtration and dried *in vacuo* to give 1-({2,4-difluoro-6-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine hydrochloride (58 mg, 48% overall yield). ^{1}H-NMR (400 MHz, D_6-DMSO): 8.67 (br s, 3H), 8.45 (s, 1H), 7.71 (d, 1H), 7.54 (d, 1H), 7.25 (tr, 1H), 6.77 (tr, 1H), 6.48 (d, 1H), 4.28-4.23 (m, 2H), 4.13-4.06 (m, 3H). MS (EI) for $C_{16}H_{13}F_3IN_3O$: 448 (MH^+).

EXAMPLE 14

1-({4,5-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine



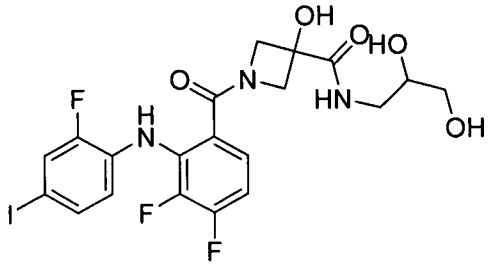
[0552] 2,4,5-Trifluorobenzoic acid (643 mg, 3.65 mmol) and 2-fluoro-4-iodoaniline (1.0 g, 4.22 mmol) were taken into acetonitrile (30 mL) followed by addition of lithium amide (290 mg, 12.7 mmol) and the mixture was heated to 60 °C under a nitrogen atmosphere for one hour. On cooling to room temperature the mixture was added to 1 N aqueous hydrochloric acid (100 mL) and the precipitate formed was collected by filtration and washed once with water then hexanes and dried *in vacuo* to give 4,5-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid (624 mg, 43% yield) as a tan solid. ^{1}H-NMR (400 MHz, D_6-DMSO): 13.65 (br s, 1H), 9.63 (s, 1H), 7.84 (tr, 1H), 7.71 (d, 1H), 7.52 (d, 1H), 7.32 (tr, 1H), 7.03-6.98 (dd, 1H).

[0553] 4,5-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid (100 mg, 0.25 mmol) was taken into DMF (1 mL) followed by addition of PyBOP (137 mg, 0.26 mmol) and the mixture was stirred for 15 minutes then NMM (60 μL, 0.5 mmol) and commercially available 1,1-dimethylethyl azetidin-3-ylcarbamate (43 mg, 0.25 mmol) were subsequently added. The mixture was allowed to stir for 12 hours at room temperature then partitioned with ethyl acetate and water. The organic phase was washed three times with additional water then brine and dried over anhydrous sodium sulfate. Filtration and concentration followed by silica gel flash chromatography of the residue using hexanes:ethyl acetate 3:1 as eluent afforded 1,1-dimethylethyl [1-({4,5-difluoro-2-[(2-fluoro-4-

iodophenyl)amino]phenyl} carbonyl)azetidin-3-yl]carbamate (131 mg) as a colorless oil. The oil was taken into trifluoroacetic acid (1 mL) and allowed to stand at room temperature for 5 minutes then concentrated *in vacuo*. The residue was portioned with ethyl acetate and saturated aqueous sodium bicarbonate and the organic phase washed with brine then dried over anhydrous sodium sulfate. The organic solution was filtered and concentrated then the residue taken into methanol (1 mL) followed by addition of 4 N HCl in dioxane until the solution was acidic. The solution was concentrated and the residue triturated with ethyl ether to give a thick precipitate. The solid was collected by filtration and dried *in vacuo* to give 1-({4,5-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine hydrochloride (67 mg, 55% overall yield). ^{1}H-NMR (400 MHz, D_6-DMSO): 9.02 (s, 1H), 8.54 (br s, 3H), 7.68 (dd, 1H), 7.53-7.47 (m, 2H), 7.22 (tr, 1H), 7.16 (dd, 1H), 4.60 (br s, 1H), 4.23 (br s, 2H), 4.03 (br m, 2H). MS (EI) for $C_{16}H_{13}F_3IN_3O$: 448 (MH^+).

EXAMPLE 15

1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2,3-dihydroxypropyl)-3-hydroxyazetidine-3-carboxamide



[0554] 1-(Diphenylmethyl)azetidin-3-ol hydrochloride (2.75 g, 9.98 mmol), prepared using procedures similar to those described for **Scheme 1** of the General Synthetic Section, 3Å molecular sieves and 4-methylmorpholine (1.1 mL, 10.0 mmol) were suspended in dichloromethane (20 mL) at 0 °C. 4-Methylmorpholine N-oxide (2.93 g, 25.0 mmol) and tetrapropylammonium perruthenate (140 mg, 0.399 mmol) were added and the mixture was stirred at ambient for 24 h. The mixture was filtered through a plug of silica using 5% triethylamine in ethyl acetate as eluent. The filtrate was concentrated *in vacuo* and the residue was partitioned between ethyl acetate and saturated sodium bicarbonate solution. The organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 8:1 hexanes:ethyl acetate) gave 1-(diphenylmethyl)azetidin-3-one (871 mg, 3.68 mmol, 37% yield): ^{1}H NMR (400 MHz, $CDCl_3$): 7.50-7.46 (m, 4H), 7.33-7.27 (m, 4H), 7.27-7.19 (m, 2H), 4.59 (s, 1H), 4.01 (s, 4H); MS (EI) for $C_{16}H_{15}NO$: 238 (MH^+).

[0555] 1-(Diphenylmethyl)azetidin-3-one (600 mg, 2.53 mmol), was dissolved in dichloromethane (1 mL) and treated with triethylamine (0.5 mL, 3.59 mmol) and trimethylsilylcyanide (0.8 mL, 6.01 mmol) at ambient for 2 h and then the mixture was concentrated *in vacuo* to afford 1-(diphenylmethyl)-3-[(trimethylsilyl)oxy]azetidine-3-carbonitrile (774 mg, 2.30 mmol, 91% yield) as a yellow solid. 1-(diphenylmethyl)-3-[(trimethylsilyl)oxy]azetidine-3-carbonitrile (250 mg, 0.744 mmol) was dissolved in dichloromethane (2 mL) at 0 °C and concentrated sulfuric acid (0.2 mL) was added dropwise. The mixture was stirred at ambient for 2 h and then was cooled to 0 °C and 25% ammonium hydroxide solution was added carefully dropwise to pH ~10-11. The mixture was extracted twice with dichloromethane. The combined organic portion was washed with brine, dried

over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to afford a residue which was triturated with hexanes/ether to afford 1-(diphenylmethyl)-3-hydroxyazetidine-3-carboxamide (160 mg, 0.567 mmol, 76% yield) as an off-white solid: ^{1}H NMR (400 MHz, $CDCl_3$): 7.92 (br s, 1H), 7.39-7.34 (m, 4H), 7.33-7.27 (m, 4H), 7.27-7.19 (m, 2H), 5.61 (br s, 1H), 4.45 (s, 1H), 4.34 (s, 1H), 3.50 (dd, 2H), 3.20 (dd, 2H); MS (EI) for $C_{17}H_{18}N_2O_2$: 283 (MH^+).

[0556] 1-(Diphenylmethyl)-3-hydroxyazetidine-3-carboxamide (1.1 g, 3.90 mmol) was treated with 10% sodium hydroxide in ethanol (15 mL) and water (2 mL) at reflux for 2 hours and then was concentrated *in vacuo*. The resiude was neutralized with 1 N hydrochloric acid (pH ~7) and the precipitate was collected by filtration and lyophilized to afford 1-(diphenylmethyl)-3-hydroxyazetidine-3-carboxylic acid (assume 3.90 mmol) which was used without further purification: ^{1}H NMR (400 MHz, d_6-DMSO): 7.45-7.40 (m, 4H), 7.31-7.25 (m, 4H), 7.21-7.15 (m, 2H), 4.52 (s, 1H), 3.46 (dd, 2H), 3.02 (dd, 2H); MS (EI) for $C_{17}H_{17}NO_3$: 284 (MH^+).

[0557] 1-(Diphenylmethyl)-3-hydroxyazetidine-3-carboxylic acid (assume 3.90 mmol) was suspended in methanol (40 mL) and 4 N hydrochloric acid in dioxane (1 mL, 4 mmol) was added. 20 wt% Palladium hydroxide on carbon (100 mg) was added to the solution and the mixture was treated with hydrogen at 40 psi for 2 h. The mixture was filtered and the filtrate was concentrated *in vacuo* to afford 3-hydroxyazetidine-3-carboxylic acid hydrochloride which was dissolved in tetrahydrofuran (5 mL) and water (5 mL) and treated with potassium carbonate (1.615 g, 11.7 mmol) and di-*tert*-butyl dicarbonate (935 mg, 4.29 mmol) were added. The mixture was stirred at ambient for 17 h and then the mixture was partitioned between ethyl acetate and water. The aqueous portion was extracted with ethyl acetate and then was acidified to pH ~3-4 and extracted twice more with ethyl acetate. The combined organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to afford 1-{[(1,1-dimethylethyl)oxy]carbonyl}-3-hydroxyazetidine-3-carboxylic acid which was dissolved in DMF (3 mL). Benzotriazol-1-yloxytris(pyrrolidino)phosphonium hexafluorophosphate (2.028 g, 3.90 mmol) and *N,N*-diisopropylethylamine (0.7 mL, 4.03 mmol) were added. The mixture was stirred at ambient for 5 minutes and then allylamine (0.6 mL, 8.03 mmol) was added and the mixture was stirred for 17 h. The mixture was partitioned between ethyl acetate and 5% lithium chloride. The organic portion was washed with 20% citric acid, saturated sodium bicarbonate and brine, then was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*.

Column chromatography (silica gel, ethyl acetate) gave 1,1-dimethylethyl 3-hydroxy-3-[(prop-2-en-1-ylamino)carbonyl]azetidine-1-carboxylate (782 mg, 3.05 mmol, 78% yield from 1-(diphenylmethyl)-3-hydroxyazetidine-3-carboxamide). 1,1-Dimethylethyl 3-hydroxy-3-[(prop-2-en-1-ylamino)carbonyl]azetidine-1-carboxylate (782 mg, 3.05 mmol) was dissolved in methanol (10 mL) and 4 N hydrochloric acid in dioxane (2 mL, 8 mmol) was added. The mixture was refluxed for 15 minutes and then was concentrated *in vacuo* to afford 3-hydroxy-*N*-prop-2-en-1-ylazetidine-3-carboxamide hydrochloride (3.05 mmol).

[0558] 3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid (1.20 g, 3.05 mmol), prepared using procedures similar to those described in US 7,019,033, 4-(dimethylamino)pyridine (1.20 g, 9.86 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (701 mg, 3.66 mmol) were dissolved in DMF (10 mL). The mixture was stirred at ambient for 5 minutes and then 3-hydroxy-*N*-prop-2-en-1-ylazetidine-3-carboxamide hydrochloride (3.05 mmol) in DMF (5 mL) was added and the mixture was stirred for 15 h. The mixture was partitioned between ethyl acetate and 5% lithium chloride. The organic portion was washed with 20% citric acid, saturated sodium bicarbonate and brine, then was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 60-85% ethyl acetate in hexanes) and then reverse phase HPLC gave 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxy-*N*-prop-2-en-1-ylazetidine-3-carboxamide (150 mg, 0.282 mmol, 9% yield): ^{1}H NMR (400 MHz, d_6-DMSO): 8.64 (br s, 1H), 8.13 (t, 1H), 7.58 (dd, 1H), 7.38 (dd, 1H), 7.34-7.28 (m, 1H), 7.21-7.12 (m, 1H), 6.84 (br s, 1H), 6.72 (ddd, 1H), 5.83-5.72 (m, 1H), 5.10-4.99 (m, 2H), 4.38 (d, 1H), 4.20 (d, 1H), 4.02 (d, 1H), 3.86 (d, 1H), 3.73-3.68 (m, 2H); MS (EI) for $C_{20}H_{17}F_3IN_3O_3$: 532 (MH^+).

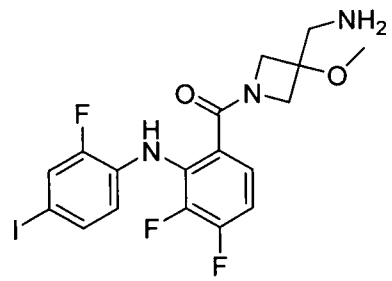
[0559] 1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxy-*N*-prop-2-en-1-ylazetidine-3-carboxamide (88 mg, 0.166 mmol) and 4-methylmorpholine *N*-oxide (58 mg, 0.496 mmol) were dissolved in acetone / water (4:1; 10 mL) and osmium tetroxide (2.5 wt.% in water; 0.1 mL) was added. The solution was stirred at ambient for 15 h, then was quenched with saturated sodium bisulfite (2 mL) and concentrated *in vacuo*. The residue was partitioned between ethyl acetate and brine. The aqueous portion was extracted with ethyl acetate. The combined organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Purification by reverse phase HPLC gave 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2,3-dihydroxypropyl)-3-hydroxyazetidine-3-carboxamide (68 mg, 0.120 mmol, 72% yield): ^{1}H

NMR (400 MHz, d_6-DMSO): 8.65 (br s, 1H), 7.72 (t, 1H), 7.58 (dd, 1H), 7.41-7.36 (m, 1H), 7.34-7.28 (m, 1H), 7.21-7.12 (m, 1H), 6.92 (br s, 1H), 6.72 (ddd, 1H), 5.00-4.10 (br, 2H), 5.10-4.99 (m, 2H), 4.39 (d, 1H), 4.20 (d, 1H), 4.02 (d, 1H), 3.54-3.45 (m, 1H), 3.34-3.21 (m, 2H), 3.06-2.96 (m, 1H); MS (EI) for $C_{20}H_{19}F_3IN_3O_5$: 566 (MH^+).

[0560] **EXAMPLE 15(a).** Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the following MEK compounds were prepared: 1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-hydroxyazetidine-3-carboxamide: ^{1}H NMR (400 MHz, d_6-DMSO): 8.63 (br s, 1H), 7.58 (dd, 1H), 7.42-7.36 (m, 3H), 7.34-7.28 (m, 1H), 7.22-7.12 (m, 1H), 6.76-6.68 (m, 2H), 4.39 (d, 1H), 4.19 (d, 1H), 4.00 (d, 1H), 3.83 (d, 1H); MS (EI) for $C_{17}H_{13}F_3IN_3O_3$: 492 (MH^+).

EXAMPLE 16

6-{[3-(aminomethyl)-3-(methyloxy)azetidin-1-yl]carbonyl}-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline



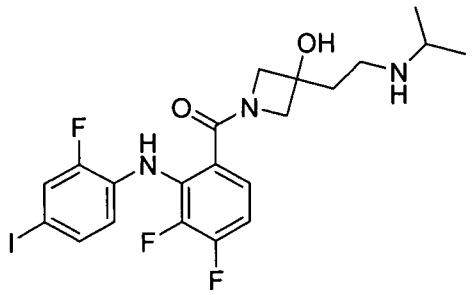
[0561] Phenylmethyl 1-oxa-5-azaspiro[2.3]hexane-5-carboxylate (165 mg, 0.75 mmol), prepared using procedures similar to those described in Reference 3, in THF (1 mL) was added to anhydrous ammonia saturated in THF (10 mL) and the mixture was allowed to stir in a sealed vessel at room temperature over 24 hours. The solution was then concentrated and taken back into THF (1 mL) followed by addition of di-*tert*-butyldicarbonate (164 mg, 0.75 mmol) and stirred for one hour at room temperature. The mixture was then concentrated and the residue purified by silica gel flash chromatography using hexanes:ethyl acetate (1:1) as eluent to give phenylmethyl 3-[({[(1,1-dimethylethyl)oxy]carbonyl}amino)methyl]-3-hydroxyazetidine-1-carboxylate (16.5 mg, 7% yield) and unreacted epoxide (120 mg, 73% recovery). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.34 (m, 5H), 5.10 (br, 1H), 5.09 (s, 2H), 4.68 (s, 1H), 3.90 (dd AB, 4H), 3.41 (d, 2H), 1.44 (s, 9H).

[0562] Phenylmethyl 3-[({[(1,1-dimethylethyl)oxy]carbonyl}amino)methyl]-3-hydroxyazetidine-1-carboxylate (16.5 mg, 0.05 mmol) and 10% Pd/C (8 mg) were taken into methanol (2 mL) and hydrogenated at ambient pressure over 12 hours. The catalyst was removed by filtration and the filtrate concentrated and dried *in vacuo*. The residue was taken into THF (1 mL) followed by addition of DIPEA (10 μL, 0.06 mmol) and 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoyl fluoride (19.8 mg, 0.05 mmol), prepared using procedures similar to those described in Reference 1, and the solution was stirred at room temperature for 30 minutes. Concentration and purification of the residue by silica gel flash chromatography using hexanes:ethyl acetate (1:1.5) afforded 1,1-dimethylethyl {[1-({3,4-difluoro-2[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidine-3-yl]methyl}carbamate (19 mg, 66% yield).

[0563] 1,1-Dimethylethyl {[1-({3,4-difluoro-2[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidine-3-yl]methyl}carbamate (8.0 mg, 0.014 mmol) and silver (I) oxide (12 mg, 0.05 mmol) were taken into methyl iodide (0.5 mL) and the mixture was brought to reflux for 4 hours. The suspension was then cooled to room temperature and diluted with an excess of ethyl ether then filtered. The filtrate was concentrated and purified by silica gel flash chromatography using hexanes:ethyl acetate (1:1) as eluent to give 1,1-dimethylethyl {[1-({3,4-difluoro-2[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(methylloxy)azetidine-3-yl]methyl}carbamate (2 mg). The material was taken into TFA (0.5 mL) and allowed to stand for 5 minutes then concentrated *in vacuo*. The residue was azetroped twice from methanol (2 mL) and the residue dried *in vacuo* to afford 6-{[3-(aminomethyl)-3-(methyloxy)azetidin-1-yl]carbonyl}-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl) aniline trifluoroacetate salt (2.3 mg, 27% yield) as an amorphous solid. MS (EI) for $C_{18}H_{17}F_3IN_3O$: 492 (MH^+).

EXAMPLE 17

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{2-[(1-methylethyl)amino]ethyl}azetidin-3-ol



[0564] A solution of *tert*-butyl acetate (566 μL, 4.2 mmol) in THF (10 mL) was cooled to -78 °C. To the solution was added LHMDS (5.25 mL of a 1.0 M solution in hexanes, 5.25 mmol), and the resulting mixture was stirred for 20 min at -78 °C. To the solution was added 1-(diphenylmethyl)azetidin-3-one (500 mg, 2.1 mmol), prepared using procedures similar to those described in Example 15. After stirring for 1 h, saturated aqueous ammonium chloride was added, and the mixture was warmed to rt. Water and ether were added, and the resulting biphasic mixture was partitioned. The aqueous phase was extracted once with ether. The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography (80% hexanes: 20% ethyl acetate) to provide 1,1-dimethylethyl [1-(diphenylmethyl)-3-hydroxyazetidin-3-yl]acetate as a pale yellow solid (644 mg, 1.8 mmol, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (m, 4H), 7.26 (m, 4H), 7.19 (m, 2H), 4.40 (s, 1H), 4.02 (s, 1H), 3.15 (m, 2H), 3.05 (m, 2H), 2.83 (s, 2H), 1.45 (s, 9H).

[0565] To a solution of 1,1-dimethylethyl [1-(diphenylmethyl)-3-hydroxyazetidin-3-yl]acetate (333 mg, 0.94 mmol) in THF (3 mL) at 0 °C was added lithium aluminum hydride (940 μL of a 1.0 M solution in THF, 0.94 mmol). The mixture was stirred for 3 h 20 min while warming to rt. Water (36 μL) was added carefully to the solution, followed by 15% sodium hydroxide (36 μL) and more water (108 μL). The resulting precipitate was removed by filtration through celite, and the filtrate was concentrated to dryness yielding 1-(diphenylmethyl)-3-(2-hydroxyethyl)azetidin-3-ol (228 mg, 0.80 mmol, 85% yield) as a colorless syrup. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (m, 4H), 7.26 (m, 4H), 7.19 (m, 2H), 4.37 (s, 1H), 3.92 (m, 2H), 3.32 (m, 2H), 2.96 (m, 2H), 2.07 (m, 2H).

[0566] Palladium hydroxide (100 mg) was suspended in a solution of 1-(diphenylmethyl)-3-(2-hydroxyethyl)azetidin-3-ol (228 mg, 0.80 mmol) in methanol (15 mL), and the mixture

was subjected to an atmosphere of hydrogen at 50 psi for 4 h. The catalyst was then removed by filtration through celite, and the filtrate was concentrated *in vacuo* to provide 3-(2-hydroxyethyl)azetidin-3-ol. This material was used in the subsequent reaction without purification. To a solution of 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid (314 mg, 0.80 mmol), prepared using procedures similar to those described in US 7,019,033, in DMF (4 mL) was added PyBOP (416 mg, 0.80 mmol) and triethylamine (223 μL, 1.6 mmol). Finally, the unpurified 3-(2-hydroxyethyl)azetidin-3-ol was added, and the resulting mixture was stirred at rt for 16 h. Water and ethyl acetate were added, and the layers were separated. The aqueous phase was extracted with once more with ethyl acetate. The combined organic extracts were washed with brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography, eluting with ethyl acetate, to provide 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(2-hydroxyethyl)azetidin-3-ol as a colorless oil (303 mg, 0.62 mmol, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46 (s, 1H), 7.39 (dd, 1H), 7.32 (m, 1H), 7.13 (m, 1H), 6.81 (m, 1H), 6.60 (m, 1H), 4.37 (br s, 1H), 4.28 (br m, 4H), 3.94 (br s, 2H), 2.19 (br s, 1H), 2.02 (m, 2H); MS (EI) for $C_{18}H_{16}F_3IN_2O_3$: 491 (M-H).

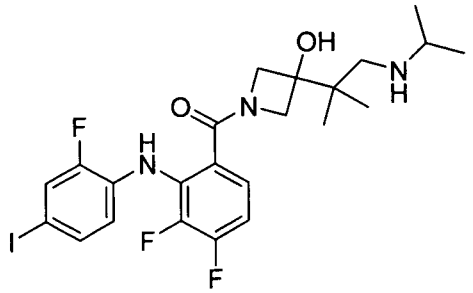
[0567] A solution of oxalyl chloride (13 μL, 0.15 mmol) in dichloromethane (1 mL) was cooled to -78 °C, and DMSO (22 μL, 0.31 mmol) was then added. To this mixture was added 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(2-hydroxyethyl) azetidin-3-ol (67.8 mg, 0.14 mmol) as a suspension in dichloromethane (1 mL). After stirring at -78 °C for 10 min, triethylamine (78 μL, 0.56 mmol) was added and the mixture was allowed to warm to rt. The solution was diluted with dichloromethane, and washed with 0.5 N HCl. The aqueous phase wash then extracted with dichloromethane. The organic extracts were combined, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by flash chromatography to provide [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]acetaldehyde as a white solid (22.1 mg, 0.045 mmol, 32% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.82 (s, 1H), 8.46 (s, 1H), 7.39 (m, 1H), 7.33 (m, 1H), 7.11 (m, 1H), 6.81 (m, 1H), 6.61 (m, 1H), 4.32-3.96 (br m, 4H), 3.41 (t, 2H), 3.07 (s, 1H); MS (EI) for $C_{18}H_{14}F_3IN_2O_3$: 491 (MH^+).

[0568] To a solution of [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-hydroxyazetidin-3-yl]acetaldehyde (38.0 mg, 0.078 mmol) in 1,2-dichloroethane (1 mL) was added isopropylamine (27 μL, 0.31 mmol) followed by sodium

triacetoxyborohydride (26 mg, 0.12 mmol). The mixture was stirred for 3 h before quenching with 1 drop of concentrated HCl. The quenched mixture was concentrated to dryness, and then purified by preparative HPLC to provide 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl) amino]phenyl}carbonyl)-3-{2-[(1-methylethyl)amino]ethyl}azetidin-3-ol (21.5 mg) as a pale yellow solid. ^{1}H NMR (400 MHz, d_6-DMSO): δ 8.54 (s, 1H), 7.57 (dd, 1H), 7.38 (dd, 1H), 7.31 (m, 1H), 7.17 (m, 1H), 6.67 (m, 1H), 4.02 (m, 1H), 3.89 (m, 2H), 3.71 (m, 1H), 2.70 (m, 1H), 2.63 (m, 2H), 1.86 (s, 3H), 1.75 (m, 2H), 0.97 (d, 6H); MS (EI) for $C_{21}H_{23}F_3IN_3O_2$: 534 (MH^+).

EXAMPLE 18

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1,1-dimethyl-2-[(1-methylethyl)amino]ethyl}azetidin-3-ol



[0569] To a solution of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)azetidin-3-one (500 mg, 1.12 mmol), prepared using procedures similar to those described in Example 6, in dichloromethane (5 mL) cooled to 0 °C was added titanium tetrachloride (125 μL, 1.12 mmol). The dark brown solution was stirred at 0 °C for 45 minutes, followed by the addition of methyltrimethylsilyl dimethylketene acetal (550 μL, 2.24 mmol) at 0 °C. Upon addition the solution was allowed to warm to room temperature, and was stirred for 1 hour. The reaction mixture was then partitioned between saturated aqueous sodium bicarbonate and ethyl acetate. The aqueous portion was extracted twice using ethyl acetate. The combined organic portion was washed with water, brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford a brown oil which was purified by column chromatography. Eluting with 10% diethyl ether in dichloromethane, the isolated product was concentrated *in vacuo* to afford 520 mg, 0.95 mmol (85%) of methyl 2-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]-2-methylpropanoate as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$): 8.34 (s, 1H), 7.38 (d, 1H), 7.31 (d, 1H), 7.13-7.08 (m, 1H), 6.85-6.77 (m, 1H), 6.63-6.56 (m, 1H), 4.26-4.20 (m, 2H), 4.13-4.09 (m, 1H), 4.00-3.93 (m, 1H), 3.70 (s, 3H), 1.23 (s, 6H). MS (EI) for $C_{21}H_{20}F_3IN_2O_4$: 547 (MH^-).

[0570] A solution of methyl 2-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-hydroxyazetidin-3-yl]-2-methylpropanoate (520 mg, 0.95 mmol) in 4N aqueous potassium hydroxide (5 mL) was stirred at 50°C for 1 hour. Using concentrated aqueous hydrochloric acid, the reaction mixture was acidified to pH 5, and then partitioned with ethyl acetate. The aqueous portion was extracted twice using ethyl acetate, and the combined organic portion was washed with brine, dried over sodium sulfate, filtered and concentrated

in vacuo to afford 300 mg, 0.56 mmol (59%) of 2-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]-2-methylpropanoic acid as a white solid. ^{1}H NMR (400 MHz, DMSO): 8.49 (s, 1H), 7.57-7.52 (m, 1H), 7.37-7.25 (m, 2H), 7.17-7.13 (m, 1H), 6.68-6.58 (m, 1H), 3.98-3.94 (m, 2H), 3.80-3.77 (m, 1H), 3.55-3.52 (m, 1H), 0.88 (s, 6H). MS (EI) for $C_{20}H_{18}F_3IN_2O_4$: 535 (MH^+).

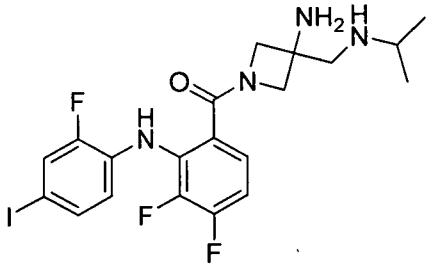
[0571] To solution of 2-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-hydroxyazetidin-3-yl]-2-methylpropanoic acid (300 mg, 0.56 mmol) in tetrahydrofuran (5 mL) was added triethylamine (80 μL, 0.56 mmol), followed by PyBOP (295 mg, 0.56 mmol) and finally sodium borohydride (64 mg, 1.68 mmol). The mixture was stirred at room temperature for 1 hour. The reaction mixture was quenched by adding 20% aqueous citric acid, and then partitioned with ethyl acetate. The organic portion was washed with saturated aqueous sodium bicarbonate, brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford a white solid which was purified by column chromatography. Eluting with 60% ethyl acetate in hexanes, the isolated product was concentrated *in vacuo* to afford 238 mg, 0.46 mmol (82%) of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl) amino]phenyl}carbonyl)-3-(2-hydroxy-1,1-dimethylethyl)azetidin-3-ol as a white solid. ^{1}H NMR (400 MHz, DMSO): 8.53 (s, 1H), 7.57 (d, 1H), 7.38-7.28 (m, 2H), 7.22-7.15 (m, 1H), 6.70-6.64 (m, 1H), 5.61 (s, 1H), 4.57 (br s, 1H), 4.30-4.27 (m, 1H), 4.18-4.15 (m, 1H), 3.80-3.77 (m, 1H), 3.68-3.64 (m, 1H), 3.25 (s, 2H), 0.76 (d, 6H); MS (EI) for $C_{20}H_{20}F_3IN_2O_3$: 521 (MH^+).

[0572] A mixture of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(2-hydroxy-1,1-dimethylethyl)azetidin-3-ol (200 mg, 0.38 mmol) and Dess-Martin periodinane (240 mg, 0.57 mmol) in dichloromethane (2 mL) was stirred at room temperature for 2 hours. 10% aqueous sodium thiosulfate (2 mL), and saturated aqueous sodium bicarbonate (2 mL) was added and the mixture was stirred at room temperature for 15 minute. The mixture was partitioned and the aqueous layer was extracted twice using dichloromethane. The combined organic portion was washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo*, to afford a white solid which was purified by column chromatography. Eluting with 30% ethyl acetate in hexanes, the isolated product was concentrated *in vacuo* to afford 100 mg, 0.20 mmol (53%) of 2-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]-2-methylpropanal as a white solid, which was immediately dissolved in tetrahydrofuran (2 mL). To the solution

was added isopropylamine (34 μL, 0.40 mmol), followed by triacetoxyborohydride (212 mg, 1.0 mmol). The solution was stirred at room temperature for 15 hours. The reaction mixture was concentrated *in vacuo* and partitioned between 20% aqueous citric acid and ethyl acetate. The aqueous portion was extracted twice using ethyl acetate, and the combined organic portion was washed with saturated aqueous sodium bicarbonate, brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford a yellow oil which was purified by preparative reverse phase HPLC. The isolated product was concentrated *in vacuo* to afford 50 mg, 0.07 mmol (36%) of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{1,1-dimethyl-2-[(1-methylethyl)amino]ethyl}azetidin-3-ol acetate salt as a white solid. ^{1}H NMR (400 MHz, DMSO): 8.47 (br s, 1H), 7.55 (d, 1H), 7.36-7.29 (m, 2H), 7.22-7.15 (m, 1H), 6.68-6.63 (m, 1H), 4.17-4.08 (m, 2H), 3.76-3.73 (m, 1H), 3.56-3.52 (m, 1H), 2.58-2.51 (m, 1H), 2.45-2.37 (m, 2H), 0.92 (t, 6H), 0.78 (d, 6H); MS (EI) for $C_{23}H_{27}F_3IN_3O_2$: 562 (MH^+).

EXAMPLE 19

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-methylethyl)amino]methyl}azetidin-3-amine



[0573] To a solution of the 1-(diphenylmethyl)-3-[(phenylmethyl)amino]azetidine-3-carbonitrile (0.80 g, 2.2 mmol), prepared using procedures similar to those described in Kozikowski and Fauq *Synlett* 1991, *11,* 783-4, in ethanol (30 mL) was added solid sodium hydroxide (7.5 mmol), and the resulting mixture was stirred at room temperature for 3 days. Water (6 mL) was added to the reaction mixture and stirring was continued at 90 °C for 2 h. The pH of the reaction mixture was adjusted to 5 with concentrated hydrochloric acid and a white solid precipitated. The mixture was cooled , diluted with water (50 mL) and the solid was collected, washed with water then dried *in vacuo* to give the 1-(diphenylmethyl)-3-[(phenylmethyl)amino]azetidine-3-carboxylic acid (0.75g, 88% yield), MS (EI) for $C_{24}H_{24}N_2O_2$: 373 (MH^+).

[0574] To a mixture of 1-(diphenylmethyl)-3-[(phenylmethyl)amino]azetidine-3-carboxylic acid (0.50 g, 1.34 mmol), *N,N*-diisopropylethylamine (0.47 mL, 2.68 mmol) in DMF (3 mL) was added 1-benzotriazolyloxytripyrrolidinylphosphonium hexafluorophosphate (1.34g, 2.68 mol) and the resulting mixture was stirred at room temperature for 10 minutes. To this mixture was added 2-propylamine (0.22 mL, 2.68 mmol) and stirring was continued for 18 h. The reaction mixture was diluted with ethyl acetate (100 mL) and washed with 2% aqueous citric acid, 5% lithium chloride, and brine solutions (50 mL each), dried over sodium sulfate, filtered and concentrated to give an oily residue which was purified by flash chromatography (silica gel, eluting with 15-25% ethyl acetate-hexane) to give 1-(diphenylmethyl)-*N*-(1-methylethyl)-3-[(phenylmethyl)amino]azetidine-3-carboxamide (0.51 g, 92% yield), MS (EI) for $C_{27}H_{31}N_3O$: 414 (MH^+).

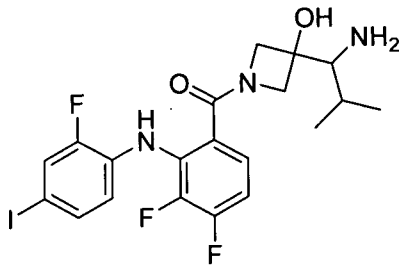
[0575] To a solution of the 1-(diphenylmethyl)-*N*-(1-methylethyl)-3-[(phenylmethyl) amino]azetidine-3-carboxamide (0.40 g, 0.97 mmol) in tetrahydrofuran (10 mL) at room was added a solution of lithium aluminum hydride in tetrahydrofuran (1M, 2.90 mL, 2.90 mmol), and the resulting mixture was stirred at 50 °C for 3h. The reaction mixture was cooled to room temperature, quenched with 20% aqueous hydroxide solution (1 mL), diluted with ether (50 mL) and filtered. The filtrate was washed with brine solution (20 mL each), dried over sodium sulfate, filtered and concentrated to give an oily residue which was purified by flash chromatography (silica gel, eluting with 5% methanol-dichloromethane) to give 1-(diphenylmethyl)-3-{[(1-methylethyl)amino]methyl}-*N*-(phenylmethyl)azetidin-3-amine (0.35g, 90% yield), ^1H NMR (400 MHz, $CDCl_3$): 7.42-7.14 (m, 15H), 4.34 (s, 1H), 3.66 (s, 2H), 3.22-3.18 (d, 2H), 2.97 (s, 2H), 2.90-2.86(d, 2H), 2.68-2.62 (p, 1H), 1.09-1.07 (d, 6H); MS (EI) for $C_{27}H_{33}N_3$: 400 (MH^+).

[0576] To a solution of the 1-(diphenylmethyl)-3-{[(1-methylethyl)amino]methyl}-*N*-(phenylmethyl)azetidin-3-amine (0.35 g , 0.88 mmol) in methanol was added a solution of hydrogen chloride in dioxane (4 molar solution, 0.96 mL, 4.40 mmol) and the resulting mixture was concentrated to give a white solid which was taken back into methanol. To this solution were added palladium hydroxide (20% on carbon, 0.50 g, 0.19 mmol) and the resulting mixture shaken at 50 psi in a Parr apparatus for 3h. The reaction mixture was filtered and concentrated to give a solid, which was washed with ether and dried *in vacuo* to give 3-{[(1-methylethyl)amino]methyl}azetidin-3-amine hydrochloride as a white solid (0.18 g, 81% yield). MS (EI) for $C_7H_{17}N_3$: 144 (MH^+).

[0577] To a mixture of the 3-{[(1-methylethyl)amino]methyl}azetidin-3-amine hydrochloride (20 mg, 0.079 mmol) in saturated sodium bicarbonate solution (1.0 mL) and dioxane (1.0 mL) was added 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoyl fluoride (31 mg, 0.079 mmol), prepared using procedures similar to those described in Reference 1, and the resulting mixture was stirred at room temperature for 18 h. The reaction mixture was diluted with water (5 mL) and extracted with ethyl acetate (3 x 5 mL). The combined extract was washed with water then brine solution (5 mL each), dried over sodium sulfate, filtered and concentrated to give an oily residue which was purified by reverse phase HPLC to afford 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-methylethyl) amino]methyl}azetidin-3-amine (15 mg, 37% yield). ^{1}H NMR (400 MHz, d_4-Methanol): 7.46-7.43 (dd, 1H), 7.35-7.33 (dd, 1H), 7.31-7.27 (m, 1H), 7.08-7.01 (dd, 1H), 6.63, 6.58 (td, 1H), 4.09-4.07 (d, 1H), 3.91-3.85 (dd, 2H), 3.76-3.73 (d, 1H). 2.80-2.74 (m, 1H), 2.73 (s, 2H), 1.07-1.05 (d, 6H); MS (EI) for $C_{20}H_{22}F_3IN_4O$: 519 (MH^+).

EXAMPLE 20

3-(1-amino-2-methylpropyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol



[0578] 1,1-Dimethylethyl 3-oxoazetidine-1-carboxylate (677.2 mg, 3.96 mmol), prepared using procedures similar to those described in Example 3, was taken into 2-methyl-1-ntropropane (5 mL) then cooled to 0 °C followed by addition of potassium *tert*-butoxide (444 mg, 3.96 mmol) and the resulting mixture was allowed to warm to room temperature over 30 minutes. The mixture was partitioned with ethyl acetate and 0.5 N aqueous hydrochloric acid then once with water and brine then dried over anhydrous magnesium sulfate. Filtration and concentration afforded a residue (1.5 g) that was further purified by silica gel flash chromatography using 3:1 hexanes:ethyl acetate as eluent to give 1,1-dimethylethyl 3-hydroxy-3-(2-methyl-1-nitropropyl)azetidine-1-carboxylate (730 mg, 67% yield) as a

colorless crystalline solid. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.50 (d, 1H), 3.93 (dd AB, 2H), 3.85 (s, 2H), 3.58 (s, 1H), 2.54-2.48 (m, 1H), 1.44 (s, 9H), 1.04 (d, 6H).

[0579] 1,1-Dimethylethyl 3-hydroxy-3-(2-methyl-1-nitropropyl)azetidine-1-carboxylate (105 mg, 0.38 mmol) was taken into methanol (1 mL) followed by addition of 4 N anhydrous hydrogen chloride in dioxane (1 mL) and the acidic solution was allowed to stand for 15 minutes at room temperature then concentrated and dried *in vacuo* to an amorphous residue. 3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid (150 mg, 0.38 mmol), prepared using procedures similar to those described in US 7,019,033, was taken into DMF (0.7 mL) followed by addition of PyBOP (198 mg, 0.38 mmol) and the solution was allowed to stir for 10 minutes at room temperature. The above amine hydrochloride salt and DIPEA (190 μL, 1.1 mmol) in DMF solution (0.7 mL) was added and the mixture was allowed to stir for one hour at room temperature. The mixture was partitioned with ethyl acetate and 0.5 N aqueous hydrochloric acid and the organic phase washed three times with water then brine and dried over anhydrous magnesium sulfate. Filtration and concentration afforded a residue that was further purified by silica gel flash chromatography using 1.5:1 hexanes:ethyl acetate as eluent to give 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(2-methyl-1-nitropropyl)azetidin-3-ol (189 mg, 90% yield) as an amorphous solid. ^{1}H-NMR (400 MHz, $CDCl_3$): 8.41 (br s, 1H), 7.41 (dd, 1H), 7.34 (d, 1H), 7.09 (br m, 1H), 6.81 (q, 1H), 6.65-6.60 (m, 1H), 4.49 (d, 1H), 4.15-4.09 (m, 4H), 3.66 (s, 1H), 2.56-2.46 (m, 1H) 1.03 (d, 6H).

[0580] 1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(2-methyl-1-nitropropyl)azetidin-3-ol (189 mg, 0.34 mmol) was taken into 4:1 THF:water (5 mL) followed by addition of iron powder (192 mg, 3.4 mmol) and ammonium formate (429 mg, 6.8 mmol) and the mixture was heated to reflux. After four hours additional aliquots of iron powder (192 mg, 3.4 mmol) and ammonium formate (429 mg, 6.8 mmol) were added and the mixture was allowed to reflux an additional 12 hours. The mixture was cooled to room temperature and diluted with ethyl acetate then filtered. The filtrate was partitioned with ethyl acetate and saturated aqueous sodium bicarbonate then the organic layer washed with brine and dried over anhydrous sodium sulfate. Filtration and concentration afforded a residue that was further purified by silica gel flash chromatography using ethyl acetate to 10% methanol in dichloromethane as eluents to give a residue (36.5 mg) that was further purified by preparative reverse phase HPLC to give 3-(1-amino-2-methylpropyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol trifluoroacetate salt

(7.9 mg) as a colorless amorphous solid after lyophillization of the combined pure fractions. ^{1}H-NMR (400 MHz, D_6-DMSO): 8.63 (s, 1H), 7.58 (dd, 1H), 7.37 (d, 1H), 7.35-7.31 (m, 1H), 7.17 (q, 1H), 6.71-6.66 (m, 1H), 4.23 (dd, 1H), 4.03 (dd, 1H), 3.80 (dd, 1H), 3.66 (dd, 1H), 2.34 (dd, 1H), 1.79-1.70 (m, 1H), 0.84-0.77 (m, 6H). MS (EI) for $C_{20}H_{21}F_3IN_3O_2$: 520 (MH^+).

[0581] Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the following MEK compounds were prepared:

[0582] **EXAMPLE 20(a).** 3-(1-aminoethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 8.56 (s, 1H), 7.91 (br s, 2H), 7.58 (d, 1H), 7.39 (d, 1H), 7.36-7.32 (m, 1H), 7.24-7.17 (m, 1H), 6.72-6.65 (m, 2H), 4.33-4.29 (m, 1H), 4.23-4.19 (m, 1H), 4.16-4.14 (m, 1H), 4.07-3.94 (m, 1H), 3.82-3.77 (m, 1H), 3.51-3.45 (m, 1H), 1.15-1.12 (m, 1H), 1.10-1.08 (m, 1H). MS (EI) for $C_{18}H_{17}F_3IN_3O_2$: 492 (MH^+).

[0583] **EXAMPLE 20(b).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(ethylamino)ethyl]azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 8.61 (d, 1H), 8.50 (s, 1H), 8.20 (s, 1H), 7.59 (d, 1H), 7.39 (d, 1H), 7.36-7.32 (m, 1H), 7.24-7.17 (m, 1H), 6.82 (s, 1H), 6.74-6.67 (m, 1H), 4.38 (d, 1H), 4.27 (d, 1H), 4.18 (d, 1H), 4.06 (d, 2H), 3.99 (d, 1H), 3.89 (d, 1H), 3.82 (d, 1H), 3.49-3.43 (m, 1H), 3.04-2.80 (m, 4H), 1.21-1.12 (m, 6H). MS (EI) for $C_{20}H_{21}F_3IN_3O_2$: 520 (MH^+).

[0584] **EXAMPLE 20(c).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-nitroethyl)azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 8.57 (d, 1H), 7.58 (d, 1H), 7.38 (d, 1H), 7.37-7.33 (m, 1H), 7.22-7.17 (m, 1H), 6.73-6.66 (m, 1H), 6.57 (s, 1H), 5.06-4.97 (m, 1H), 4.54 (d, 0.5H), 4.37 (d, 0.5 H), 4.29 (d, 0.5H), 4.14 (d, 0.5 H), 4.05 (d, 0.5 H), 3.95 (d, 0.5H), 3.86 (d, 0.5H), 3.80 (d, 0.5H), 1.44-1.38 (m, 3H). MS (EI) for $C_{18}H_{16}F_3IN_3O_4$: 523 (MH^+).

[0585] **EXAMPLE 20(d).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(methylamino)ethyl]azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 8.63-8.55 (m, 1H), 8.44-8.23 (m, 1H), 7.79 (br s, 1H), 7.60 (d, 1H), 7.39 (d, 1H), 7.36-7.31 (m, 1H), 7.24-7.17 (m, 1H), 6.82 (br s, 0.5H), 6.73-6.65 (m, 1H), 4.38-3.77 (m, 4H), 1.18-1.07 (m, 3H). MS (EI) for $C_{19}H_{19}F_3IN_3O_2$: 505 (M^+).

[0586] **EXAMPLE 20(e).** methyl {1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}carbamate: ^{1}H NMR (400 MHz, d_6-DMSO): 8.59 (d, 1H), 7.58 (d, 1H), 7.41-7.05 (m, 4H), 6.72-6.64 (m, 1H), 5.84 (d, 1H), 4.20 (d,

0.5H), 4.08-4.04 (m, 1H), 3.92-3.85 (m, 1.5H), 3.76-3.71 (m, 1H), 3.69-3.63 (m, 1H), 3.46 (d, 2H), 0.99-0.95 (m, 3H). MS (EI) for $C_{20}H_{19}F_3IN_3O_4$: 550 (MH^+).

[0587] EXAMPLE 20(f). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-[1-(dimethylamino)ethyl]azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 9.45 (s, 1H), 8.61 (d, 1H), 7.60 (d, 1H), 7.39 (d, 1H), 7.38-7.33 (m, 1H), 7.24-7.18 (m, 1H), 7.05 (s, 1H), 6.73-6.66 (m, 1H), 4.48 (d, 0.5H), 4.36 (d, 0.5 H), 4.26 (d, 0.5H), 4.16-4.11 (m, 1H), 4.00-3.94 (m, 1H), 3.86 (d, 0.5H), 3.60-3.54 (m, 1H), 2.75-2.70 (m, 3H), 2.66-2.62 (br s, 3H), 1.22 (dd, 3H). MS (EI) for $C_{20}H_{21}F_3IN_3O_2$: 520 (MH^+).

[0588] EXAMPLE 20(g). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-(1-nitropropyl)azetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.46 (m, 1H), 7.35 (m, 1H), 7.28 (m, 1H), 7.07 (m, 1H), 6.61 (m, 1H), 4.65 (m, 1H), 4.44 (m, 1H), 4.25 (m, 1H), 4.02 (m, 1H), 3.86 (m, 1H), 2.04 (m, 1H), 1.76 (m, 1H), 0.94 (m, 3H). MS (EI) for $C_{19}H_{17}F_3IN_3O_4$: 536 (MH^+).

[0589] EXAMPLE 20(h). 3-(1-aminopropyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.45 (m, 1H), 7.34 (m, 1H), 7.28 (m, 1H), 7.05 (m, 1H), 6.61 (m, 1H), 4.21 (m, 1H), 4.09-3.86 (m, 2H), 3.78 (m, 1H), 2.63 (m, 1H), 1.50 (m, 1H), 1.24 (m, 1H), 0.98 (m, 3H). MS (EI) for $C_{19}H_{19}F_3IN_3O_2$: 506 (MH^+).

[0590] EXAMPLE 20(i). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-[1-(ethylamino)propyl]azetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.45 (m, 1H), 7.34 (m, 1H), 7.28 (m, 1H), 7.05 (m, 1H), 6.61 (m, 1H), 4.23 (m, 1H), 4.02 (m, 1H), 3.90 (m, 1H), 3.79 (m, 1H), 2.70 (m, 1H), 2.54 (m, 1H), 1.53 (m, 1H), 1.40 (m, 1H), 1.05 (m, 3H), 0.95 (m, 3H). MS (EI) for $C_{21}H_{23}F_3IN_3O_2$: 534 (MH^+).

[0591] EXAMPLE 20(j). 3-[1-(diethylamino)propyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.44 (m, 1H), 7.33 (m, 1H), 7.27 (m, 1H), 7.07 (m, 1H), 6.60 (m, 1H), 4.21 (m, 1H), 4.10 (m, 1H), 4.03-3.70 (m, 2H), 2.71-2.45 (m, 5H), 1.67 (m, 1H), 1.49 (m, 1H), 0.94 (m, 9H). MS (EI) for $C_{23}H_{27}F_3IN_3O_2$: 562 (MH^+).

[0592] EXAMPLE 20(k). 3-[amino(phenyl)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol): MS (EI) for $C_{23}H_{19}F_3IN_3O_2$: 554 (MH^+).

[0593] EXAMPLE 20(m). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-(3-methyl-1-nitrobutyl)azetidin-3-ol): ^{1}H NMR (400MHz, $CDCl_3$): 8.38 (s, 1H), 7.39 (dd, 1H), 7.34-7.31 (m, 1H), 7.14-7.10 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.58 (m,

1H), 4.68 (dd, 1H), 4.23-4.04 (br m, 4H), 2.13 (t, 2H), 1.64-1.44 (br m, 3H), 0.93 (d, 6H); MS (EI) for $C_{21}H_{21}F_3IN_3O_4$: 564 (MH^+).

[0594] EXAMPLE 20(n). 3-(1-aminobutyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.48-7.43 (d, 1H), 7.38-7.33 (d, 1H), 7.32-7.26 (m, 1H), 7.09-7.00 (q, 1H), 6.66-6.58 (t, 1H), 4.33-4.22 (d, 1H), 4.13-3.81 (m, 3H), 3.17-3.09 (t, 1H), 1.93-1.89 (s, 3H), 1.89-1.82 (t, 3H), 1.56-1.24 (m, 4H), 0.97-0.88 (t, 3H); MS (EI) for $C_{20}H_{21}F_3IN_3O_2$: 520 (MH^+).

[0595] EXAMPLE 20(o). 3-(1-aminocyclopentyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, $CDCl_3$): 8.27-8.21 (s, 1H), 7.42-7.36 (d, 1H), 7.34-7.29 (d, 1H), 7.15-7.09 (t, 1H), 7.09-7.01 (q, 1H), 6.88-6.79 (q, 1H), 6.63-6.53 (m, 1H), 4.18-3.92 (m, 4H), 2.12-2.08 (s, 3H), 2.06-1.70 (m, 7H), 0.92-0.68 (m, 4H); MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 532 (MH^+).

[0596] EXAMPLE 20(p). *N*-{1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}acetamide: ^{1}H NMR (400 MHz, CDCl3): 8.42 (s, 1H), 7.41-7.38 (dd, 1H), 7.34-7.32 (dt, 1H), 7.12-7.09 (m, 1H), 6.85-6.78 (m, 1H), 6.63-6.57 (m, 1H), 5.76 (b, 1H), 4.28-3.98 (m, 5H), 2.00 (s, 3H), 1.20-1.19 (d, 3H); MS (EI) for $C_{20}H_{19}F_3IN_3O_3$: 534 (MH^+).

[0597] EXAMPLE 20(q). (2R)-*N*-{1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanamide: ^{1}H NMR (400 MHz, CDCl3): 8.47 (s, 1H), 7.45-7.40 (m, 5H), 7.33-7.31 (m, 1H), 7.21-7.19 (m, 1H), 7.12-7.05 (m, 1H), 6.85-6.76 (m, 1H), 6.63-6.58 (m, 1H), 4.20-3.99 (m, 5H), 3.36 (s, 1.5H), 3.34 (s,1.5H), 1.27-1.25 (d, 1.5H), 1.24-1.22 (d, 1.5H); MS (EI) for $C_{28}H_{24}F_6IN_3O_4$: 708 (MH^+).

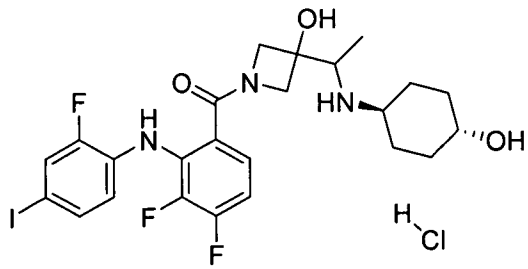
[0598] EXAMPLE 20(r). (2R)-*N*-{(1R)-1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanamide: ^{1}H NMR (400 MHz, CDCl3): 8.49 (s, 1H), 7.46-7.391 (m, 5H), 7.33-7.31 (m, 1H), 7.21-7.16 (m, 1H), 7.14-7.10 (m, 1H), 6.85-6.79 (m, 1H), 6.64-6.58 (m, 1H), 4.24-4.00 (m, 5H), 3.35 (s, 3H), 1.25-1.23 (d, 3H); MS (EI) for $C_{28}H_{24}F_6IN_3O_4$: 708 (MH^+).

[0599] EXAMPLE 20(s). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methyl-1-nitroethyl)azetidin-3-ol: ^{1}H NMR (400 MHz, CDCl3): 8.28 (s, 1H), 7.41-7.38 (dd, 1H), 7.34-7.32 (dt, 1H), 7.14-7.10 (m, 1H), 6.87-6.81 (m, 1H), 6.64-6.59 (m, 1H), 4.33-4.15 (m, 4H), 1.64 (s, 6H); MS (EI) for $C_{19}H_{17}F_3IN_3O_4$: 536 (MH^+).

[0600] **EXAMPLE 20(t).** 3-(1-amino-1-methylethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: ^{1}H NMR (400 MHz, CDCl3): 8.30 (s, 1H), 7.39-7.36 (dd, 1H), 7.32-7.30 (dt, 1H), 7.13-7.09 (m, 1H), 6.85-6.79 (m, 1H), 6.62-6.56 (m, 1H), 4.25-3.97 (m, 4H), 1.14 (s, 6H); MS (EI) for $C_{19}H_{19}F_3IN_3O_2$: 506 (MH^+).

EXAMPLE 21

1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1-[(*trans*-4-hydroxycyclohexyl)amino]ethyl}azetidin-3-ol hydrochloride



[0601] Potassium *tert*-butoxide (1.672 g, 14.9 mmol) and ethyltriphenylphosphonium bromide (5.538 g, 14.9 mmol) were stirred in ether (30 mL) at amibient for 1 h. 1,1-Dimethylethyl 3-oxoazetidine-1-carboxylate (954 mg, 6.0 mmol), prepared using procedures similar to those described in Example 3, was added and the mixture was 35 °C for 4.5 h. Mixture was filtered through celite and the solid was washed with ether. The filtrate was washed with water, brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 20% ether in hexanes) gave 1,1-dimethylethyl 3-ethylideneazetidine-1-carboxylate (506 mg, 2.76 mmol, 49% yield): ^{1}H NMR (400 MHz, $CDCl_3$): 5.37-5.28 (m, 1H), 4.47-4.39 (m, 4H), 1.56-1.51 (m, 3H), 1.45 (s, 9H).

[0602] 1,1-Dimethylethyl 3-ethylideneazetidine-1-carboxylate (506 mg, 2.76 mmol), and 4-methylmorpholine *N*-oxide (1.04 g, 8.89 mmol) were dissolved in acetone / water (4:1; 30 mL) and osmium tetroxide (2.5 wt.% in *t*-butanol; 0.2 mL) was added. The solution was stirred at ambient for 5 days, then was quenched with saturated sodium bisulfite (2 mL) and concentrated *in vacuo*. The residue was partitioned between ethyl acetate and brine. The aqueous portion was extracted with ethyl acetate. The combined organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, ethyl acetate) gave 1,1-dimethylethyl 3-hydroxy-3-(1-hydroxyethyl)azetidine-1-carboxylate (375 mg, 1.73 mmol, 63% yield): ^{1}H NMR (400 MHz, $CDCl_3$): 4.00-3.77 (m, 5H), 2.65 (br s, 1H), 1.86, (br s, 1H), 1.44 (s, 9H), 1.25 (d, 3H).

[0603] 1,1-Dimethylethyl 3-hydroxy-3-(1-hydroxyethyl)azetidine-1-carboxylate (200 mg, 0.922 mmol) was dissolved in methanol (5 mL) and 4 N hydrochloric acid in dioxane (1 mL, 4 mmol) was added. The mixture was refluxed for 15 minutes and then was concentrated *in vacuo* to afford 3-(1-hydroxyethyl)azetidin-3-ol hydrochloride (0.922 mmol).

[0604] 3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid (362 mg, 0.921 mmol), prepared using procedures similar to those described in US 7,019,033, 4-(dimethylamino)pyridine (337 mg, 2.76 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (212 mg, 1.11 mmol) were dissolved in DMF (3 mL). The mixture was stirred at ambient for 5 minutes and then 3-(1-hydroxyethyl)azetidin-3-ol hydrochloride (0.922 mmol) in DMF (2 mL) was added and the mixture was stirred for 15 h. The mixture was partitioned between ethyl acetate and 5% lithium chloride. The organic portion was washed with 20% citric acid, saturated sodium bicarbonate and brine, then was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 80% ethyl acetate in hexanes) gave 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-hydroxyethyl)azetidin-3-ol (296 mg, 0.602 mmol, 65% yield): MS (EI) for $C_{18}H_{16}F_3IN_2O_3$: 493 (MH^+).

[0605] 1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-hydroxyethyl)azetidin-3-ol (267 mg, 0.543 mmol), was dissolved in dichloromethane (10 mL) and treated with 4-(dimethylamino)pyridine (80 mg, 0.661 mmol) and 2,4,6-triisopropylbenzenesulfonyl chloride (183 mg, 0.604 mmol) at ambient for 15 h. Triethylamine (0.076 mL, 0.545 mmol) was added and the mixture was stirred at ambient for 3 h and then at 35 °C for 4 h and then at ambient for a furhter 15 h. 2,4,6-Triisopropyl-benzenesulfonylchloride (110 mg, 0.363 mmol) was added and the mixture was stirred at 35 °C for 3 h and then 4-(dimethylamino)pyridine (80 mg, 0.661 mmol) was added and the mixture was stirred at 35 °C for 2 h. 2,4,6-Triisopropylbenzenesulfonyl chloride (303 mg, 1.0 mmol) was added and the mixture was stirred at 35 °C for a further 18 h. The mixture was adsorbed on to silica and purified by column chromatography (silica gel, 30-50% ethyl acetate in hexanes) to give 1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-hydroxyazetidin-3-yl]ethyl 2,4,6-tris(1-methylethyl)benzenesulfonate (201 mg, 0.265 mmol, 49% yield): MS (EI) for $C_{33}H_{38}F_3IN_2O_5S$: 759 (MH^+).

[0606] 1-[1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl 2,4,6-tris(1-methylethyl)benzenesulfonate (194 mg, 0.256 mmol) was dissolved in tetrahydrofuran (2 mL) and was cooled to 0 °C. Sodium hydride (60 wt%

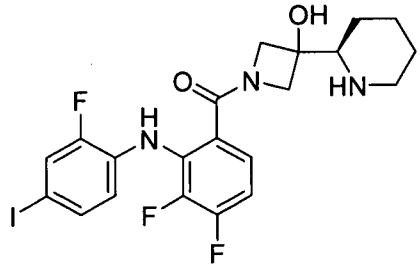
dispersion in oil; 31 mg, 0.775 mmol) was added and the mixture was stirred at 0 °C for 15 minutes. The mixture was quenched with saturated sodium bicarbonate solution and partitioned with ethyl acetate. The aqueous portion was extracted with ethyl acetate. The combined organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 50% ethyl acetate in hexanes) gave 2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)-6-[(2-methyl-1-oxa-5-azaspiro[2.3]hex-5-yl)carbonyl]aniline (120 mg, 0.253 mmol, 99% yield): MS (EI) for $C_{18}H_{14}F_3IN_2O_2$: 475 (MH^+).

[0607] 2,3-Difluoro-*N*-(2-fluoro-4-iodophenyl)-6-[(2-methyl-1-oxa-5-azaspiro[2.3]hex-5-yl)carbonyl]aniline (50 mg, 0.105 mmol) was dissolved in dimethylsulfoxide (0.8 mL) and treated with *trans*-4-cyclohexanolamine (70 mg, 0.609 mmol) with 100 W microwave power at 100 °C for 45 minutes. The mixture was purified by reverse phase HPLC and the clean fractions were combined, neutralized with saturated sodium bicarbonate solution and the organic solvent was removed *in vacuo*. The remaining aqueous residue was extracted twice with ethyl acetate. The combined organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to give a residue which was treated with aqueous hydrochloric acid and then was lyophilized to afford 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1-[(*trans*-4-hydroxycyclohexyl)amino]ethyl}azetidin-3-ol hydrochloride (36 mg, 0.058 mmol, 55% yield): ^{1}H NMR (400 MHz, d_6-DMSO): 8.61 (br s, 0.5H), 8.55 (br s, 0.5H), 8.49-8.33 (m, 1H), 8.08-7.90 (m, 1H), 7.59 (dd, 1H), 7.39 (br d, 1H), 7.37-7.30 (m, 1H), 7.21 (br q, 1H), 6.81 (br d, 1H), 6.77-6.65 (m, 1H), 4.20 (br d, 1H), 4.09-4.02 (m, 1H), 3.97 (br d, 1H), 3.93-3.80 (m, 1H), 3.62-3.47 (m, 1H), 3.03-2.90 (m, 1H), 2.07-1.93 (m, 2H), 1.93-1.77 (m, 2H), 1.54-1.06 (m, 8H); MS (EI) for $C_{24}H_{27}F_3IN_3O_3$: 590 (MH^+).

[0608] **EXAMPLE 21(a).** Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the following MEK compound was prepared: 1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1-[(1,1-dimethylethyl)amino]ethyl}azetidin-3-ol: ^{1}H NMR (400 MHz, d_6-DMSO): 8.63 (br s, 0.4H), 8.53 (br s, 0.6H), 7.56 (dt, 1H), 7.40-7.34 (m, 1H), 7.32-7.26 (m, 1H), 7.25-7.13 (m, 1H), 6.72-6.62 (m, 1H), 5.43 (br s, 1H), 4.14-3.56 (m, 4H), 2.69-2.53 (m, 1H), 1.00-0.85 (br, 12H); MS (EI) for $C_{22}H_{25}F_3IN_3O_2$: 548 (MH^+).

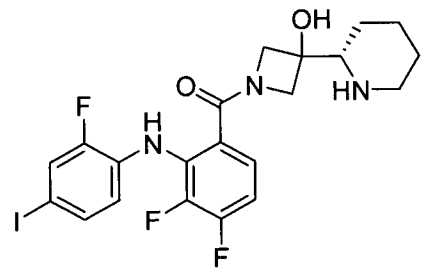
EXAMPLE 22(a) and 22(b)

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2R)-piperidin-2-yl]azetidin-3-ol



and

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol



[0609] To a solution of 1,1-dimethylethyl 2-(3-hydroxy-1-{[(phenylmethyl)oxy] carbonyl}azetidin-3-yl)piperidine-1-carboxylate (368 mg, 0.94 mmol), prepared using procedures similar to those described in Reference 5, in dichloromethane (5 mL) was added DMAP (115 mg, 0.94 mmol) and the resulting solution was cooled to 0°C. (*R*)-(-)-α-Methoxy-α-trifluoromethylphenylacetyl chloride (105 μL, 0.56 mmol) was added to the solution by syringe and the mixture was allowed to warm to room temperature then stirred an additional 12 hours. The solution was then partitioned with saturated aqueous soldium bicarbonate and the organic phase dried over anhydrous magnesium sulfate then filtered and concentrated to an oily residue. Silica gel flash chromatography using hexanes:ethyl acetate 3:1 as eluent afforded the less polar 1,1-dimethylethyl (2*R*)-2-(1-{[(phenylmethyl)oxy] carbonyl}-3-{[(2*R*)-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanoyl]oxy}azetidin-3-yl)piperidine-1-carboxylate (27.5 mg, 5% yield), the more polar 1,1-dimethylethyl (2*S*)-2-(1-{[(phenylmethyl)oxy]carbonyl}-3-{[(2*R*)-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanoyl]oxy}azetidin-3-yl)piperidine-1-carboxylate (105 mg, 19% yield) and starting material (253 mg, 69% recovery).

[0610] The starting material thus recovered was taken into dichloromethane (3 mL) followed by addition of DMAP (115 mg, 0.94 mmol) and (*R*)-(-)-α-methoxy-α-trifluoromethylphenylacetyl chloride (105 μL, 0.56 mmol) and the mixture was allowed to stir at room temperature over 12 hours. Proceeding as before afforded combined 1,1-dimethylethyl (2R)-2-(1-{[(phenylmethyl)oxy]carbonyl}-3-{[(2*R*)-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanoyl]oxy}azetidin-3-yl)piperidine-1-carboxylate (46.6 mg, 8% yield), the more polar 1,1-dimethylethyl (2*S*)-2-(1-{[(phenylmethyl)oxy]carbonyl}-3-{[(2*R*)-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanoyl]oxy}azetidin-3-yl)piperidine-1-carboxylate (228 mg, 41% yield) and starting material (100.8 mg, 27% recovery).

[0611] The starting material thus recovered was taken into tetrahydrofuran-dichloromethane (1:1, 2 mL) followed by addition of DMAP (47 mg, 0.39 mmol) and (R)-(-)-α-methoxy-α-trifluoromethylphenylacetyl chloride (80 μL, 0.43 mmol) and the mixture was heated to 60 °C over 12 hours. Proceeding as before afforded combined less polar 1,1-dimethylethyl (2*R*)-2-(1-{[(phenylmethyl)oxy]carbonyl}-3-{[(2*R*)-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanoyl]oxy}azetidin-3-yl)piperidine-1-carboxylate (144 mg, 26 % yield). The chiral ester derivatives thus obtained were again subject to silica gel flash chromatography using hexanes:ethyl acetate 3:1 as eluent to give the pure less polar 1,1-dimethylethyl (2*R*)-2-(1-{[(phenylmethyl)oxy]carbonyl}-3-{[(2*R*)-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanoyl]oxy}azetidin-3-yl)piperidine-1-carboxylate (122.8 mg, 22% yield) and the more polar 1,1-dimethylethyl (2*S*)-2-(1-{[(phenylmethyl)oxy]carbonyl}-3-{[(2*R*)-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanoyl]oxy}azetidin-3-yl)piperidine-1-carboxylate (177.6 mg, 32% yield) both as colorless amorphous residues.

[0612] 1,1-Dimethylethyl (2*R*)-2-(1-{[(phenylmethyl)oxy]carbonyl}-3-{[(2*R*)-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanoyl]oxy}azetidin-3-yl)piperidine-1-carboxylate (122.8 mg, 0.21 mmol) was taken into methanol (4 mL) followed by addition of 1M aqueous sodium hydroxide (1 mL) and the resulting solution was stirred for one hour at room temperature. The solution was then partitioned with ethyl acetate and 1N aqueous hydrochloric acid. The organic layer was washed with brine, dried over anhydrous magnesium sulfate then filtered and concentrated. The residue was purified by silica gel flash chromatography using hexanes:ethyl acetate 2:1 to give 1,1-dimethylethyl (2*R*)-2-(3-hydroxy-1-{[(phenylmethyl)oxy]carbonyl}azetidin-3-yl)piperidine-1-carboxylate (60.8 mg, 81% yield) a colorless amorphous solid. 1,1-dimethylethyl (2*S*)-2-(3-hydroxy-1-

{[(phenylmethyl)oxy]carbonyl}azetidin-3-yl)piperidine-1-carboxylate (87.4 mg, 75% yield) was prepared analogously.

[0613] 1,1-Dimethylethyl (2*R*)-2-(3-hydroxy-1-{[(phenylmethyl)oxy]carbonyl}azetidin-3-yl)piperidine-1-carboxylate (60.8 mg, 0.16 mmol) and 10% Pd/C (30 mg) were taken into methanol (2 mL) and the mixture hydrogenated at ambient pressure for one hour. The suspension was then filtered through a celite pad and concentrated then dried *in vacuo* to a colorless solid. The solid amine was taken into THF (1 mL) followed by addition of DIPEA (42 μL, 0.24 mmol) and 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoyl fluoride (63 mg, 0.16 mmol), prepared using procedures similar to those described in Reference 1, and the mixture stirred at room temperature for 30 minutes. The reaction mixture was partitioned with ethyl acetate and 1 N aqueous hydrochloric acid and the organic layer washed with brine, dried over anhydrous magnesium sulfate then filtered and concentrated. Purification of the residue by silica gel flash chromatography using hexanes:ethyl acetate 3:2 as eluent afforded 1,1-dimethylethyl (2*R*)-2-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate (74.9 mg, 74% yield) as an amorphous solid. 1,1-Dimethylethyl (2*R*)-2-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate ^{1}H NMR (400 MHz, $CDCl_3$): 8.53 (br s, 0.5H), 8.40 (br s, 0.5H), 7.41-7.38 (dd, 1H), 7.34-7.31(dt, 1H), 7.17-7.14 (m, 1H), 6.86-6.79 (m, 1H), 6.63-6.587 (m, 1H), 4.24-3.90 (m, 4H), 3.37-3.23 (m, 1H), 2.90-2.80 (m, 1H), 1.85-1.54 (m, 7H), 1.43 (s, 9H); MS (EI) for $C_{26}H_{29}F_3IN_3O_4$: 576 ($M\text{-}C_4H_9^+$).

[0614] 1,1-dimethylethyl (2*R*)-2-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate (74.9 mg, 0.12 mmol) was taken into methanol (1 mL) followed by addition of 4 N HCl in dioxane (1 mL) and the solution was stirred at room temperature for one hour. The solution was then concentrated and the residue partitioned with chloroform and saturated aqueous sodium bicarbonate. The organic layer was washed with brine, dried over anhydrous sodium sulfate then filtered and concentrated. Purification of the residue by silica gel flash chromatography using ethyl acetate then concentrated aqueous ammonia in chloroform and methanol (0.1:10:1) as eluents afforded 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*R*)-piperidin-2-yl]azetidin-3-ol (57.3 mg) as a colorless amorphous solid. The free base was taken into methanol (1 mL) then brought to about pH 1 by addition of 4 N HCl in dioxane

and the solution concentrated. The residue was triturated with ethyl ether to afford a suspension. The solid was collected by filtration to afford 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*R*)-piperidin-2-yl]azetidin-3-ol hydrochloride salt (49 mg, 72% yield) as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): 8.43-8.39 (d, 1H), 7.41-7.38 (dd, 1H), 7.33-7.31(dt, 1H), 7.14-7.10 (m, 1H), 6.84-6.80 (m, 1H), 6.63-6.57 (m, 1H), 4.12-3.99 (m, 4H), 3.10-3.08 (d, 1H), 2.72-2.69 (d, 1H), 2.64-2.62 (m, 1H), 1.61-1.58 (m, 2H), 1.36-1.16 (m, 4H); MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 532 (MH^+).

[0615] Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the following MEK compounds were prepared:

[0616] **EXAMPLE 22(c).** 1,1-dimethylethyl (2S)-2-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate: ^{1}H NMR (400 MHz, $CDCl_3$): 8.52 (br s, 0.5H), 8.39 (br s, 0.5H), 7.41-7.38 (dd, 1H), 7.34-7.31(dt, 1H), 7.17-7.12 (m, 1H), 6.85-6.79 (m, 1H), 6.63-6.57 (m, 1H), 4.25-3.88 (m, 4H), 3.34-3.26 (m, 1H), 2.80-2.90 (m, 1H), 1.85-1.54 (m, 7H), 1.43 (s, 9H); MS (EI) for $C_{26}H_{29}F_3IN_3O_4$: 576 ($M-C_4H_9^+$).

[0617] **EXAMPLE 22(d).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol hydrochloride: ^{1}H NMR (400 MHz, d_4-Methanol): 7.49-7.46 (dd, 1H), 7.37-7.35(dt, 1H), 7.35-7.30 (m, 1H), 7.10-7.04 (m, 1H), 6.64-6.59 (m, 1H), 4.39-4.32 (dd, 1H), 4.21-4.18 (dd, 1H), 4.13-4.07 (m, 1H), 3.97-3.88 (dd, 1H), 3.57-3.32 (m, 1H), 3.02-2.96 (dd,1H), 1.90-1.50 (m, 7H); MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 532 (MH^+).

[0618] **EXAMPLE 22(e).** 1-({2-[(4-bromo-2-chlorophenyl)amino]-3,4-difluorophenyl} carbonyl)-3-piperidin-2-ylazetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.56 (d, 1H), 7.29-7.38 (m, 2H), 7.08-7.16 (m, 1H), 6.64-6.70 (m, 1H), 4.30-4.40 (m, 1H), 4.18-4.26 (m, 1H), 4.04-4.14 (m, 1H), 3.90-4.00 (m, 1H), 3.16-3.26 (m, 2H), 2.86-2.96 (m, 1H), 1.91 (s, 3H), 1.76-1.88 (m, 3H), 1.44-1.64 (m, 3H). MS (EI) for $C_{21}H_{21}BrClF_2N_3O_2$: 500 (M-H).

[0619] **EXAMPLE 22(f).** 1-({2-[(4-bromo-2-fluorophenyl)amino]-3,4-difluorophenyl} carbonyl)-3-piperidin-2-ylazetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, DMSO): 8.52 (br s, 1H), 7.50 (d, 1H), 7.35-7.15 (m, 3H), 6.88-6.79 (m, 1H), 4.15-3.96 (m, 1H), 3.84-3.78 (m, 1H), 3.68-3.63 (m, 1H), 2.95-2.88 (m, 1H), 2.48-2.40 (m, 2H), 1.71-1.42 (m, 3H), 1.25-1.14 (m, 2H), 1.03-0.90 (m, 1H); MS (EI) for $C_{21}H_{21}BrF_3N_3O_2$: 485 (MH^+).

[0620] **EXAMPLE 22(g).** 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-pyrrolidin-2-ylazetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.45 (dd, 1H), 7.37-

7.31 (m, 1H), 7.30-7.25 (m, 1H), 7.13-6.99 (m, 1H), 6.67-6.54 (m, 1H), 4.20-4.09 (m,1H), 4.08-3.91 (m, 2H), 3.88-3.79 (m, 1H), 3.27 (t, 1H), 2.99-2.89 (m, 1H), 2.88-2.81 (m, 1H), 1.93-1.67 (m, 3H), 1.55-1.42 (m, 1H). MS (EI) for $C_{20}H_{19}F_3IN_3O_2$: 518 (MH^+)

[0621] EXAMPLE 22(h). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-(1-methylpyrrolidin-2-yl)azetidin-3-ol acetate (salt): ^{1}H NMR (400 MHz, CD_3OD): 7.46 (dd, 1H), 7.38-7.26 (m, 2H), 7.12-6.99 (m, 1H), 6.66-6.56 (m, 1H), 4.37-3.87 (m,4H), 2.94-2.82 (m, 1H), 2.75-2.63 (m, 3H), 2.20-2.06 (m, 1H), 2.00-1.67 (m, 8H). MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 532 (MH^+).

[0622] EXAMPLE 22(i). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-(1-ethylpyrrolidin-2-yl)azetidin-3-ol acetate (salt): ^{1}H NMR (400 MHz, CD_3OD): 7.46 (d, 1H), 7.38-7.33 (m, 1H), 7.32-7.27 (m, 1H), 7.12-7.01 (m, 1H), 6.66-6.57 (m, 1H), 4.34-3.89 (m,4H), 3.57 (t, 1H), 3.51-3.40 (m, 1H), 3.28-2.81(m, 3H), 2.25-1.72 (m, 8H), 1.31-1.18 (m, 3H). MS (EI) for $C_{22}H_{23}F_3IN_3O_2$: 546 (MH^+).

[0623] EXAMPLE 22(j). 1-({4-fluoro-5-[(2-fluoro-4-iodophenyl)amino]-1-methyl-1*H*-benzimidazol-6-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, d_4-MeOH): 8.30 (s, 1H), 7.56 (s, 1H), 7.42 (d, 1H), 7.24 (d, 1H), 6.34 (m, 1H), 4.20 (d, 2H), 3.92 (s, 3H), 3.38-3.24 (m, 3H), 3.08 (bs, 1H), 2.88 (bs (1*H*), 1.90-1.70 (m, 3H), 1.66-1.32 (m, 3H); MS (EI) for $C_{23}H_{24}F_2IN_5O_2$: 568 (MH^+).

[0624] EXAMPLE 22(k). 1-({7-fluoro-6-[(2-fluoro-4-iodophenyl)amino]-1-methyl-1*H*-benzimidazol-5-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, d_4-MeOH): 8.22 (s, 1H), 7.60 (s, 1H), 7.42 (d, 1H), 7.26 (d, 1H), 6.46 (m, 1H), 4.21 (d, 2H), 4.06 (s, 3H), 3.88 (m, 1H), 3.38-3.24 (m, 3H), 3.10 (bs, 1H), 2.88 (bs (1*H*), 1.88-1.70 (m, 3H), 1.64-1.28 (m, 3H); MS (EI) for $C_{23}H_{24}F_2IN_5O_2$: 568 (MH^+).

[0625] EXAMPLE 22(m). 4-[(4-bromo-2-fluorophenyl)amino]-3-fluoro-5-({3-hydroxy-3-[(2S)-piperidin-2-yl]azetidin-1-yl}carbonyl)-1-methylpyridin-2(1*H*)-one: MS (EI) for $C_{21}H_{23}BrF_2N_4O_3$: 498 (MH^+).

[0626] EXAMPLE 22(n). 1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol: ^{1}H NMR (400MHz, d_6-DMSO): 8.79 (s, 1H), 8.04 (d, 1H), 7.91 (d, 1H), 7.64 (dd, 1H), 7.55 (d, 1H), 6.95-7.02 (m, 1H), 4.38 (d, 1H), 4.15 (dd, 1H), 3.99 (dd, 1H), 3.72 (q, 1H), 3.32-3.39 (m, 1H), 3.00-3.12 (m, 1H), 1.93 (t, 3H), 1.51-1.70 (m, 3H); MS (EI) for $C_{22}H_{22}ClFIN_5O_2$: 532 (MH^+).

[0627] EXAMPLE 22(o). 1-({7-[(4-bromo-2-chlorophenyl)amino]-8-chloroimidazo[1,2-a]pyridin-6-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol: ^{1}H NMR (400MHz, d_4-

MeOH): 8.85 (s, 1H), 8.06 (d, 1H), 7.91 (d, 1H), 7.71 (d, 1H), 7.45 (d, 1H), 7.01 (d, 1H), 4.48 (d, 1H), 4.10-4.27 (m, 2H), 3.87 (q, 1H), 3.37 (d, 2H), 3.02 (s, 1H), 1.88-1.94 (m, 3H), 1.58-1.69 (m, 3H); $C_{22}H_{22}BrCl_2N_5O_2$: 540 (MH^+).

[0628] EXAMPLE 22(p). 1-({6-[(4-bromo-2-chlorophenyl)amino]-7-fluoro-3-methyl-1,2-benzisoxazol-5-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol: ^1H NMR (400MHz, $CDCl_3$): 8.50 (m, 1H), 7.51 (d, 1H), 7.42 (s, 1H), 7.26 (dd, 1H), 6.79 (dd, 1H), 4.20-3.98 (br m, 4H), 3.11 (d , 1H), 2.77-2.50 (br m, 5H), 1.80-1.15 (br m, 6H); MS (EI) for $C_{23}H_{23}BrClFN_4O_3$: 537 (MH^+).

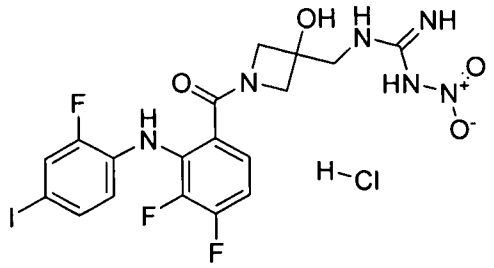
[0629] EXAMPLE 22(q). 1-({3-fluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol: ^1H NMR (400 MHz, d_4-MeOH): 7.53 (2d, 1H), 7.46 (m, 2H), 7.16 (t, 1H), 6.86 (m, 1H), 6.63 (m, 1H), 4.36 (m, 1H), 4.22 (m, 1H), 4.02 (m, 1H), 3.88 (m, 1H), 3.08 (d, 1H), 2.66 (dd, 1H), 2.56 (m, 1H), 1.82 (bs, 1H), 1.66 (d, 1H), 1.58 (d, 1H), 1.38 (m, 2H), 1.22 (m, 1H); MS (EI) for $C_{21}H_{22}F_2IN_3O_2$: 514 (MH^+).

[0630] EXAMPLE 22(r). 1-({4-fluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol: ^1H NMR (400 MHz, d_4-MeOH): 7.42 (2d, 1H), 7.34-7.18 (m, 4H), 6.46 (m, 1H), 4.10 (m, 2H), 3.84 (m, 2H), 3.04 (d, 1H), 2.52 (dd, 2H), 1.76 (bs, 0.5H), 1.58 (m, 2.5H), 1.32 (m, 2H), 1.18 (m, 0.5H), 1.04 (m, 0.5H); MS (EI) for $C_{21}H_{22}F_2IN_3O_2$: 514 (MH^+).

[0631] EXAMPLE 22(s). 5-[(2-fluoro-4-iodophenyl)amino]-6-({3-hydroxy-3-[(2S)-piperidin-2-yl]azetidin-1-yl}carbonyl)-2-methylpyridazin-3(2*H*)-one: ^1H NMR (400MHz, d_6-DMSO): 10.19 (s, 1H), 7.78 (dd, 1H), 7.59 (d, 1H), 7.32 (t, 1H), 5.95 (s, 1H), 4.59 (q, 1H), 4.13-4.27 (m, 2H), 3.77 (d, 1H), 3.62 (s, 3H), 3.02 (d, 2H), 2.71 (d, 1H), 1.78 (s, 1H), 1.68 (d, 1H), 1.53 (d, 1H), 1.32 (s, 2H), 1.17 (t, 1H); MS (EI) for $C_{20}H_{23}FIN_5O_3$: 528 (MH+).

Example 23

1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-3-nitroguanidine hydrochloride

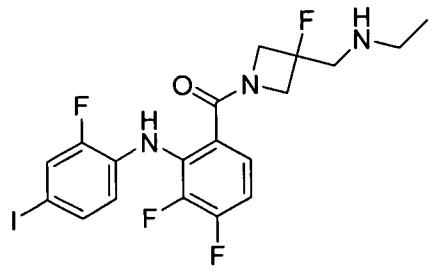


[0632] To a mixture of 2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)-6-(1-oxa-5-azaspiro[2,3]hex-5-ylcarbonyl)aniline (0.15g, 0.33 mmol), prepared using procedures similar to those described in Example 21, and nitroguanidine (0.1 g, 1.00 mmol) in tetrahydrofuran (3.00 mL) an aqueous solution of sodium hydroxide (1.0 mL, 2.0 mmol) was added and the reaction mixture was stirred at 70 °C for 16 hours. The reaction mixture was concentrated *in vacuo*. The crude product was purified by reverse phase preparative HPLC. The fractions were collected, and the solvent was concentrated. The residue was partitioned with ethyl acetate. The organic layer was washed with saturated aqueous sodium bicarbonate, brine and dried over anhydrous sodium sulfate. Filtration and concentration resulted in an amorphous residue, which was dissolved in methanol, and 4 N HCl in dioxane (80 μL, 0.33 mmol) was added to the solution. A white precipitate formed and was collected by filtration. The solid was washed with hexane, and dried to afford 76 mg (38%) 1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-3-nitroguanidine hydrochloride. ^{1}H NMR (400 MHz, d_4-MeOH): 7.46 (2d, 1H), 7.36 (m, 1H), 7.29 (m, 1H), 7.02 (m, 1H), 6.63 (m, 1H), 4.22 (m, 1H), 4.01 (m, 2H), 3.86 (m, 1H), 3.51 (d, 2H); MS (EI) for $C_{18}H_{16}F_3IN_6O_4$: 565 (MH^+).

[0633] **EXAMPLE 23(a).** Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the following MEK compounds were prepared: 1-cyano-3-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino] phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}guanidine hydrochloride. ^{1}H NMR (400 MHz, d_4-MeOH): 7.47 (2d, 1H), 7.36 (m, 1H), 7.27 (m, 1H), 7.03 (m, 1H), 6.63 (m, 1H), 4.18 (m, 1H), 3.98 (m, 2H), 3.80 (m, 1H), 3.43 (s, 2H); MS (EI) for $C_{19}H_{16}F_3IN_6O_2$: 545 (MH^+).

EXAMPLE 24

6-({3-[(ethylamino)methyl]-3-fluoroazetidin-1-yl}carbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline

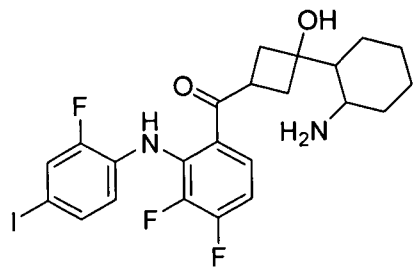


[0634] To 1,1-dimethylethyl [{1-({3,4-difuoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-hydroxyazetidin-3-yl]methyl}ethylcarbamate (27 mg, 0.044 mmol), prepared using procedures similar to those in Example 3 and followed by Boc-protection, in chloroform (2.5 mL) added DAST (11.8 μL, 0.089 mmol) and stirred for 3.5 hr at room temperature. Quenched with water (15 mL), partitioned phases and extracted aqueous phase with chloroform (2 X 15mL). The combined chloroform extracts were dried over sodium sulfate, filtered and the filtrate concentrated *in vacuo*. The residue was purified on a silica gel column to afford 1,1-dimethylethyl [{1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino] phenyl}carbonyl)-3-fluoroazetidin-3-yl]methyl}ethylcarbamate (19.0 mg, 70%).

[0635] To the 1,1-dimethylethyl [{1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino] phenyl}carbonyl)-3-fluoroazetidin-3-yl]methyl}ethylcarbamate (19.0 mg, 0.031 mmol) in acetonitrile (1.0 mL) added a solution 4.0N hydrogen chloride in dioxane (1.0 mL). After 1.5hr the solution was concentrated *in vacuo*. The residue was purified by preparative reverse phase HPLC to afford the title compound (4.30 mg, 27%). ^{1}H NMR (400MHz, $CDCl_3$): 8.25 (s, 1H), 7.33 (dd, 1H), 7.33-7.25 (m, 1H), 7.18-7.14 (m, 1H), 6.84-6.77 (m, 1H), 6.63-6.58 (m, 1H), 4.33-4.05 (br m, 4H), 3.07-2.95 (br m, 2H), 2.65 (q, 2H), 1.08 (t, 3H); MS (EI) for $C_{19}H_{18}F_4IN_3O$: 508 (MH^+).

EXAMPLE 25

3-(2-aminocyclohexyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol



[0636] A solution of 1-(trimethylsiloxy)cyclohexene (200 mg, 1.17 mmol) and benzyl 3-oxoazetidine-1-carboxylate (289 mg, 1.41 mmol), prepared using procedures similar to those described in Reference 3, in tetrahydrofuran (3.90 mL) was cooled to -78 °C for 10 minutes followed by the addition of titanium tetrachloride (0.13 mL, 1.17 mmol). The reaction mixture stirred for an additional 5 hours at -78 °C. The mixture was quenched with aqueous sodium bicarbonate and the aqueous layer was extracted with ether (2x). The

organic layer was separated, dried over anhydrous sodium sulfate, filtered and the filtrate was concentrated *in vacuo*. The residue was purified on silica gel chromatography column (3:2 hexanes/ethyl acetate) to afford benzyl 3-hydroxy-3-(2-oxocyclohexyl)azetidine-1-carboxylate (328 mg, 37%) . ^{1}H NMR ($CDCl_3$): 7.28-7.34 (m, 5H), 5.08 (s, 2H), 4.02 (d, 1H), 3.89 (d, 1H), 3.87 (s, 1H), 3.55 (s, 1H), 2.71 (q, 1H), 2.29-2.43 (m, 2H), 2.11 (s, 2H), 1.95 (s, 1H), 1.66 (d, 3H); MS (EI) for $C_{17}H_{21}NO_4$: 303 (MH+).

[0637] A solution of benzyl 3-hydroxy-3-(2-oxocyclohexyl)azetidine-1-carboxylate (100 mg, 330 mmol) in methanol (1.60 mL) in the presence of ammonium acetate (191 mg, 2.48 mmol was cooled to 0 °C for 1 hour. Sodium cyanoborohydride (81.5 mg, 1.30 mmol) was added and the mixture was stirred at room temperature for 16 hours. To the reaction mixture was added 6 N hydrogen chloride (800 μL) and extracted with ethyl acetate. The aqueous layer was basified with aqueous sodium bicarbonate (pH 9) and extracted with dichloromethane. The combined organic portion was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to afford benzyl-3-(2-aminocyclohexyl)-3-hydroxyazetidine-1-carboxylate (73.7 mg, 73%) . MS (EI) for $C_{17}H_{24}N_2O_3$: 305 (MH+).

[0638] To a solution of benzyl-3-(2-aminocyclohexyl)-3-hydroxyazetidine-1-carboxylate (202 mg, 0.663 mmol) in dioxane-water (1:1, 2.5 mL) was added di-*tert*-butyl dicarbonate (138 mg, 0.630 mmol) and solid sodium bicarbonate (112 mg, 1.33 mmol). The reaction mixture was stirred at room temperature for 2 hours and evaporated. The residue was partitioned between ethyl acetate and water. The organic layer was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to afford benzyl 3-(2-*tert*-butoxycarbonylamino)cyclohexyl)-3-hydroxyazetidine-1-carboxylate (237 mg, 100%). ^{1}H NMR (CH_3OH): 7.15-7.21 (m, 5H), 5.45 (s, 0.5H), 5.20 (d, 0.5H), 4.95 (s, 2H), 4.81 (s, 1H), 3.81 (d, 2H), 1.43-1.74 (m, 5H), 1.39 (s, 1H), 1.31 (s, 11H), 1.20 (s, 1H). MS (EI) for $C_{22}H_{32}N_2O_5$: 405 (MH+).

[0639] A solution of benzyl 3-(2-tert-butoxycarbonylamino)cyclohexyl)-3-hydroxyazetidine-1-carboxylate (237 mg, 0.586 mmol) in ethyl acetate (2 mL) was hydrogenated over 10% palladium-carbon (200 mg, 0.586 mmol) at 40 psi for 16 hours. The reaction mixture was filtered and concentrated *in vacuo* to provide *tert*-butyl 2-(3-hydroxyazetidin-3-yl)cyclohexylcarbamate (181 mg, 100%). ^{1}H NMR ($CDCl_3$): 5.10 (s, 1H), 4.80 ((s, 1H), 3.78-3.86 (m, 1H), 3.61 (d, 1H), 3.57 (s, 1H), 3.36 (d, 1H), 1.77 (s, 2H). 1.40-1.53 (m, 1H), 1.36 (d, 9H), 1.25 (s, 2H). MS (EI) for $C_{14}H_{26}N_2O_3$: 271 (MH+).

[0640] To a solution of *tert*-butyl 2-(3-hydroxyazetidin-3-yl)cyclohexylcarbamate (181 mg, 0.669 mmol) and 3,4-difluoro-2-(2-fluoro-4-iodophenylamino)benzoyl fluoride (265 mg, 0.669 mmol), prepared using procedures similar to those described in Reference 1, in tetrahydrofuran (2.2 mL) was added *N,N*-diisopropylethylamine (110 μL) at room temperature. After an hour, the reaction mixture was heated to 50 °C and stirred for 45 minutes, at which time it was cooled to room temperature and evaporated. The residue was partitioned between ethyl acetate and 10% citric acid. The organic layer was washed with aqueous sodium chloride, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to afford *tert*-butyl-2-(1-(3,4-difluoro-2-(2-fluoro-4-iodophenylamino)benzoyl)-3-hydroxyazetidin-3-yl)cyclohexylcarbamate. This crude material was taken into the next step without further purification.

[0641] *Tert*-butyl-2-(1-(3,4-difluoro-2-(2-fluoro-4-iodophenylamino)benzoyl)-3-hydroxyazetidin-3-yl)cyclohexylcarbamate was dissolved in a mixture of methanol (4 mL) and hydrogen chloride (4 M in dioxane) (3 mL). The solution was heated to reflux then cooled to room temperature and stirred for 16 hours. The reaction mixture was concentrated and purified by reverse phase HPLC. The purified fractions were evaporated to dryness and partitioned between ethyl acetate and aqueous sodium bicarbonate. The organic layer was dried over sodium sulfate, filtered and concentrated *in vacuo* to afford an oil. The residue was taken up in methanol (2 mL) and was added hydrogen chloride (4M in dioxane) (700 μL) and evaporated to dryness to afford the title compound 3-(2-aminocyclohexyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol hydrochloride (44.7 mg, 12%).

^{1}H NMR (400MHz, d_6-DMSO): 8.58 (d, 1H), 7.59 (dd, 1H), 7.54 (s, 2H), 7.38 (d, 1H), 7.33 (t, 1H), 7.16-7.25 (m, 1H), 6.69 (dt, 1H), 6.41 (s, 1H), 4.26 (d, 0.5H), 4.17 (d, 0.5H), 4.04 (t, 1H), 3.90 (t, 1H), 3.79 (d, 0.5H), 3.65-3.73 (m, 0.5H), 3.45-3.51 (m, 1H), 1.88 (s, 1H), 1.65-1.88 (m, 2H), 1.47 (s, 4H), 1.16-1.37 (m, 2H); MS (EI) for $C_{22}H_{23}F_3IN_3O_2$: 546 (MH^+).

[0642] Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the following MEK compounds were prepared:

[0643] **EXAMPLE 25(c).**3-(2-aminocyclopentyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol; ^{1}H NMR (400MHz, d_6-DMSO): 8.56 (d, 1H), 7.82 (d, 1H), 7.59 (td, 1H), 7.45 (s, 1H), 7.38 (d, 1H), 7.30-7.35 (m, 1H), 7.18-7.24 (m, 1H), 6.68-6.72 (m, 1H0, 6.41 (s, 0.5H), 6.17 (s, 0.5H), 3.91-4.27 (m, 2.5H), 3.78-3.86 (m,

1H), 3.65-3.73 (m, 1H), 3.44-3.52 (m, 0.5H), 2.19-2.26 (m, 1H), 1.54-1.94 (m, 5H), 1.30-1.39 (m, 1H); MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 532 (MH^+).

EXAMPLE 25(a) and **EXAMPLE 25(b)**

(±)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(trans)-2-hydroxycyclohexyl]azetidin-3-ol

and

(±)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(cis)-2-hydroxycyclohexyl]azetidin-3-ol

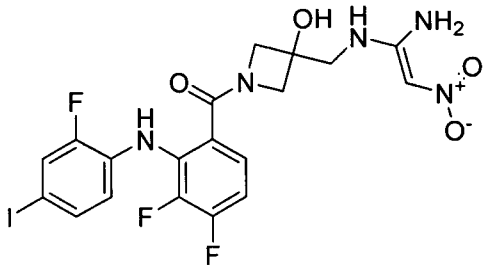
[0644] The compounds of examples 25a and 25b were synthesized starting from benzyl 3-hydroxy-3-(2-oxycyclohenyl)azetidine-1-carboxylate prepared according to the procedure given in example 25. The ketone was reduced to give benzyl 3-hydroxy-3-(2-hydroxycyclohexyl)azetidine-1-carboxylate as a mixture of racemic diastereomers which were subjected to hydrogenation to afford 3-(2-hydroxycyclohexyl)azetidin-3-ol. 3-(2-hydroxycyclohexyl)azetidin-3-ol was then carried forward in a coupling step with 3,4-difluoro-2-(2-fluoro-4-iodophenylamino)benzoyl fluoride in the usual manner. The coupled material thus obtained was purified by preparative reverse phase HPLC wherein fraction 1 was tentatively assigned as (±)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(trans)-2-hydroxycyclohexyl]azetidin-3-ol (Example 25a) and fraction 2 was tentatively assigned as (±)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(cis)-2-hydroxycyclohexyl]azetidin-3-ol.

[0645] **EXAMPLE 25(a). First eluting fraction:** ^{1}H NMR (400 MHz, d_4-MeOH): 7.44 (2d, 1H), 7.34 (t, 1H), 7.25 (m, 1H), 7.03 (m, 1H), 6.60 (m, 1H), 4.46 (d, 0.5H), 4.28 (d, 0.5H), 4.22 (d, 0.5H), 3.98 (dd, 1H), 3.89 (d, 0.5H), 3.85 (s, 0.5H), 3.77 (d, 0.5H), 3.56 (m, 1H), 1.90 (m, 1H), 1.46-1.74 (m, 4H), 0.98-1.32 (m, 4H); MS (EI) for $C_{22}H_{22}F_3IN_2O_3$: 547 (MH^+).

[0646] **EXAMPLE 25(b). Second eluting fraction:** ^{1}H NMR (400 MHz, d_4-MeOH): 7.44 (2d, 1H), 7.33 (d, 1H), 7.26 (m, 1H), 7.04 (m, 1H), 6.59 (dd, 1H), 4.20 (m, 1.5H), 4.19 (s, 0.5H), 4.00 (m, 1.5H), 3.86 (dd, 1H), 3.74 (d, 0.5H), 1.76 (m, 2H), 1.50-1.68 (m, 5H), 1.18-1.46 (m, 4H); MS (EI) for $C_{22}H_{22}F_3IN_2O_3$: 547 (MH^+).

Example 26

3-({[(E)-1-amino-2-nitroethenyl]amino}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

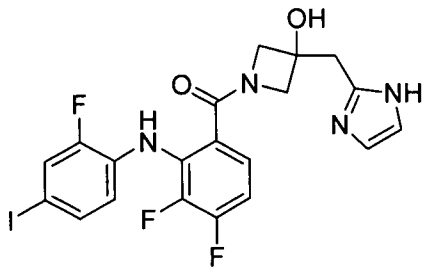


[0647] A solution of 3-(aminomethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol (0.24 g, 0.5 mmol), prepared using procedures similar to those described in Example 3, and commercially available 1,1-bis(methylthio)-2-nitroethylene (0.083 g, 0.5 mmol) in ethanol (5 mL) was stirred at 70 °C for 16 hours. The reaction mixture was concentrated *in vacuo*. The residue was partitioned between ethyl acetate and water. The organic layer was washed with brine, dried over sodium sulfate, filtered and concentrated to afford 0.10 g, (39%) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(Z)-1-(methylthio)-2-nitroethenyl]amino}methyl)azetidin-3-ol. MS (EI) for $C_{20}H_{18}F_3IN_4O_4S$: 595 (MH^+).

[0648] To a solution of (0.05 g 0.08 mmol) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(Z)-1-(methylthio)-2-nitroethenyl]amino}methyl)azetidin-3-ol in ethanol (2 mL) was added ammonium hydroxide (0.1 mL, 0.8 mmol) and the reaction mixture was stirred at 70 °C for 16 hours. The reaction mixture was concentrated *in vacuo*. The crude product was purified by reverse phase preparative HPLC. The fractions were collected and the solvent was concentrated. The residue was partitioned with ethyl acetate. The organic layer was washed with saturated aqueous sodium bicarbonate, brine and dried over anhydrous sodium sulfate. Filtration and concentration resulted in an amorphous residue, which was dissolved in methanol, and 4 N HCl in dioxane (40 µL, 0.16 mmol) was added to the solution. A white precipitate formed and was collected by vacuum filtration. The solid was washed with hexane, and dried to afford 42 mg (87%) 3-({[(E)-1-amino-2-nitroethenyl]amino}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol hydrochloride. ^{1}H NMR (400 MHz, d_4-MeOH): 7.58 (t, 0.5H), 7.44 (t, 0.5H), 7.36 (m, 1H), 7.31 (m, 1H), 7.04 (m, 1H), 6.63 (m, 1H), 3.90-4.30 (m, 4H) 3.72 (s, 2H); MS (EI) for $C_{19}H_{17}F_3IN_5O_4$: 564 (MH^+).

EXAMPLE 27

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-imidazol-2-ylmethyl)azetidin-3-ol



[0649] A solution of 2-methyl-1-({[2-(trimethylsilyl)ethyl]oxy}methyl)-1*H*-imidazole (0.5 g, 2.3 mmol) (prepared using procedures similar to those described in Clader *et. al. J. of Med. Chem.* 1995, *38(10),* 1600-7) in tetrahydrofuran (5 mL) was cooled to –78 °C, and *n*-butyllithium was added (2.5 M in hexanes, 0.990 mL, 2.5 mmol). After 2 hours, 1,1-dimethylethyl 3-oxoazetidine-1-carboxylate (0.60 g, 3.5 mmol), prepared using procedures similar to those described in Example 3, in 2.0 mL tetrahydrofuran was added and the solution was allowed to warm to room temperature and stirred overnight. The reaction mixture was quenched with an excess of saturated aqueous ammonium chloride solution and partitioned between water and ethyl acetate. The layers were separated and the aqueous layer was extracted with ethyl acetate (2 x 10 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 3:1 hexanes/ethyl acetate) gave 0.37 g (41%) of 3-{[1-({[2-(trimethylsilyl)ethyl]oxy}methyl)-1*H*-imidazol-2-yl]methyl}azetidin-3-ol: ^{1}H NMR (400 MHz, $CDCl_3$): 6.96-6.92 (m, 1H), 5.23 (s, 2H), 3.98 (d, 2H), 3.79 (d, 2H), 3.52-3.47 (m, 2H), 3.13 (s, 2H), 1.43 (s, 9H), 0.94-0.88 (m, 2H), 0.00 (s, 9H).

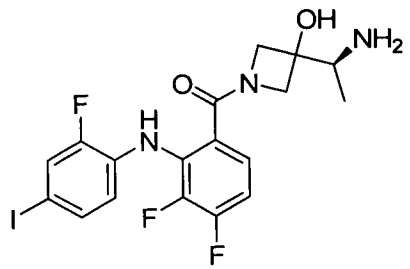
[0650] 3-{[1-({[2-(trimethylsilyl)ethyl]oxy}methyl)-1*H*-imidazol-2-yl]methyl}azetidin-3-ol (0.19 g, 0.49 mmol) was dissolved in dichloromethane (1.5 mL) and trifluroacetic acid (1.5 mL) was added. The reaction mixture was stirred at room temperature overnight and the solvent was removed under vacuum to give 0.16 g of 3-(1*H*-imidazol-2-ylmethyl)azetidin-3-ol trifluoroacetate salt (87%). The crude residue was used without further purification for the next step.

[0651] To a solution of 3-(1*H*-imidazol-2-ylmethyl)azetidin-3-ol trifluoroacetate salt (0.16 g, 0.42 mmol) and *N,N*-diisopropylethylamine (0.370 mL, 2.13 mmol) in tetrahydrofuran (2.0

mL) 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoyl fluoride (0.17 g, 0.42 mmol), prepared using procedures similar to those described in Reference 1, was added and the reaction mixture was stirred for 3 hours at room temperature. The solution was partitioned between ethyl acetate and saturated aqueous sodium bicarbonate and the organic layer was dried over sodium sulfate and concentrated *in vacuo*. Purification by reverse-phase HPLC followed by lyophilization of the pure fractions gave 0.032 g (13%) of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-imidazol-2-ylmethyl)azetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, CD_3OD): 7.45 (dd, 1H), 7.38-7.33 (m, 1H), 7.25-7.18 (m, 1H), 7.08-6.96 (m, 1H), 6.89 (s, 2H), 6.65-6.56 (m, 1H), 4.33-4.22 (m, 1H), 4.17-4.00 (m, 2H), 3.91-3.80 (m, 1H), 3.08 (s, 2H), 1.96 (s, 3H). MS (EI) for $C_{20}H_{16}F_3IN_4O_2$: 529 (MH^+).

EXAMPLE 28

3-[(1*R*)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol



[0652] To a solution of diisopropylamine (6.5 mL, 46.3 mmol) in THF (200 mL) at -78 °C was added butyllithium (17 mL of a 2.5 M solution in hexanes, 42.5 mmol) over 5 min. The solution of lithium diisopropylamide was stirred for 15 min at -78 °C. A solution of (*S*)-4-benzyl-3-propionyl-2-oxazolidinone (9.0 g, 38.6 mmol) in THF (100 mL) was added to the lithium diisopropylamide by addition funnel over 26 min. The reaction temperature was kept below -70 °C during the course of the addition. After the addition, the mixture was stirred for a further 30 min at -78 °C. Then phenylmethyl 3-oxoazetidine-1-carboxylate (9.5 g, 46.3 mmol) was added by addition funnel over 25 minutes as a solution in THF (100 mL). Again, the reaction mixture was kept below -70 °C during the reagent addition. After stirring for an additional 1 hour at -78 °C, the reaction mixture was quenched with saturated ammonium chloride solution and was then allowed to warm to rt. Water was added to dissolve any precipitated ammonium chloride, and ethyl acetate was added. The layers were partitioned, and the aqueous phase was extracted twice with ethyl acetate. The combined organic

extracts were washed with 5% aqueous sodium bicarbonate, dried over sodium sulfate, filtered, and concentrated. The residue was purified by column chromatography (50% ethyl acetate: 50% hexanes) to provide phenylmethyl 3-hydroxy-3-{(1*R*)-1-methyl-2-oxo-2-[(4*S*)-2-oxo-4-(phenylmethyl)-1,3-oxazolidin-3-yl]ethyl}azetidine-1-carboxylate as a white crystalline solid (6.03 g, 13.8 mmol, 36% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (m, 8H), 7.20 (d, 2H), 5.12 (s, 2H), 4.66 (m, 1H), 4.27-4.20 (m, 2H), 4.10 (q, 1H), 4.03-3.93 (m, 3H), 3.28 (dd, 1H), 2.77 (dd, 1H), 1.29 (d, 3H).

[0653] A solution of lithium hydroxide monohydrate (1.16 g, 27.6 mmol) in 30% hydrogen peroxide (13.2 mL, 138 mmol) was prepared and was subsequently added slowly to a solution of phenylmethyl 3-hydroxy-3-{(1*R*)-1-methyl-2-oxo-2-[(4*S*)-2-oxo-4-(phenylmethyl)-1,3-oxazolidin-3-yl]ethyl}azetidine-1-carboxylate (6.03 g, 13.8 mmol) in THF (80 mL) and water (20 mL) at 0 °C. After the mixture was stirred for 1 hour at rt, the hydrogen peroxide was quenched carefully with 1 M sodium sulfite (150 mL, 150 mmol). The THF was removed *in vacuo*, and the mixture was then acidified to pH=2 with concentrated hydrochloric acid. The aqueous mixture was extracted twice with ethyl acetate. The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The resulting residue was purified by column chromatography (gradient, 5% methanol: 95% dichloromethane to 10% methanol: 90% dichloromethane) to provide (2*R*)-2-(3-hydroxy-1-{[(phenylmethyl)oxy]carbonyl}azetidin-3-yl)propanoic acid as a colorless oil (2.77 g, 9.9 mmol, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.31 (m, 5H), 5.10 (s, 2H), 3.99 (s, 2H), 3.93 (s, 2H), 2.88 (q, 1H), 1.28 (d, 3H); MS (EI) for $C_{14}H_{17}NO_5$: 280 (MH^+).

[0654] To a solution of (2*R*)-2-(3-hydroxy-1-{[(phenylmethyl)oxy]carbonyl}azetidin-3-yl)propanoic acid (2.77 g, 9.9 mmol) in toluene (100 mL) was added triethylamine (1.52 mL, 10.9 mmol) followed by diphenyl phosphoryl azide (2.24 mL, 10.4 mmol). The mixture was heated to 80 °C for 2 h and was then cooled to rt. The volatile materials were removed *in vacuo*, and the residue was purified by column chromatography (gradient: 50% hexanes: 50% ethyl acetate up to 100% ethyl acetate). The desired product, (8*R*)-8-methyl-6-oxo-5-oxa-2,7-diazaspiro[3.4]octane-2-carboxylic acid phenylmethyl ester, was isolated as a viscous, colorless syrup (1.84 g, 6.6 mmol, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.32 (m, 5H), 5.66 (br s, 1H), 5.12 (s, 2H), 4.34 (dd, 1H), 4.30 (dd, 1H), 4.17 (dd, 1H), 4.05 (dd, 1H), 3.98 (q, 1H), 1.34 (d, 3H).

[0655] To a solution of (8*R*)-8-methyl-6-oxo-5-oxa-2,7-diazaspiro[3.4]octane-2-carboxylic acid phenylmethyl ester (1.84 g, 6.6 mmol) in methanol (66 mL) was added wet 10% palladium on carbon (50% by mass, 500 mg). The resulting suspension was stirred under 1 atm of hydrogen for 1 h. The catalyst was then removed by filtration through celite. The filtrate was concentrated *in vacuo* to provide (8*R*)-8-methyl-5-oxa-2,7-diazaspiro[3.4]octan-6-one as a white solid (0.99 g, quantitative yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (br s, 1H), 4.07 (d, 1H), 4.02 (d, 1H), 3.92 (d, 1H), 3.79 (d, 1H), 3.58 (d, 1H), 1.38 (d, 3H); MS (EI) for $C_6H_{10}N_2O_2$: 143 (MH^+).

[0656] A solution of (8*R*)-8-methyl-5-oxa-2,7-diazaspiro[3.4]octan-6-one (937 mg, 6.6 mmol), acetic acid (0.756 mL, 13.2 mmol), and benzaldehyde (1.0 mL, 9.9 mmol) in methanol (65 mL) was treated with sodium cyanoborohydride (829 mg, 13.2 mmol) at rt for 30 min. The mixture was then cooled to 0 °C, and 3 N hydrochloric acid (100 mL) was added. The methanol was then removed *in vacuo*. The resulting aqueous solution was washed with ethyl acetate. The ethyl acetate wash was back extracted with 1 N hydrochloric acid, and the aqueous acidic phases were combined and basified with potassium carbonate. The organic phase was discarded. The aqueous mixture was then extracted three times with ethyl acetate. The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The desired (8*R*)-8-methyl-2-(phenylmethyl)-5-oxa-2,7-diazaspiro[3.4]octan-6-one was obtained in 93% purity as a milky colorless liquid (1.33 g, 5.73 mmol, 87% yield). MS (EI) for $C_{13}H_{16}N_2O_2$: 233 (MH^+).

[0657] To a solution of (8*R*)-8-methyl-2-(phenylmethyl)-5-oxa-2,7-diazaspiro[3.4]octan-6-one (1.33 g, 5.7 mmol) in dioxane (40 mL) and water (20 mL) was added barium hydroxide octahydrate (9.0 g, 28.5 mmol), and the mixture was heated to reflux for 2 h. After cooling to rt, the mixture was acidified with 3 N hydrochloric acid (10 mL) and dichloromethane (50 mL) was added. The biphasic mixture was treated with potassium carbonate (1.6 g, 11.4 mmol) and di-*tert*-butyl dicarbonate (2.11 g, 9.7 mmol). After stirring vigorously at rt for 17 h, solids were removed by filtration, and the layers were partitioned. The aqueous phase was extracted with dichloromethane, and the organic extracts were combined and dried over magnesium sulfate, filtered, and concentrated. The residue was taken up in methanol (60 mL) and was treated with potassium carbonate (3.0 g, 22 mmol) added in two portions over 4 h at reflux. After cooling, the methanol was removed *in vacuo*, and the residual solids were loaded directly on to a silica column. After purification (5%

methanol: 95% dichloromethane), 1,1-dimethylethyl {(1*R*)-1-[3-hydroxy-1-(phenylmethyl)azetidin-3-yl]ethyl}carbamate was obtained as a colorless syrup (1.07 g, 3.5 mmol, 62% yield). MS (EI) for $C_{17}H_{26}N_2O_3$: 307 (MH^+).

[0658] To a solution of 1,1-dimethylethyl {(1*R*)-1-[3-hydroxy-1-(phenylmethyl)azetidin-3-yl]ethyl}carbamate (1.07 g, 3.5 mmol) in methanol was added wet 10% palladium on carbon (50% by mass, 250 mg). The resulting suspension was subjected to 1 atmosphere of hydrogen for 7 h, and an additional 250 mg of catalyst was added over the course of the reaction. The catalyst was then removed by filtration through celite. The filtrate was then concentrated *in vacuo* to provide 1,1-dimethylethyl [(1*R*)-1-(3-hydroxyazetidin-3-yl)ethyl]carbamate as a colorless syrup (800 mg, quantitative yield). MS (EI) for $C_{10}H_{20}N_2O_3$: 161 (M - *tert*-butyl + H).

[0659] To a solution of 1,1-dimethylethyl [(1*R*)-1-(3-hydroxyazetidin-3-yl)ethyl]carbamate (200 mg, 0.92 mmol) in dichloromethane (5 mL) was added diisopropylethylamine (228 μL, 1.38 mmol) and 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoyl fluoride (prepared according to the procedures described in Reference 1) (363 mg, 0.92 mmol). The mixture was stirred at rt for 16 h, after which the volatile materials were removed *in vacuo*. The residue was purified by column chromatography (50% hexanes : 50% ethyl acetate) to provide 1,1-dimethylethyl {(1*R*)-1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}carbamate as a colorless film (333 mg, 0.56 mmol, 61% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (br s, 1H), 7.40 (dd, 1H), 7.32 (d, 1H), 7.12 (m, 1H), 6.81 (m, 1H), 6.61 (m, 1H), 4.74 (br d, 1H), 4.22 (d, 1H), 4.15-4.07 (m, 2H), 3.96 (br s, 1H), 3.77 (m, 1H), 1.43 (s, 9H), 1.18 (d, 3H); MS (EI) for $C_{23}H_{25}F_3IN_3O_4$: 536 (M - *tert*-butyl + H).

[0660] A solution of 1,1-dimethylethyl {(1*R*)-1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}carbamate (333 mg, 0.56 mmol) in methanol (10 mL) was treated with hydrochloric acid (4 N in dioxane, 1.4 mL, 5.6 mmol) at 60 °C for 30 min. After cooling, the volatile materials were removed *in vacuo* to provide 3-[(1*R*)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol hydrochloride as a white solid (285 mg, 0.54 mmol, 97% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.56 (s, 1H), 7.83 (br s, 3H), 7.59 (dd, 1H), 7.39 (d, 1H), 7.34 (m, 1H), 7.21 (q, 1H), 6.69 (m, 1H), 6.65 (s, 1H), 4.25 (dd, 1H), 4.10 (dd, 1H), 3.98 (dd, 1H), 3.80 (m, 1H), 3.48 (m, 1H), 1.11 (dd, 3H); MS (EI) for $C_{18}H_{17}F_3IN_3O_2$: 492 (MH^+).

[0661] To establish the enantiomeric excess (ee) of this material, 3-[(1*R*)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol hydrochloride (21 mg, 0.040 mmol) was dissolved in dichloromethane (400 μL) and was treated with diisopropylethylamine (20 μL, 0.12 mmol) and (*R*)-(-)-α-methoxy-α-(trifluoromethyl) phenylacetylchloride at rt for 15 min. An aliquot was removed and was analyzed by chiral HPLC. The diastereomeric excess of (2*S*)-N-{(1*R*)-1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanamide was found to be 91%, and by extrapolation the ee of 3-[(1*R*)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl) azetidin-3-ol was also assigned to be 91%.

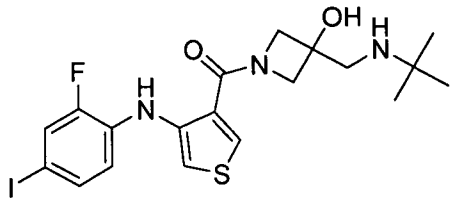
[0662] **Example 28a.** Using the sequence described above, beginning with (*R*)-4-benzyl-3-propionyl-2-oxazolidinone, 3-[(1*S*)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol was prepared using similar procedures except that the phenylmethyl 3-hydroxy-3-{(1*S*)-1-methyl-2-oxo-2-[(4*R*)-2-oxo-4-(phenylmethyl)-1,3-oxazolidin-3-yl]ethyl}azetidine-1-carboxylate required additional recrystallizations from isopropanol. Using the same method described above in Example 28, 3-[(1*S*)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl) azetidin-3-ol was determined to have 98.4% ee. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.56 (s, 1H), 7.84 (br s, 3H), 7.59 (dd, 1H), 7.39 (d, 1H), 7.34 (m, 1H), 7.21 (q, 1H), 6.69 (m, 1H), 6.65 (s, 1H), 4.25 (dd, 1H), 4.10 (dd, 1H), 3.98 (dd, 1H), 3.80 (m, 1H), 3.48 (m, 1H), 1.11 (dd, 3H); MS (EI) for $C_{18}H_{17}F_3IN_3O_2$: 492 (MH^+).

[0663] **Example 28b.** To 3-[(1*S*)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol (87.4 mg, 0.18 mmol), prepared using procedures similar to those described in Example 28, was added formaldehyde (37% aqueous, 14 mg, 0.18 mmol) in methanol (2 mL) and sodium borohydride (7 mg, 0.18 mmol). The mixture was stirred for 3 h at rt, after which sodium borohydride (16 mg, 0.42 mmol) was added. Upon stirring an additional 1.25 h, more formaldehyde (37% aqueous, 1 drop) was added, and the mixture was stirred 3 days at rt. A further small spatula (~50 mg) of sodium borohydride was then added, and the mixture was stirred at rt for 30 min. After quenching with 1 N HCl, the reaction mixture was purified directly by preparative HPLC. The clean material was converted to its hydrochloride salt to provide 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1*S*)-1-(methylamino)ethyl]azetidin-3-ol as

a yellow solid (21.7 mg, 0.040 mmol, 22% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.47 (dd, 1H), 7.36 (d, 1H), 7.31 (m, 1H), 7.06 (q, 1H), 6.62 (dt, 1H), 4.36 (dd, 1H), 4.21-3.91 (m, 3H), 3.44 (q, 1H), 2.66 (s, 3H), 1.29 (br m, 3H); MS (EI) for $C_{19}H_{19}F_3IN_3O_2$: 506 (MH^+).

EXAMPLE 29

3-{[(1,1-Dimethylethyl)amino]methyl}-1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-ol



[0664] To a mixture of methyl 4-oxotetrahydrothiophene-3-carboxylate (1.75 g, 11 mmol) (commercially available or prepared using procedures similar to those described in Rossy *et. al. J. Org. Chem.* 1980, *45(4),* 617-2) in 15 mL of ethanol was added 2-fluoro-4-iodoaniline (2.6 g, 11 mmol) followed by addition of several drops of acetic acid . The mixture was refluxed for 3 hrs. The mixture was cooled to room temperature and the product precipitated. This product was filtered off, washed with ethyl acetate, ether, dried *in vacuo* to afford the methyl 4-[(2-fluoro-4-iodophenyl)amino]-2,5-dihydrothiophene-3-carboxylate (1.7 g, 42%). ^{1}HNMR(d_6-DMSO):9.80 (s,1H), 7.71 (d, 1H), 7.49 (dd, 1H), 7.24 (t, 1H), 4.10 (t, 2H), 3.79 (t, 2H), 3.69 (s, 3H); MS(EI) for $C_{12}H_{11}FINO_2S$: 380 (MH^+).

[0665] To a mixture of methyl 4-[(2-fluoro-4-iodophenyl)amino]-2,5-dihydrothiophene-3-carboxylate (1.2 g, 3.16 mmol) in 10 ml of anhydrous toluene was added 2,3,5,6-tetrachlorocyclohexa-2,5-diene-1,4-dione (0.78 g, 3.16 mmol). The mixture was refluxed for 2 hours. The mixture was cooled to 50 °C and concentrated *in vacuo* to dryness and cooled to room temperature. To the residue was added ethanol and the mixture was refluxed for several minutes, cooled to room temperature and light blue crystalline product was filtered off and dried *in vacuo* to afford methyl 4-[(2-fluoro-4-iodophenyl)amino]thiophene-3-carboxylate (0.74 g, 62%). ^{1}HNMR(d_6-DMSO): 8.78 (s, 1H), 8.42(d, 1H), 7.64 (d, 1H), 7.46 (d, 1H), 7.37(t, 1H), 7.14 (s, 1H), 3.85(s, 3H); MS(EI) for $C_{12}H_9FINO_2S$: 378 (MH^+).

[0666] A mixture of methyl 4-[(2-fluoro-4-iodophenyl)amino]thiophene-3-carboxylate (0.74g, 1.96 mmol) in the solution of potassium hydroxide (0.3g) in ethanol / water

(4ml/4ml) was heated up to 60 °C and stirred at this temperature for 30 min. The mixture was cooled to room temperature, diluted with 4 ml of water and extracted with ether. The water layer was acidified with 1 N HCl to pH 2, the product precipitated and was filtered off, washed several times with water and dried *in vacuo* to afford 4-[(2-fluoro-4-iodophenyl)amino]thiophene-3-carboxylic acid (0.59 g, 83%). ^{1}H NMR (d_6-DMSO): 13.20(s, 1H), 9.13 (s, 1H), 8.35 (d, 1H), 7.62 (dd, 1H), 7.48-7.38 (m, 2H), 7.11 (s, 1H); MS(EI) for $C_{11}H_7FINO_2S$: 362 (MH^-).

[0667] 4-[(2-fluoro-4-iodophenyl)amino]thiophene-3-carboxylic acid (200 mg, 0.551 mmol), 4-(dimethylamino)pyridine (202 mg, 1.65 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (127 mg, 0.662 mmol) were dissolved in DMF (3 mL). The mixture was stirred at ambient for 5 minutes and then 3-(hydroxymethyl)azetidin-3-ol hydrochloride (72 mg, 0.516 mmol) was added and the mixture was stirred for 15 h. The mixture was partitioned between ethyl acetate and 20% citric acid. The aqueous portion was extracted with ethyl acetate. The combined organic portion was washed with 5% lithium chloride, saturated sodium bicarbonate and brine, then was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The residue was crystallized from dichloromethane to afford 1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)-3-(hydroxymethyl)azetidin-3-ol (247 mg, 0.551 mmol, quantitative yield) as off-white crystals: MS (EI) for $C_{15}H_{14}FIN_2O_3S$: 449 (MH^+).

[0668] 1-({4-[(2-Fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)-3-(hydroxymethyl) azetidin-3-ol (247 mg, 0.551 mmol), was suspended in dichloromethane (10 mL) and treated with 4-(dimethylamino)pyridine (80 mg, 0.661 mmol), and 2,4,6-triisopropylbenzenesulfonyl chloride (183 mg, 0.604 mmol) at ambient for 15 hours. The mixture was adsorbed on to silica and purified by column chromatography (silica gel, 30% ethyl acetate in hexanes) to give [1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl 2,4,6-tris(1-methylethyl)benzenesulfonate (101 mg, 0.141 mmol, 26% yield): MS (EI) for $C_{30}H_{36}FIN_2O_5S_2$: 715 (MH^+).

[0669] [1-({4-[(2-Fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl 2,4,6-tris(1-methylethyl)benzenesulfonate (101 mg, 0.141 mmol) was dissolved in tetrahydrofuran (2 mL) and was treated with sodium hydride (60 wt% dispersion in oil; 17 mg, 0.425 mmol) at ambient for 20 minutes. Tetrahydrofuran (2 mL) and *tert*-butylamine (0.1 mL) were added and the mixture was stirred at ambient for 16 hours. The mixture was concentrated *in vacuo* and partitioned between ethyl acetate and water. The organic portion

was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by reverse phase HPLC and the clean fractions were combined, neutralized with saturated sodium bicarbonate solution and the organic solvent was removed *in vacuo*. The remaining aqueous residue was extracted twice with ethyl acetate. The combined organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to afford 3-{[(1,1-dimethylethyl)amino]methyl}-1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-ol (8 mg, 0.016 mmol, 11% yield): ^{1}H NMR (400 MHz, d_6-DMSO): 9.64 (br, 1H), 8.08 (d, 1H), 7.59 (dd, 1H), 7.44 (dd, 1H), 7.36 (t, 1H), 7.12 (d, 1H), 4.39 (d, 1H), 4.22 (d, 1H), 4.03 (d, 1H), 3.80 (d, 1H), 2.68 (br, 2H) 1.04 (s, 9H); MS (EI) for $C_{19}H_{23}FIN_3O_2S$: 504 (MH^+).

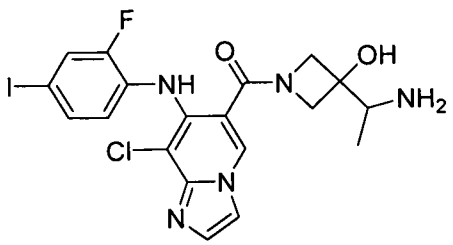
[0670] Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the following MEK compounds were prepared:

[0671] **EXAMPLE 29(a).** 3-[(dimethylamino)methyl]-1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-ol: ^{1}H NMR (400 MHz, CD_3OD): 7.91 (d, 1H), 7.46- 7.41 (m, 2H), 7.33 (t, 1H), 7.00 (d, 1H), 4.66 (s, 1H), 4.49 (s, 1H), 4.30 (s, 1H), 4.15 (s, 1H), 3.54 (s, 1H), 3.17- 3.13 (m, 3H), 2.90 (s, 2H), 1.87- 1.83 (m, 3H); MS(EI) for $C_{17}H_{19}FIN_3O_2S$: 476 (MH^+).

[0672] **EXAMPLE 29(b).** 1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl) azetidin-3-amine: ^{1}H NMR (400 MHz, CD_3OD): 7.90 (d, 1H), 7.46-7.41 (m, 2H), 7.31 (t, 1H), 6.99 (d, 1H), 4.47 (br.s, 2H), 4.22-4.16 (m, 2H); MS(EI) for $C_{14}H_{13}FIN_3OS$: 418 (MH^+).

EXAMPLE 30

3-(1-aminoethyl)-1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)azetidin-3-ol



[0673] To a suspension of sodium hydride (72 mg, 1.75 mmol, 60% wt) in tetrahydrofuran (1 mL) cooled to 0 °C was added nitroethane (125 µL, 1.75 mmol). The suspension was allowed to warm to room temperature and was stirred for 15 minutes, then cooled back to 0 °C. To the suspension was added dropwise a solution of 1,1-dimethylethyl 3-oxoazetidine-1-

carboxylate (300 mg, 1.75 mmol, in 2 mL of tetrahydrofuran), prepared using procedures similar to those described in Reference 3. The suspension was stirred at room temperature for 1 hour. The reaction mixture was quenched by adding 20% aqueous citric acid, and then was partitioned with ethyl acetate. The aqueous portion was extracted twice using ethyl acetate and the combined organic portion was washed with saturated sodium bicarbonate, brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford a colorless oil that was purified by column chromatography. Eluting with 30% ethyl acetate in hexanes, the isolated product was concentrated *in vacuo* to afford 250 mg, 1.02 mmol (58%) of 1,1-dimethylethyl 3-hydroxy-3-(1-nitroethyl)azetidine-1-carboxylate as a colorless oil. ^{1}H NMR (400 MHz, DMSO): 6.46 (s, 1H), 5.01 (q, 1H), 4.24-3.97 (m, 2H), 3.77-3.60 (m, 2H), 1.41 (d, 3H), 1.39 (s, 9H).

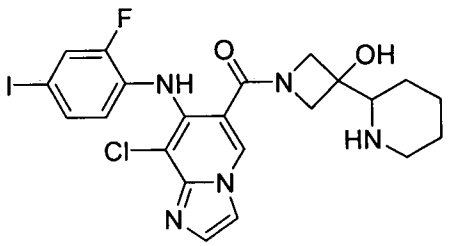
[0674] 1,1-Dimethylethyl 3-hydroxy-3-(1-nitroethyl)azetidine-1-carboxylate was dissolved in methanol (5 mL) and treated with 4 N HCl in dioxane. The solution was briefly heated to reflux and then was concentrated *in vacuo* to afford 178 mg, 0.98 mmol (96%) of 3-(1-nitroethyl)azetidin-3-ol hydrochloride as a white solid. ^{1}H NMR (400 MHz, DMSO): 9.30 (br s, 1H), 8.96 (br s, 1H), 5.12 (q, 1H), 4.44-4.38 (m, 1H), 4.22-4.17 (m, 1H), 3.94-3.87 (m, 1H), 3.85-3.77 (m, 1H), 1.44 (d, 3H).

[0675] A solution of 8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-*a*]pyridine-6-carboxylic acid (150 mg, 0.35 mmol) (prepared using procedures similar to those described in US 2006030610 and US 2005054701), *N,N*-diisopropylethylamine (300 μL, 1.74 mmol), PyBOP (180 mg, 0.35 mmol) and 3-(1-nitroethyl)azetidin-3-ol hydrochloride (76 mg, 0.42 mmol) in dimethylformamide (3 mL) was stirred at room temperature for 15 hours. The reaction mixture was then partitioned between 5% aqueous lithium chloride, and ethyl acetate. The aqueous portion was extracted twice using ethyl acetate. The combined organic portion was washed with 20% aqueous citric acid, brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford a brown residue which was purified by column chromatography. Eluting with 5% methanol in dichloromethane, the isolated product was concentrated *in vacuo* to afford 195 mg, 0.35 mmol (100%) of 1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-*a*]pyridin-6-yl}carbonyl)-3-(1-nitroethyl)azetidin-3-ol as a yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$): 8.28 (s, 1H), 7.68 (s, 1H), 7.59 (s, 1H), 7.43 (d, 1H), 7.31 (d, 1H), 7.23 (br s, 1H), 6.55-6.51 (m, 1H), 6.02 (br s, 1H), 4.79 (q, 1H), 4.45-3.96 (4H), 1.56 (d, 3H). MS (EI) for $C_{20}H_{19}ClFIN_6O_4$: 560 (MH^+).

[0676] To a solution of 1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-*a*]pyridin-6-yl}carbonyl)-3-(1-nitroethyl)azetidin-3-ol (195 mg 0.35 mmol) in tetrahydrofuran/water (5 mL, 4:1) was added iron powder (193 mg, 3.5 mmol) and ammonium formate (438 mg, 7.0 mmol). The mixture was stirred at 80°C for 1 hour, then cooled to room temperature and filtered through a pad of celite. The celite was washed three times with boiling ethanol (20 mL). The filtrate was concentrated *in vacuo* and the residue was diluted with ethyl acetate. The precipitate which formed was filtered through a pad a celite and the filtrate was partitioned with water. The aqueous portion was extracted twice with ethyl acetate. The combined organic portion was washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford a yellow residue which was purified by preparative reverse phase HPLC. The isolated product was concentrated *in vacuo* to afford 35 mg, 0.05 mmol (15%) of 3-(1-aminoethyl)-1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)azetidin-3-ol acetate salt as a white solid. ^{1}H NMR (400 MHz, DMSO): 8.79 (s, 1H), 8.00 (s, 1H), 7.61 (s, 1H), 7.54 (d, 1H), 7.32 (d, 1H), 6.54-6.48 (m, 1H), 4.24-4.13 (m, 1H), 3.98-3.84 (m, 2H), 3.61-3.56 (m, 1H), 2.83 (q, 1H), 0.92-0.88 (m, 3H); MS (EI) for $C_{19}H_{18}ClFIN_5O_2$: 530 (MH^+).

EXAMPLE 31

1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol



[0677] To a solution of 1,1-dimethylethyl 2-(3-hydroxy-1-{[(phenylmethyl)oxy]carbonyl}azetidin-3-yl)piperidine-1-carboxylate (595 mg, 1.52 mmol), prepared using procedures similar to those described in Reference 5, in methanol (5 mL) was added catalytic palladium on carbon (5% wt). The heterogeneous mixture was stirred under a hydrogen gas atmosphere for 15 hours at ambient pressure and then was filtered. The filtrate was concentrated *in vacuo* to afford 385 mg, 1.50 mmol (98%) of 1,1-dimethylethyl 2-(3-hydroxyazetidin-3-yl)piperidine-1-carboxylate as a colorless film without further purification.

A solution of 8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-*a*]pyridine-6-carboxylic acid (78 mg, 0.18 mmol) (prepared using procedures similar to those described in US 2006030610 and US 2005054701), 1,1-dimethylethyl 2-(3-hydroxyazetidin-3-yl)piperidine-1-carboxylate (46.7 mg, 0.18 mmol), 4-(dimethylamino)pyridine (66 mg, 0.55 mmol), and finally 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (42 mg, 0.21 mmol) in dimethylformamide (2 mL) was stirred at room temperature for 15 hours. The reaction mixture was partition between 5% aqueous lithium chloride and ethyl acetate and the aqueous portion was extracted twice using ethyl acetate. The combined organic portion was washed with 1 N HCl, brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford a brown residue which was purified by column chromatography. Eluting with ethyl acetate, the isolated product was concentrated *in vacuo* to afford 101 mg, 0.15 mmol (83%) of 1,1-dimethylethyl 2-[1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate as a white solid. The solid was immediately dissolved in methanol (5 mL) and 4 N HCl in dioxane was added. The solution was briefly heated to reflux and then was concentrated *in vacuo*. The resultant residue was purified by preparative reverse phase HPLC. Isolated product was concentrated *in vacuo* to afford 36 mg, 0.06 mmol (40%) of 1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol acetate as a white solid. ^{1}H NMR (400 MHz, DMSO): 8.78 (s, 1H), 8.19 (s, 0.5H), 8.15 (s, 0.5H), 8.00 (s, 1H), 7.62 (s, 1H), 7.55 (d, 1H), 7.31 (d, 1H), 6.54-6.49 (m, 1H), 4.24-4.12 (m, 1H), 3.97-3.86 (m, 2H), 3.63-3.56 (m, 1H), 2.98-2.90 (m, 1H), 2.50-2.40 (m, 1H), 1.72-1.61 (m, 1H), 1.56-1.43 (m, 2H), 1.32-1.14 (m, 2H), 1.07-0.94 (m, 1H); MS (EI) for $C_{22}H_{22}ClFIN_5O_2$: 570 (MH^+).

[0678] Using the same or analogous synthetic techniques and/or substituting with alternative reagents, the following MEK compounds were prepared:

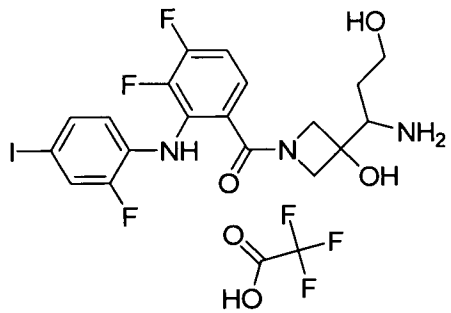
[0679] **EXAMPLE 31(a).** 1-({4-fluoro-5-[(2-fluoro-4-iodophenyl)amino]-1-methyl-1*H*-benzimidazol-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol acetate salt: ^{1}H NMR (400 MHz, DMSO): 8.35 (s, 1H), 7.84-7.77 (m, 1H), 7.54-7.49 (m, 2H), 7.25 (d, 1H), 6.31-6.25 (m, 1H), 4.04-3.92 (m, 2H), 3.90 (s, 3H), 3.86-3.78 (m, 1H), 3.70-3.62 (m, 1H), 2.94-2.85 (m, 1H), 2.45-2.32 (m, 2H), 1.66-1.36 (m, 3H), 1.26-1.08 (m, 2H), 1.01-0.80 (m, 1H); MS (EI) for $C_{23}H_{24}F_2IN_5O_2$: 568 (MH^+).

[0680] **EXAMPLE 31(a).** 1-({7-[(4-bromo-2-chlorophenyl)amino]-8-chloroimidazo[1,2-a]pyridin-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol acetate salt: ^{1}H NMR (400 MHz,

DMSO): 8.87 (s, 1H), 8.29 (s, 0.5H), 8.21 (s, 0.5H), 8.04 (s, 1H), 7.67-7.63 (m, 2H), 7.32 (d, 1H), 6.59 (d, 1H), 4.35-4.22 (m, 1H), 4.08-3.98 (m, 2H), 3.72-3.67 (m, 1H), 2.96-2.88 (m, 1H), 2.50-2.44 (m, 2H), 1.66-1.42 (m, 3H), 1.26-1.17 (m, 2H), 1.04-0.94 (m, 1H); MS (EI) for $C_{22}H_{22}BrCl_2N_5O_2$: 540 (MH^+).

EXAMPLE 32

3-(1-Amino-3-hydroxypropyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol trifluoroacetate salt



[0681] Potassium *tert*-butoxide (1.393 g, 12.4 mmol) and [2-(1,3-dioxolan-2-yl)ethyl]-triphenylphosphonium bromide (5.51 g, 12.4 mmol) were stirred in ether (30 mL) at amibient for 1 h. Phenylmethyl 3-oxoazetidine-1-carboxylate (1.025 g, 5.0 mmol), prepared using procedures similar to those described in Reference 3, was added and the mixture was stirred at 35 °C for 6 h and then at ambient for 4 days. Mixture was filtered through celite and the solid was washed with ether. The filtrate was washed with water, brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 20% ether in hexanes) gave phenylmethyl 3-[2-(1,3-dioxolan-2-yl)ethylidene]azetidine-1-carboxylate (220 mg, 0.761 mmol, 15% yield): ^{1}H NMR (400 MHz, $CDCl_3$): 7.39-7.28 (m, 5H), 5.43-5.35 (m, 1H), 5.11 (s, 2H), 4.89 (t, 1H), 4.56 (br d, 4H), 4.00-3.92 (m, 2H), 3.91-3.83 (m, 2H), 2.27 (br t, 2H).

[0682] Phenylmethyl 3-[2-(1,3-dioxolan-2-yl)ethylidene]azetidine-1-carboxylate (220 mg, 0.761 mmol), and 4-methylmorpholine N-oxide (287 mg, 2.45 mmol) were dissolved in acetone / water (4:1; 10 mL) and osmium tetroxide (4 wt.% in water; 0.05 mL) was added. The solution was stirred at ambient for 20 h, then was quenched with saturated sodium bisulfite (2 mL) and concentrated *in vacuo*. The residue was partitioned between ethyl acetate and brine. The aqueous portion was extracted with ethyl acetate. The combined organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, ethyl acetate) gave phenylmethyl

3-[2-(1,3-dioxolan-2-yl)-1-hydroxyethyl]-3-hydroxyazetidine-1-carboxylate (244 mg, 0.755 mmol, 99% yield): ^{1}H NMR (400 MHz, $CDCl_3$): 7.38-7.28 (m, 5H), 5.11-5.07 (m, 3H), 4.14-4.01 (m, 4H), 3.96-3.86 (m, 5H), 3.47 (d, 1H), 2.97-2.94 (m, 1H), 1.98-1.84 (m, 2H). Phenylmethyl 3-[2-(1,3-dioxolan-2-yl)-1-hydroxyethyl]-3-hydroxyazetidine-1-carboxylate (235 mg, 0.728 mmol) was dissolved in methanol (5 mL) and treated with 5 wt% palladium on carbon (50 mg) under hydrogen at ambient for 1.5 h. The mixture was filtered and the filtrate was concentrated *in vacuo* to afford 3-[2-(1,3-dioxolan-2-yl)-1-hydroxyethyl]azetidin-3-ol (0.729 mmol): MS (EI) for $C_8H_{15}NO_4$: 190 (MH^+).

[0683] 3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid (287 mg, 0.730 mmol), prepared using procedures similar to those described in US 7,019,033, 4-(dimethylamino)pyridine (178 mg, 1.46 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (168 mg, 0.88 mmol) were dissolved in DMF (3 mL). The mixture was stirred at ambient for 10 minutes and then 3-[2-(1,3-dioxolan-2-yl)-1-hydroxyethyl]azetidin-3-ol (0.729 mmol) in DMF (2 mL) was added and the mixture was stirred for 15 h. The mixture was partitioned between ethyl acetate and 5% lithium chloride. The organic portion was washed with 20% citric acid, saturated sodium bicarbonate and brine, then was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, gradient 90% ethyl acetate in hexanes to 100% ethyl acetate) gave 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[2-(1,3-dioxolan-2-yl)-1-hydroxyethyl]azetidin-3-ol (148 mg, 0.262 mmol, 36% yield): MS (EI) for $C_{21}H_{20}F_3IN_2O_5$: 565 (MH^+).

[0684] 1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[2-(1,3-dioxolan-2-yl)-1-hydroxyethyl]azetidin-3-ol (148 mg, 0.262 mmol), was dissolved in dichloromethane (10 mL) and treated with 4-(dimethylamino)pyridine (38 mg, 0.31 mmol), triethylamine (0.036 mL, 0.262 mmol) and 2,4,6-triisopropylbenzenesulfonyl chloride (303 mg, 1.0 mmol) at 35 °C for 15 h. 2,4,6-Triisopropylbenzenesulfonyl chloride (100 mg, 0.33 mmol) was added and the mixture was stirred at 35 °C for 3.5 h. The mixture was adsorbed on to silica and purified by column chromatography (silica gel, 40-50% ethyl acetate in hexanes and then 100% ethyl acetate) to give 1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]-2-(1,3-dioxolan-2-yl)ethyl 2,4,6-tris(1-methylethyl)benzenesulfonate (30 mg, 0.0361 mmol, 14% yield): MS (EI) for $C_{36}H_{42}F_3IN_2O_7S$: 831 (MH^+).

[0685] 1-[1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]-2-(1,3-dioxolan-2-yl)ethyl 2,4,6-tris(1-methylethyl)benzenesulfonate (50 mg, 0.060 mmol) was dissolved in tetrahydrofuran (1 mL) and was cooled to 0 °C. Sodium hydride (60 wt% dispersion in oil; 7 mg, 0.18 mmol) was added and the mixture was stirred at 0 °C for 45 minutes. The mixture was quenched with saturated sodium bicarbonate solution and partitioned with ethyl acetate. The aqueous portion was extracted with ethyl acetate. The combined organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 50% ethyl acetate in hexanes) gave 6-{[2-(1,3-dioxolan-2-ylmethyl)-1-oxa-5-azaspiro[2.3]hex-5-yl]carbonyl}-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline (31 mg, 0.057 mmol, 94% yield): MS (EI) for $C_{21}H_{18}F_3IN_2O_4$: 547 (MH^+).

[0686] 6-{[2-(1,3-Dioxolan-2-ylmethyl)-1-oxa-5-azaspiro[2.3]hex-5-yl]carbonyl}-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline (31 mg, 0.057 mmol) was dissolved in dimethylformamide (0.5 mL) and sodium azide (20 mg, 0.308 mmol) was added. The mixture was stirred at ambient for 22 h. The mixture was partitioned between ethyl acetate and 5% lithium chloride. The aqueous portion was extracted with ethyl acetate. The combined organic portion was washed with water, brine, then was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 50% ethyl acetate in hexanes) gave 3-[1-azido-2-(1,3-dioxolan-2-yl)ethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol (25 mg, 0.042 mmol, 74% yield): MS (EI) for $C_{21}H_{19}F_3IN_5O_4$: 590 (MH^+).

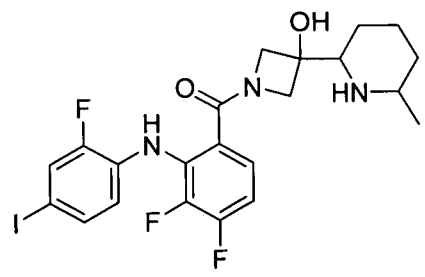
[0687] 3-[1-Azido-2-(1,3-dioxolan-2-yl)ethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol (24 mg, 0.041 mmol) was dissolved in tetrahydrofuran (0.5 mL) and treated with 5% aqueous hydrochloric acid (0.5 mL) at ambient for 15 hours. The misture was neutralised with saturated sodium bicarbonate solution and was extracted twice with ethyl acetate. The combined organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to afford 3-azido-3-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]propanal (21 mg, 0.0385 mmol) which was suspended in ethanol (2 mL) and treated with sodium borohydride (5 mg, 0.132 mmol) at ambient for 2 hours. The mixture was quenched with acetic acid (4 drops) and concentrated *in vacuo*. The residue was partitioned between saturated sodium bicarbonate solution and ethyl acetate. The aqueous portion was extracted with ethyl acetate. The combined organic portion was washed with

brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (silica gel, 70-80% ethyl acetate in hexanes) gave 3-(1-azido-3-hydroxypropyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol (14 mg, 0.0255 mmol, 62% yield from 3-[1-azido-2-(1,3-dioxolan-2-yl)ethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol): ^{1}H NMR (400 MHz, $CDCl_3$): 8.33 (br s, 1H), 7.40 (dd, 1H), 7.32 (br d, 1H), 7.13 (br t, 1H), 6.83 (br q, 1H), 6.61 (ddd, 1H), 4.32-3.94 (m, 4H), 3.92-3.84 (m, 1H), 3.82-3.71 (m, 2H), 2.56 (br, 1H), 1.94 (br, 2H), 1.26 (br, 1H); MS (EI) for $C_{19}H_{17}F_3IN_5O_3$: 548 (MH^+).

[0688] 3-(1-Azido-3-hydroxypropyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol (14 mg, 0.0255 mmol) was dissolved in tetrahydrofuran and water (1:1, 0.5 mL) and polymer supported triphenylphosphine (~3 mmol/g; 20 mg, 0.06 mmol) was added. The mixture was stirred at 55 °C for 1 h. Triphenylphosphine (10 mg, 0.038 mmol) was added and the mixture was stirred at 55 °C for 1.5 h. The mixture was filtered and the filtrate was purified by reverse phase HPLC to afford 3-(1-amino-3-hydroxypropyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol trifluoroacetate salt (1.7 mg, 0.003 mmol, 10% yield): ^{1}H NMR (400 MHz, CD_3OD): 7.47 (dd, 1H), 7.36 (br d, 1H), 7.33-7.28 (m, 1H), 7.05 (br q, 1H), 6.62 (ddd, 1H), 4.38-4.26 (m, 1H), 4.18-4.00 (m, 2H), 3.98-3.88 (m, 1H), 3.78-3.67 (m, 2H), 3.61-3.56 (m, 1H), 1.87-1.70 (m, 2H); MS (EI) for $C_{19}H_{19}F_3IN_3O_3$: 522 (MH^+).

EXAMPLE 33

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(6-methylpiperidin-2-yl)azetidin-3-ol



[0689] To a solution of *N,N*-diisopropylamine (1.6 mL, 11.2 mmol) cooled to -78 °C in THF (15 mL) was added a 2.5 M solution of n-BuLi in hexane (4.5 mL, 11.2 mmol)

dropwise over 5 minutes and the mixture was stirred at this temperature for an addition 15 minutes. 6-methyl-1-(phenylmethyl)piperidine-2-carbonitrile (2.4 g, 11.2 mmol) (prepared using procedures similar to those in Bonin *et. al. Tet. Lett.* 1982, *23(33),* 3369-72) in THF (10 mL) was then added dropwise over 20 minutes and the reaction mixture was stirred for a further 30 minutes. Next a solution of 1,1-dimethylethyl 3-oxoazetidine-1-carboxylate (1.3 g, 7.5 mmoL), prepared using procedures similar to those in Example 3, in THF (10 mL) was added dropwise over 30 minutes. The reaction mixture was gradually warmed to room temperature and allowed to stir overnight. The reaction mixture was quenched with 10% citric acid and extracted with ethyl acetate (3 x 50 mL). The combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate then filtered and concentrated *in vacuo* to give crude product as yellow oil. Further purification by flash chromatography (30% ethyl acetate in hexanes) afforded 1,1-dimethylethyl 3-[2-cyano-6-methyl-1-(phenylmethyl)piperidin-2-yl]-3-hydroxyazetidine-1-carboxylate as a pale yellow oil (0.2 g, 7% yield). ^{1}H NMR (400 MHz, $CDCl_3$): 7.17-7.40 (m, 5H), 4.42 (d, 1H), 4.04-4.18 (m, 1H), 3.83-4.00 (m, 1H), 3.70-3.75 (m, 2H), 1.70-1.87 (m, 4H), 1.45 (s, 3H), 1.41 (s, 9H), 1.22-1.26 (m,1H), 1.13-1.18 (m, 2H); MS (EI) for $C_{22}H_{31}N_3O_3$: 386 (MH^+).

[0690] To a stirred solution of 1,1-dimethylethyl 3-[2-cyano-6-methyl-1-(phenylmethyl)piperidin-2-yl]-3-hydroxyazetidine-1-carboxylate (180 mg, 0.47 mmol) in ethanol (1 mL) was added acetic acid (53.5 µL, 0.94 mmol) followed by sodium cyanoborohydride (58.7 mg, 0.94 mmol) and the reaction mixture stirred at 70 °C overnight. After cooling to room temperature the suspension was filtered through celite and the solid washed with additional ethanol. The filtrate was concentrated *in vacuo* and taken up in ethyl acetate (30 mL). The organic layer was washed with 2 M sodium hydroxide solution. The sodium hydroxide layer was separated and washed with ethyl acetate (10 mL). The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate and concentrated *in vacuo* to give crude1,1-dimethylethyl 3-hydroxy-3-[6-methyl-1-(phenylmethyl)piperidin-2-yl]azetidine-1-carboxylate as yellow oil (60 mg, 36% yield). Crude product was used further without purification. ^{1}H NMR (400 MHz, $CDCl_3$): 7.22-7.35 (m, 5H), 4.08 (d, 1H), 3.85-3.96 (m, 3H), 3.57 (d, 1H), 3.33-3.36 (m, 1H), 2.91-3.06 (m, 2H), 1.63-1.70 (m, 4H), 1.44 (s, 9H), 1.23 (d,3H), 1.05 (d, 2H); MS (EI) for $C_{21}H_{32}N_2O_3$: 361 (MH^+).

[0691] To a solution of 1,1-dimethylethyl 3-hydroxy-3-[6-methyl-1-(phenylmethyl) piperidin-2-yl]azetidine-1-carboxylate (60 mg, 0.16 mmol) in methanol (0.5 mL) was added

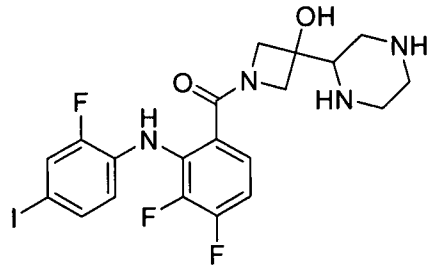
hydrogen chloride (4N in dioxane, 0.5 mL) and the reaction mixture stirred at 60 °C for one hour. The reaction mixture was cooled to room temperature and concentrated *in vacuo* and aezotroped 3 times from methanol and diethyl ether. On drying the hydrochloride salt of 3-[6-methyl-1-(phenylmethyl)piperidin-2-yl]azetidin-3-ol was obtained as a dark brown residue (40 mg, 81% yield), which was used further without purification. ^{1}H NMR (400MHz, CD_3OD): 7.58-7.63 (m, 2H), 7.47-7.49 (m, 3H), 4.78 (d, 1H), 4.44-4.62 (m, 2H), 4.29 (s, 2H), 4.22-4.26 (m, 1H), 4.12-4.18 (m, 1H), 4.08 (s, 1H), 1.60-2.00 (m, 8H), 1.48 (d, 3H); MS (EI) for $C_{16}H_{25}ClN_2O$: 261 (MH^+).

[0692] To a solution of 3-[6-methyl-1-(phenylmethyl)piperidin-2-yl]azetidin-3-ol hydrochloride (40 mg, 0.13 mmol) in ethyl acetate (3 mL) was added acetic acid (0.5 mL) and Pd/C (50 mg) and the mixture was hydrogenated at 35 psi for 3 hours. The reaction mixture was filtered through celite. The filtrate was concentrated *in vacuo*. The obtained residue was dissolved in a small amount of ethyl acetate and concentrated hydrochloric acid was added and the mixture was concentrated *in vacuo* to give the crude dihydrochloride salt of 3-[6-methylpiperidin-2-yl]azetidin-3-ol (20 mg, 54%). The crude product was used further without purification. ^{1}H NMR (400MHz, CD_3OD): 4.20-4.40 (m, 1H), 4.00-4.10 (m, 1H), 3.60-3.90 (m, 2H), 1.50-2.00 (m, 6H), 1.45 (d, 3H), 1.26-1.30 (m, 1H); MS (EI) for $C_9H_{20}Cl_2N_2O$: 171 (MH^+).

[0693] To a 0 °C solution of 3-[6-methylpiperidin-2-yl]azetidin-3-ol dihydrochloride (20 mg, 0.08 mmol) in DMF (1 mL) was added *N,N*-diisopropylethylamine (42 µL, 0.26 mmol) followed by 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino] benzoyl fluoride (32 mg, 0.08 mmol), prepared using procedures similar to those described in Reference 1, and the reaction mixture stirred at 0 °C for 30 min. The mixture was diluted with acetonitrile and purified by preparative reverse phase HPLC (CH_3CN/H_2O with 0.1% TFA). Fractions were collected and lyophilized to give 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(6-methylpiperidin-2-yl)azetidin-3-ol acetate salt (7 mg, 16% yield) as a white solid. ^{1}H NMR (400MHz, CD_3OD): 7.44-7.50 (m, 1H), 7.34-7.37 (m, 1H), 7.28-7.32 (m, 1H), 7.02-7.12 (m, 1H), 6.60-6.63 (m, 1H), 4.10-4.30 (m, 2H), 3.95-4.09 (m, 2H), 3.80-3.95 (m, 1H), 3.55-3.65 (m, 1H), 3.34-3.36 (m, 1H), 1.90 (s, 3H), 1.62-1.84 (m, 6H), 1.40-1.52 (m, 1H), 1.33 (d, 3H); MS (EI) for $C_{22}H_{23}F_3IN_3O_2$: 546 (MH^+).

EXAMPLE 34

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-piperazin-2-ylazetidin-3-ol



[0694] To a solution of commercially available 1,4-bis(phenylmethyl)piperazine-2,5-dione (2.0 g, 6.8 mmol) in dry THF (50 mL) at -78 °C was added lithium diisopropylamide (2.0 M solution in heptane/THF/ethylbenzene, 3.4 mL, 6.8 mmol). The resulting reddish brown suspension was stirred for 23 min at -78 °C, and then a solution of 1,1-dimethylethyl 3-oxoazetidine-1-carboxylate (770 mg, 4.5 mmol) in THF (10 mL) was added over 30 min by syringe pump. The mixture became a bright yellow solution as it was allowed to warm to room temperature over 3 hours. The mixture was quenched with saturated aqueous ammonium chloride. Water was added to dissolve precipitated salts, and the resulting mixture was extracted twice with ethyl acetate. The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography (60% ethyl acetate: 40% hexanes) to provide 1,1-dimethylethyl 3-[3,6-dioxo-1,4-bis(phenylmethyl)piperazin-2-yl]-3-hydroxyazetidine-1-carboxylate as a colorless foam (1.04 g, 2.23 mmol, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$): 7.39-7.29 (m, 7H), 7.23-7.19 (m, 3H), 5.34 (d, 1H), 4.82 (d, 1H), 4.58 (d, 1H), 4.37 (d, 1H), 4.37 (d, 1H), 4.22 (d, 1H), 4.15 (s, 1H), 4.08 (d, 1H), 3.97 (d, 1H), 3.75 (d, 1H), 3.74 (d, 1H), 3.67 (d, 1H), 3.64 (br s, 1H), 1.43 (s, 9H).

[0695] A solution of 1,1-dimethylethyl 3-[3,6-dioxo-1,4-bis(phenylmethyl)piperazin-2-yl]-3-hydroxyazetidine-1-carboxylate (1.04 g, 2.2 mmol) in methanol (10 mL) was treated with hydrogen chloride in dioxane (4 N, 5.5 mL, 22 mmol) at 60 °C for 25 min. After cooling to room temperature the solution was concentrated. Ethyl acetate and 2 N hydrochloric acid were added to the residue and the phases were separated. The organic phase was discarded. The aqueous phase was basified with 5 M sodium hydroxide and the resulting solution was extracted 4 times with ethyl acetate. The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography (85% dichloromethane: 14% methanol: 1% aqueous ammonium

hydroxide) to provide 3-(3-hydroxyazetidin-3-yl)-1,4-bis(phenylmethyl)piperazine-2,5-dione as a colorless film (493 mg, 1.35 mmol, 61% yield). ^{1}H NMR (400 MHz, $CDCl_3$): 7.39-7.28 (m, 6H), 7.25-7.20 (m, 4H), 5.39 (d, 1H), 4.80 (d, 1H), 4.44 (d, 1H), 4.36 (d, 1H), 4.26 (d, 1H), 4.11 (s, 1H), 3.97 (d, 1H), 3.83 (d, 1H), 3.71 (d, 1H), 3.27 (m, 2H); MS (EI) for $C_{21}H_{23}N_3O_3$: 366 (MH^+).

[0696] A solution 3-(3-hydroxyazetidin-3-yl)-1,4-bis(phenylmethyl)piperazine-2,5-dione (493 mg, 1.35 mmol) in ethyleneglycol dimethylether (12 mL) was treated with sodium borohydride (511 mg, 13.5 mmol) followed by slow addition of boron trifluoride-diethyl etherate. The reaction mixture was then heated to reflux for 3 hours. After cooling to 0 °C, methanol (17 mL) was added followed by careful addition of concentrated hydrochloric acid (7 mL). The resulting mixture was heated to reflux for 70 minutes. After cooling to room temperature, insoluble residue was removed by filtration. The filtrate was concentrated to an aqueous mixture of about 10 mL in volume. This mixture was cooled to 0 °C and was then basified to pH 10 with 5 M sodium hydroxide (approximately 17 mL). Dichloromethane (10 mL) was then added followed by di-*tert*-butyl dicarbonate (442 mg, 2.03 mmol). The mixture was warmed to room temperature and stirred for 15 minutes. The layers were separated and the aqueous phase was extracted twice with dichloromethane. The organic extracts were combined, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography (70% hexanes: 30% ethyl acetate) to provide 1,1-dimethylethyl 3-[1,4-bis(phenylmethyl)piperazin-2-yl]-3-hydroxyazetidine-1-carboxylate as a white foam (408 mg, 0.93 mmol, 69% yield). ^{1}H NMR (400 MHz, $CDCl_3$): 7.35-7.24 (m, 10H), 4.12 (br s, 1H), 3.88 (d, 1H), 3.78-3.65 (m, 4H), 3.53 (d, 1H), 3.43 (d, 1H), 3.21 (m, 1H), 2.80 (br s, 1H), 2.66 (m, 1H), 2.57-2.37 (m, 4H), 1.41 (s, 9H); MS (EI) for $C_{26}H_{35}N_3O_3$: 438 (MH^+).

[0697] To a solution of 1,1-dimethylethyl 3-[1,4-bis(phenylmethyl)piperazin-2-yl]-3-hydroxyazetidine-1-carboxylate (408 mg, 0.93 mmol) in methanol (15 mL) was added 10% palladium on carbon (wet), and the resulting suspension was subjected to an atmosphere of hydrogen for 21 hours. The catalyst was removed by filtration through celite, and the filter cake was rinsed with methanol. The combined filtrate was concentrated to provide 1,1-dimethylethyl 3-hydroxy-3-piperazin-2-ylazetidine-1-carboxylate as a brown syrup (227 mg, 0.88 mmol, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$): 3.94-3.76 (m, 5H), 3.12 (m, 1H), 3.01 (m, 1H), 2.94-2.81 (m, 3H), 2.78-2.70 (m, 2H); MS (EI) for $C_{12}H_{23}N_3O_3$: 258 (MH^+).

[0698] To a solution of 1,1-dimethylethyl 3-hydroxy-3-piperazin-2-ylazetidine-1-carboxylate (227 mg, 0.88 mmol) and *N,N*-diisopropylethylamine (436 μL, 2.64 mmol) in THF (5 mL) was added 2-nitrobenzenesulfonyl chloride (195 mg, 0.88 mmol). The mixture was stirred at room temperature for 2 hours. The solution was concentrated and the residue was purified by column chromatography (95% dichloromethane: 5% methanol) to provide 1,1-dimethylethyl 3-hydroxy-3-{4-[(2-nitrophenyl)sulfonyl]piperazin-2-yl}azetidine-1-carboxylate as a white foam (308 mg, 0.70 mmol, 79% yield). ^{1}H NMR (400 MHz, $CDCl_3$): 7.98 (m, 1H), 7.72 (m, 2H), 7.64 (m, 1H), 3.96 (d, 1H), 3.94 (d, 1H), 3.85 (d, 1H), 3.79 (d, 1H), 3.79-3.73 (m, 2H), 3.11 (m, 1H), 3.05 (dd, 1H), 3.00 (br s, 1H), 2.94 (dt, 1H), 2.78 (dt, 1H), 2.68 (dd, 1H), 1.45 (s, 9H).

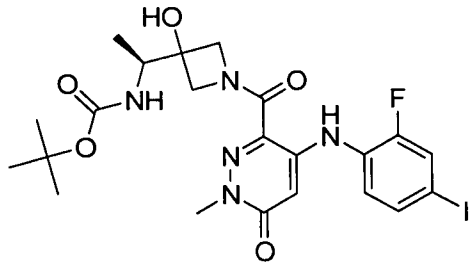
[0699] To a solution of 1,1-dimethylethyl 3-hydroxy-3-{4-[(2-nitrophenyl) sulfonyl]piperazin-2-yl}azetidine-1-carboxylate (308 mg, 0.70 mmol) in methanol (10 mL) was added HCl in dioxane (4 N, 1.75 mL, 7.0 mmol), and the mixture was heated to 60 °C for 30 minutes. The solution was concentrated to provide 3-{4-[(2-nitrophenyl) sulfonyl]piperazin-2-yl}azetidin-3-ol as a sticky white solid. This material was dissolved in dichloromethane (7 mL). To the solution was added *N,N*-diisopropylethylamine (1.16 mL, 7.0 mmol) followed by 3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoyl fluoride (277 mg, 0.7 mmol), prepared using procedures similar to those described in Reference 1, and the resulting mixture was stirred at room temperature for 16 hours. The solution was concentrated and the residue was purified by column chromatography (95% dichloromethane: 5% methanol) to provide 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{4-[(2-nitrophenyl)sulfonyl]piperazin-2-yl}azetidin-3-ol as a pale yellow foam (453 mg, 0.63 mmol, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$): 8.49 (s, 1H), 7.96 (dd, 1H), 7.71 (m, 2H), 7.53 (dd, 1H), 7.39 (dd, 1H), 7.33 (d, 1H), 7.15 (m, 1H), 6.84 (br s, 1H), 6.62 (m, 1H), 4.29-3.97 (br m, 4H), 3.79-3.62 (m, 3H), 3.26-2.99 (br m, 3H), 2.92-2.62 (br m, 3H); MS (EI) for $C_{26}H_{23}F_3IN_5O_6S$: 718 (MH^+).

[0700] To a solution of 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-{4-[(2-nitrophenyl)sulfonyl]piperazin-2-yl}azetidin-3-ol (139.4 mg, 0.19 mmol) in DMF (1 mL) was added potassium carbonate (79 mg, 0.57 mmol) and thiophenol (21 μL, 0.21 mmol). The mixture was stirred for 45 min at room temperature then quenched with water. The aqueous mixture was extracted twice with ethyl acetate, and the combined organic extracts were dried over magnesium sulfate, filtered, and concentrated. The residue

was purified by preparative reverse phase HPLC to provide 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-piperazin-2-ylazetidin-3-ol as a white solid (26.8 mg, 0.05 mmol). ^{1}H NMR (400 MHz, CD_3OD): 7.45 (dd, 1H), 7.36 (m, 1H), 7.32 (m, 1H), 7.03 (m, 1H), 6.62 (ddd, 1H), 4.51 (br dd, 1H), 4.31 (br dd, 1H), 4.17-3.92 (m, 4H), 3.73-3.56 (m, 3H), 3.46 (br m, 1H), 3.26 (m, 1H); MS (EI) for $C_{20}H_{20}F_3IN_4O_2$: 533 (MH^+).

EXAMPLE 36

1,1-Dimethylethyl {(1*S*)-1-[1-({4-[(2-fluoro-4-iodophenyl)amino]-1-methyl-6-oxo-1,6-dihydropyridazin-3-yl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}carbamate



[0701] To a suspension of 4-[(2-fluoro-4-iodophenyl)amino]-1-methyl-6-oxo-1,6-dihydropyridazine-3-carboxylic acid (50 mg, 0.13 mmol) in DMF (2 mL), prepared using similar procedures to those described in Reference 4, at room temperature was added 1-hydroxybenzotriazole (36.3 mg, 0.27 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (52 mg, 0.27 mmol) and the reaction was stirred for 2 hours. 1,1-Dimethylethyl [(1*S*)-1-(3-hydroxyazetidin-3-yl)ethyl]carbamate (30 mg, 0.13 mmol), prepared using procedures similar to those in Example 28, and triethylamine (0.04 mL) were added and the mixture was stirred for 15 hours. The reaction mixture was partitioned between saturated sodium chloride and ethyl acetate. The organic layer was washed with 5% lithium chloride solution, saturated sodium bicarbonate, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to give crude product as yellow oil. The oil was purified by column chromatography (silica gel, ethyl acetate) to afford 1,1-dimethylethyl {(1*S*)-1-[1-({4-[(2-fluoro-4-iodophenyl)amino]-1-methyl-6-oxo-1,6-dihydropyridazin-3-yl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}carbamate as a yellow oil (55 mg, 73% yield): ^{1}H NMR (400 MHz, $CDCl_3$): 10.24-10.23 (m, 1H), 7.52-7.50 (m, 2H), 7.12-7.07 (m, 1H), 6.10-6.09 (m, 1H), 5.13-5.09 (m, 1H), 4.91-4.82 (m, 1H), 4.60-4.39 (m, 2H), 4.10-4.08 (m, 1H), 4.00-3.87 (m, 2H), 3.70 (d, 3H), 1.43 (s, 9H), 1.24-1.20 (m, 3H); MS (EI) for $C_{22}H_{27}FIN_5O_5$: 588 (MH^+).

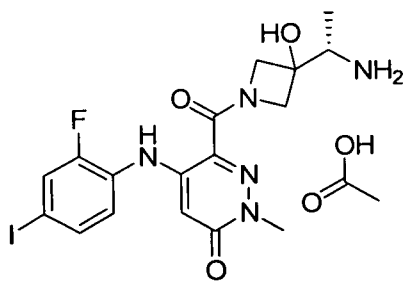
[0702] Using the same or analogous synthetic techniques and substituting, as necessary, with alternative reagents, the following MEK compounds were prepared:

[0703] **EXAMPLE 36(a).** 1,1-Dimethylethyl {(1*S*)-1-[1-({5-[(4-bromo-2-chlorophenyl) amino]-4-fluoro-1-methyl-1*H*-benzimidazol-6-yl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}carbamate: ^{1}H NMR (400 MHz, $CDCl_3$): 7.95 (s, 1H), 7.45-7.44 (m, 1H), 7.33-7.27 (m, 2H), 7.15-7.12 (m, 1H), 6.50-6.47 (m, 1H), 4.82-4.74 (m, 1H), 4.17-3.92 (m, 4H), 3.86 (s, 3H), 3.74-3.60 (m, 1H), 1.40 (s, 9H), 1.11-1.06 (m, 3H). MS (EI) for $C_{25}H_{28}BrClFN_5O_4$: 598 (MH^+) with a chloro, bromo isotope pattern.

[0704] **EXAMPLE 36(b).** 1,1-Dimethylethyl (2*S*)-2-[1-({5-[(4-bromo-2-chlorophenyl) amino]-4-fluoro-1-methyl-1*H*-benzimidazol-6-yl}carbonyl)-3-hydroxyazetidin-3-yl] piperidine-1-carboxylate: MS (EI) for $C_{28}H_{32}BrClFN_5O_4$: 638 (MH^+) with a chloro, bromo isotope pattern.

Example 37

6-({3-[(1*S*)-1-aminoethyl]-3-hydroxyazetidin-1-yl}carbonyl)-5-[(2-fluoro-4-iodophenyl)amino]-2-methylpyridazin-3(2*H*)-one acetate salt



[0705] 1,1-Dimethylethyl {(1*S*)-1-[1-({4-[(2-fluoro-4-iodophenyl)amino]-1-methyl-6-oxo-1,6-dihydropyridazin-3-yl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}carbamate (55 mg, 0.09 mmol), prepared using procedures similar to those described in Example 36, was taken up in methanol (2 mL) and hydrochloric acid (4N in dioxane, 1 mL, 4 mmol) was added and the reaction was stirred at 60 °C for 2 hours. The reaction mixture was concentrated *in vacuo* and was purified by reverse-phase HPLC followed by lyophilization of the pure fractions to afford 6-({3-[(1*S*)-1-aminoethyl]-3-hydroxyazetidin-1-yl}carbonyl)-5-[(2-fluoro-4-iodophenyl)amino]-2-methylpyridazin-3(2*H*)-one acetate as yellow solid (40 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): 10.17 (d, 1H), 7.52-7.46 (m, 2H), 7.09 (t, 1H), 6.13-6.12 (m, 1H), 4.51-4.48 (m, 2H), 4.18-4.03 (m, 2H), 3.73 (d, 3H), 3.35-3.28 (m, 1H), 3.22-2.80 (br, 3H), 1.21-1.19 (m, 3H); MS (EI) for $C_{17}H_{19}FIN_5O_3$: 488 (MH^+).

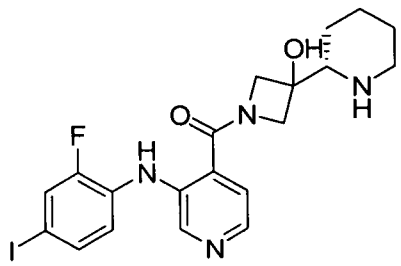
[0706] Using the same or analogous synthetic techniques and/or substituting with alternative reagents, the following MEK compounds were prepared:

[0707] **Example 37(a).** 3-[(1*S*)-1-Aminoethyl]-1-({5-[(4-bromo-2-chlorophenyl)amino]-4-fluoro-1-methyl-1*H*-benzimidazol-6-yl}carbonyl)azetidin-3-ol hydrochloride. MS (EI) for $C_{20}H_{20}BrClFN_5O_2$: 498 (MH^+) with a chloro, bromo isotope pattern

[0708] **Example 37(b).** 1-({5-[(4-Bromo-2-chlorophenyl)amino]-4-fluoro-1-methyl-1*H*-benzimidazol-6-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol hydrochloride. ^{1}H NMR (400 MHz, CD_3OD): 9.42 (s, 1H), 7.97-7.96 (m, 1H), 7.57 (s, 1H), 7.30-7.27 (m, 1H), 6.70-6.66 (m, 1H), 4.60-4.55 (m, 1H), 4.28 (t, 1H), 4.19 (s, 3H), 4.13-3.98 (m, 2H), 3.38-3.32 (m, 2H), 3.00 (t, 1H), 1.86-1.30 (m, 6H). MS (EI) for $C_{23}H_{24}BrClFN_5O_2$. HCl: 538 (MH^+) with a chloro, bromo isotope pattern

EXAMPLE 38

1-({3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol



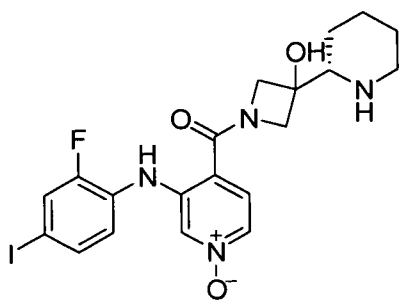
[0709] 3-[(2-Fluoro-4-iodophenyl)amino]pyridine-4-carboxylic acid (200 mg, 0.559 mmol), prepared using procedures similar to those described in WO 2006/045514, was suspended in DMF (7 mL) and 1-hydroxybenzotriazole (151 mg, 1.12 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (214 mg, 1.12 mmol) were added. The mixture was stirred at ambient for 10 minutes and then triethylamine (0.078 mL, 0.559 mmol) was added. After a further 20 minutes, 1,1-dimethylethyl (2*S*)-2-(3-hydroxyazetidin-3-yl)piperidine-1-carboxylate (143 mg, 0.559 mmol), prepared using similar procedures to those described in Example 22(a) and 22(b), and triethylamine (0.16 mL, 1.15 mmol) were added and the mixture was stirred for 15 hours. The mixture was partitioned between ethyl acetate and saturated ammonium chloride. The organic portion was washed with 5% lithium chloride and twice with saturated sodium bicarbonate, then was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 60-80% ethyl acetate in hexanes) to give 1,1-dimethylethyl (2*S*)-

2-[1-({3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate (368 mg, 0.587 mmol, 74% yield): ^{1}H NMR (400 MHz, $CDCl_3$): 8.73 (br m, 1H), 8.62 (br s, 1H), 8.14 (d, 1H), 7.47 (dd, 1H), 7.43-7.39 (m, 1H), 7.20-7.12 (m, 2H), 4.38-4.21 (m, 2H), 4.16-4.01 (m, 2H), 4.01-3.88 (m, 1H), 3.44-3.30 (m, 1H), 2.98-2.83 (m, 1H), 2.00-1.88 (m, 1H), 1.71-1.50 (m, 6H), 1.44 (s, 9H); MS (EI) for $C_{25}H_{30}FIN_4O_4$: 597 (MH^+).

[0710] 1,1-Dimethylethyl (2*S*)-2-[1-({3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate (24 mg, 0.040 mmol) was dissolved in methanol (2 mL) and treated with 4 N hydrochloric acid in dioxane (0.25 mL, 1 mmol) at reflux for 20 minutes. The mixture was concentrated *in vacuo* and was purified by reverse-phase HPLC followed by lyophilization of the pure fractions to afford 1-({3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol acetate (14 mg, 0.025 mmol, 63% yield): ^{1}H NMR (400 MHz, d_6-DMSO): 8.62 (br s, 1H), 8.46 (s, 1H), 8.18 (dd, 1H), 7.65 (dd, 1H), 7.45 (d, 1H), 7.37 (t, 1H), 7.16-7.08 (m, 1H), 4.25 (dd, 1H), 4.04 (dd, 1H), 3.90 (t, 1H), 3.70 (d, 1H), 2.95 (br d, 1H), 2.52-2.42 (m, 2H), 1.78-1.68 (m, 1H), 1.57 (br t, 1H), 1.47 (br d, 1H), 1.35-1.13 (m, 2H), 1.10-0.96 (m, 1H); MS (EI) for $C_{20}H_{22}FIN_4O_2$: 497 (MH^+).

EXAMPLE 39

1-({3-[(2-fluoro-4-iodophenyl)amino]-1-oxidopyridin-4-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol



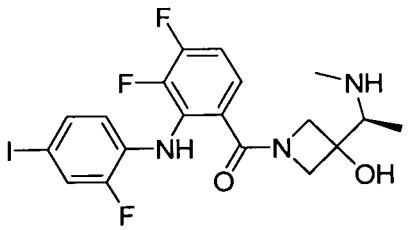
[0711] 1,1-Dimethylethyl (2*S*)-2-[1-({3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate (80 mg, 0.134 mmol), prepared using procedures similar to those described in Example 38, was dissolved in dichloromethane (3 mL) and treated with 3-chloroperoxybenzoic acid (73% pure; 32 mg, 0.135 mmol) at ambient for 7 hours. 3-chloroperoxybenzoic acid (73% pure; 32 mg, 0.135 mmol) was added and the mixture was stirred for 15 hours. The mixture was purified by

column chromatography (silica gel, 0-10% ethanol in ethyl acetate) to give 1,1-dimethylethyl (2*S*)-2-[1-({3-[(2-fluoro-4-iodophenyl)amino]-1-oxidopyridin-4-yl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate (57 mg, 0.093 mmol, 69% yield): ^{1}H NMR (400 MHz, $CDCl_3$): 9.38 (s, 1H), 8.00 (s, 1H), 7.68 (dd, 1H), 7.51 (dd, 1H), 7.46 (d, 1H), 7.19 (br d, 1H), 7.09 (t, 1H), 5.78 (br, 1H), 4.44-3.98 (m, 3H), 3.98-3.87 (m, 1H), 3.49-3.39 (m, 1H), 3.07-2.88 (m, 1H), 2.01-1.91 (m, 1H), 1.70-1.47 (m, 6H), 1.45 (s, 9H); MS (EI) for $C_{25}H_{30}FIN_4O_5$: 613 (MH^+).

[0712] 1,1-Dimethylethyl (2*S*)-2-[1-({3-[(2-fluoro-4-iodophenyl)amino]-1-oxidopyridin-4-yl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate (57 mg, 0.093 mmol) was dissolved in methanol (2 mL) and treated with 4N hydrochloric acid in dioxane (0.25 mL, 1 mmol) at 50 °C for 2.25 hours. The mixture was concentrated *in vacuo* and was purified by reverse-phase HPLC followed by lyophilization of the pure fractions to afford 1-({3-[(2-fluoro-4-iodophenyl)amino]-1-oxidopyridin-4-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol acetate (35 mg, 0.061 mmol, 66% yield): ^{1}H NMR (400 MHz, d_6-DMSO): 7.83 (s, 1H), 7.72 (dt, 2H), 7.55-7.51 (m, 1H), 7.47-7.41 (m, 1H), 7.24 (t, 1H), 4.45-4.32 (m, 1H), 4.14-3.95 (m, 2H), 3.72 (d, 1H), 2.97 (d, 1H), 2.58-2.43 (m, 2H), 1.80-1.73 (m, 1H), 1.67-1.55 (m, 1H), 1.49 (br d, 1H), 1.38-1.16 (m, 2H), 1.16-1.01 (m, 1H); MS (EI) for $C_{20}H_{22}FIN_4O_3$: 513 (MH^+).

EXAMPLE 40

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1*S*)-1-(methylamino)ethyl]azetidin-3-ol



[0713] To 3-[(1*S*)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl) amino]phenyl}carbonyl)azetidin-3-ol (87.4 mg, 0.18 mmol), prepared using similar procedures to those described in Example 28, was added formaldehyde (37% aqueous, 14 mg, 0.18 mmol) in methanol (2 mL) and sodium borohydride (7 mg, 0.18 mmol). The mixture was stirred for 3 h at rt, after which sodium borohydride (16 mg, 0.42 mmol) was added. Upon stirring an additional 1.25 h, more formaldehyde (37% aqueous, 1 drop) was

added, and the mixture was stirred 3 days at rt. A further small spatula (~50 mg) of sodium borohydride was then added, and the mixture was stirred at rt for 30 min. After quenching with 1 N HCl, the reaction mixture was purified directly by preparative HPLC. The clean material was converted to its hydrochloride salt to provide 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1*S*)-1-(methylamino)ethyl]azetidin-3-ol as a yellow solid (21.7 mg, 0.040 mmol, 22% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 7.47 (dd, 1H), 7.36 (d, 1H), 7.31 (m, 1H), 7.06 (q, 1H), 6.62 (dt, 1H), 4.36 (dd, 1H), 4.21-3.91 (m, 3H), 3.44 (q, 1H), 2.66 (s, 3H), 1.29 (br m, 3H); MS (EI) for $C_{19}H_{19}F_3IN_3O_2$: 506 (MH^+).

Biological Example 1

Biochemical Assay

[0714] For a biochemical measurement of MEK1 inhibitory activity, MEK compounds were screened in a triple coupled cRaf-MEK-ERK2 assay using ALPHASCREEN (Registered Trademark of Perkin Elmer) technology (Perkin Elmer). The MEK compound 0.5 μL of 100% DMSO stock solution, is diluted into an assay buffer composed of 20 mM Tris (pH = 7.5), 10 mM magnesium chloride, 0.03% CHAPS and 1 mM DTT. Subsequently, 10 μL of substrate mixture is added composed of unactive MEK1 (3 nM), ATP (50 μM), unactive ERK2 (4 nM), biotinylated MBP peptide (b-FFKNIVTPRTPPPSQGK, 1 μM) and antiphospho MBP peptide (0.5 nM). The mixture is then gently shaken for 30 minutes at room temperature followed by addition of active cRaf (5 μL at 0.5 nM) to initiate reaction. The mixture is then shaken for 100 minutes at room temperature then quenched by addition of 10 μL of a mixture of 5μg/mL streptavidin donor beads and 5μg/mL protein A acceptor beads in detection buffer (75 mM Hepes pH = 7.5, 300 mM sodium chloride, 120 mM EDTA, 0.3% BSA and 0.03% Tween), followed by incubation overnight and signal detection on an ALPHAQuest® (Registered Trademark of Perkin Elmer) plate reader (Perkin Elmer).

[0715] The extent to which these MEK compounds inhibitor MEK can be determined by one of ordinary skill in the art. In particular, the compounds can be tested in the assay described in Biological Example 1. When tested in that assay, MEK compounds demonstrated the ability to bind to MEK. In one embodiment the MEK inhibitor is selected from the MEK compounds in Table 1 having a MEK-binding affinity of about 4 μM or less. In another embodiment, the MEK inhibitor is selected from the MEK compounds in Table 1 having a MEK-binding affinity of about 3 μM or less. In another embodiment, the MEK

inhibitor is selected from the MEK compounds in Table 1 having a MEK-binding affinity of about 2 μM or less. In another embodiment, the MEK inhibitor is selected from the MEK compounds in Table 1 having a MEK-binding affinity of about 1.6 μM or less. In another embodiment, the MEK inhibitor is selected from the MEK compounds in Table 1 having a MEK-binding affinity of about 1 μM or less. In another embodiment, the MEK inhibitor is selected from the MEK compounds in Table 1 having a MEK-binding affinity of about 0.7 μM or less. In another embodiment, the MEK inhibitor is selected from the MEK compounds in Table 1 having a MEK-binding affinity of about 0.3 μM or less. In another embodiment, the MEK inhibitor is selected from the MEK compounds in Table 1 having a MEK-binding affinity of about 0.2 μM or less. In another embodiment, the MEK inhibitor is selected from the MEK compounds in Table 1 having a MEK-binding affinity of about 0.1 μM or less. In another embodiment, the MEK inhibitor is selected from the MEK compounds in Table 1 having a MEK-binding affinity of about 0.05 μM or less.

Biological Example 2

Endogenous ERK Phosphorylation ELISA Assay

[0716] MDA-MB-231T (ATCC), Calu-6 (ATCC), HCT 116 (ATCC), A2058 (ATCC), and A375 (ATCC) cells were seeded at 20000, 30000, 30000, 20000, and 30000 cells/well, respectively, onto black 96-well microtiter plates (Costar 3904), in DMEM (Cellgro) containing 10% FBS (Heat-Inactivated, Cellgro), 1% NEAA (Cellgro), and 1% Pen/Strep (Cellgro). SK-MEL-28 (ATCC) cells were seeded at 20000 cells/well in MEM (ATCC) containing 10% FBS (Heat-Inactivated, Cellgro), and 1% Pen/Strep (Cellgro). The cells were then incubated at 37°C, 5% CO_2 for 24 hours. Serum starvation was performed by replacing the medium with serum-free DMEM or MEM for an additional 24 hours. Serial dilutions of test compounds in fresh serum-free medium in a final concentration of 0.3% DMSO (vehicle) were added to the cells and incubated for 1 hour. Negative control wells were in serum-free medium + 0.3% DMSO only. After treatment, the medium was removed and cells were fixed with 4% formaldehyde, followed by quenching of endogenous peroxidases with 0.6% H_2O_2. Plates were then blocked (10% FBS, Cellgro) and incubated with mouse monoclonal anti-phospho-p44/42 MAPK, E10 (1:2000, Cell Signaling), followed by secondary antibody (HRP-conjugated, goat anti-mouse IgG, 1:3000 from Jackson ImmunoResearch Laboratories, Inc). Washing of the plates was performed with PBS-T (0.1% Triton X-100) in between all

incubation steps. A luminol-based substrate solution was then added and plates read using the Victor Wallac machine. IC_{50} values were determined based on total ERK phosphorylation with compound treatment versus total ERK phosphorylation with 0.3% DMSO treatment alone.

Biological Example 3

BrdU Cell Proliferation Assay

[0717] MDA-MB-231T (ATCC), Calu-6 (ATCC), HCT 116 (ATCC), A2058 (ATCC), A375 (ATCC), and Colo-205 (ATCC) cells were plated at densities of 2500, 3500, 3500, 2500, 3500, and 15000 cells/well onto 96-well microtiter plates (Cat# 3904, Costar), in DMEM (Cellgro) containing 10% FBS (Heat Inactivated, Cellgro), 1% Pen/Strep (Cellgro), and 1% NEAA (Cellgro). SK MEL-28 (ATCC) and WM-266-4 (ATCC) were plated at densities of 2000 and 6000 cells/well in MEM (ATCC) containing 10% FBS (Heat-Inactivated, Cellgro), and 1% Pen/Strep (Cellgro). The cells were incubated overnight at 37°C, 5% CO_2 for 18 h. The next day, cells were treated with a serial dilution of compound in medium (containing a final concentration of 0.3% DMSO). Triplicate wells were used for each compound concentration. The control wells received 0.3% DMSO media. The cultures were incubated at 37°C, 5% CO_2 for an additional 48 hours. The cells were assayed for proliferation according to the "Cell Proliferation ELISA, Bromo Deoxyuridine (BrdU) (chemiluminescence) kit" from Roche. The cells were treated with the BrdU labeling solution and then fixed with FixDenat solution. Anti-BrdU-POD (PerOxiDase) conjugate was added to the cells, after which the plates were washed 3x with 1X PBS. Substrate solution was added, and the plates were read for luminescence using the Victor Wallac machine. IC_{50} values were calculated based on the cell proliferation with compound treatment compared to the vehicle control.

Biological Example 4

In vivo mouse models

[0718] Female athymic nude mice (NCr) 5-8 weeks of age and weighing approximately 20g were purchased from Taconic (Germantown, NY). Prior to initiation of a study, the animals were allowed to acclimate for a minimum of 48 hours. During these studies, animals were provided food and water ad libitum and housed in a room conditioned at 70-75°F and 60% relative humidity. A 12 hours light and 12 hours dark cycle was maintained with automatic timers.

[0719] Colo-205 human colorectal carcinoma cells were cultured in vitro in DMEM (Mediatech) supplemented with 10% Fetal Bovine Serum (Hyclone), Penicillin-Streptomycin and non-essential amino acids at 37 °C in a humidified, 5% CO_2 atmosphere. On day 0, cells were harvested by trypsinization, and $3x10^6$ cells (passage #3, 92% viability) in 0.1 ml ice-cold Hank's balanced salt solution were implanted intradermally in the hind-flank of 5-8 week old female athymic nude mice.

[0720] A375 human melanoma cells were cultured in vitro in DMEM (Mediatech) supplemented with 10% Fetal Bovine Serum (Hyclone), Penicillin-Streptomycin and non-essential amino acids at 37 °C in a humidified, 5% CO_2 atmosphere. On day 0, cells were harvested by trypsinization, and $5x10^6$ cells (passage #8, >99% viability) in 0.1 mL ice-cold Hank's balanced salt solution were implanted intradermally in the hind-flank of 5-8 week old female athymic nude mice.

[0721] A2058 human melanoma cells were cultured in vitro in DMEM (Mediatech) supplemented with 10% Fetal Bovine Serum (Hyclone), Penicillin-Streptomycin and non-essential amino acids at 37 °C in a humidified, 5% CO_2 atmosphere. On day 0, cells were harvested by trypsinization, and $3x10^6$ cells (passage #5, 80% viability) in 0.1 mL ice-cold Hank's balanced salt solution were implanted intradermally in the hind-flank of 5-8 week old female athymic nude mice.

[0722] MDA-MB-231 human breast adenocarcinoma cells were cultured in vitro in DMEM (Mediatech) supplemented with 10% Fetal Bovine Serum (Hyclone), Penicillin-Streptomycin and non-essential amino acids at 37 °C in a humidified, 5% CO_2 atmosphere. On day 0, cells were harvested by trypsinization, and $1x10^6$ cells (passage #6, >99% viability) in 0.1 mL ice-cold Hank's balanced salt solution were implanted subcutaneously into the mammary fat pad of 5-8 week old female athymic nude mice.

[0723] Calu-6 human lung anaplastic carcinoma cells were cultured in vitro in DMEM (Mediatech) supplemented with 10% Fetal Bovine Serum (Hyclone), Penicillin-Streptomycin and non-essential amino acids at 37 °C in a humidified, 5% CO_2 atmosphere. On day 0, cells were harvested by trypsinization, and $5x10^6$ cells (passage #8, 96% viability) in 0.1 mL ice-cold Hank's balanced salt solution were implanted intradermally in the hind-flank of 5-8 week old female athymic nude mice.

[0724] For subcutaneous or intradermal tumors, the mean tumor weight of each animal in the respective control and treatment groups was determined twice weekly during the study. Tumor weight (TW) was determined by measuring perpendicular diameters with a caliper,

using the following formula: tumor weight (mg) = [tumor volume = length (mm) x width^2 (mm^2)]/2.

[0725] Percent inhibition of tumor growth (TGI) is determined with the following formula:

$$\left[1 - \left[\frac{(X_f - X_0)}{(Y_f - X_0)}\right]\right] * 100$$

wherein X_0 = average TW of all tumors on group day; X_f = TW of treated group on Day f; Y_f = TW of vehicle control group on Day f

[0726] If tumors regress below their starting sizes, then the percent tumor regression is determined with the following formula:

$$\left[\frac{(X_0 - Xf)}{X_0}\right] * 100$$

[0727] TGI is calculated individually for each tumor to obtain a mean ± SEM value for each experimental group. Statistical significance is determined using the 2-tailed Student's t-test (significance defined as $P<0.05$).

Pharmaceutical Composition Examples

[0728] The following are representative pharmaceutical formulations containing a compound of Formula I(M) or Formula I(N).

Tablet Formulation

[0729] The following ingredients are mixed intimately and pressed into single scored tablets.

Ingredient	Quantity per tablet, mg
compound of formula I(M) or I(N)	400
Cornstarch	50
croscarmellose sodium	25
Lactose	120
magnesium stearate	5

Capsule Formulation

[0730] The following ingredients are mixed intimately and loaded into a hard-shell gelatin capsule.

Ingredient	Quantity per tablet, mg
compound of formula I(M) or I(N)	200
lactose, spray-dried	148
magnesium stearate	2

Suspension Formulation

[0731] The following ingredients are mixed to form a suspension for oral administration.

Ingredient	Amount
compound of formula I(M) or I(N)	1.0 g
fumaric acid	0.5 g
sodium chloride	2.0 g
methyl paraben	0.15 g
propyl paraben	0.05 g
granulated sugar	25.5 g
sorbitol (70% solution)	12.85 g
Veegum K (Vanderbilt Co.)	1.0 g
Flavoring	0.035 mL
Colorings	0.5 mg
distilled water	q.s. to 100 mL

Injectable Formulation

[0732] The following ingredients are mixed to form an injectable formulation.

Ingredient	Amount
compound of formula I(M) or I(N)	1.2 g
sodium acetate buffer solution	0.4 M 2.0 mL
HCl (1 N) or NaOH (1 M)	q.s. to suitable pH
water (distilled, sterile)	q.s.to 20 mL

[0733] All of the above ingredients, except water, are combined and heated to 60-70 °C. with stirring. A sufficient quantity of water at 60 °C. is then added with vigorous stirring to emulsify the ingredients, and water then added q.s. to 100 g.

Suppository Formulation

[0734] A suppository of total weight 2.5 g is prepared by mixing the MEK compound described herein with Witepsol®. H-15 (triglycerides of saturated vegetable fatty acid; Riches-Nelson, Inc., New York), and has the following composition:

Ingredient	Quantity per tablet, mg
compound of Formula I(M) or I(N)	500
Witepsol® H-15	Balance

UTILITY OF JAK-2 COMPOUNDS

[0735] The compounds of Formula I(J) are useful for treating diseases, particularly myeloproliferative disorders, for example, myelofibrosis, thrombocythemia, polycythemia vera (PV), essential thrombocythemia (ET), agnogenic myeloid metaplasia (AMM), also referred to as idiopathic myelofibrosis (IMF), and chronic myelogenous leukemia (CML); and cancer, for example, ovarian cancer, cervical cancer, breast cancer, colorectal cancer, glioblastomas, prostrate, colon, melanoma, leukemia and haematopoietic malignancies, as described above, in which JAK-2 activity contributes to the pathology and/or symptomatology of the disease.

[0736] Suitable *in vitro* assays for measuring JAK-2 activity and the inhibition thereof by compounds are known. For further details of an *in vitro* assay for measuring JAK-2 activity see Biological Examples.

[0737] Assays for measurement of efficacy in treatment of various cancers are described in Biological Examples.

[0738] Suitable *in vivo* models of various cancers are known to those of ordinary skill in the art. For further details of *in vivo* assays see Biological Examples.

Synthetic Procedures for JAK-2 Compounds

[0739] The JAK-2 compounds of the invention, or their pharmaceutically acceptable salts, can have asymmetric carbon atoms, oxidized sulfur atoms or quaternized nitrogen atoms in their structure.

[0740] The JAK-2 compounds of the invention and their pharmaceutically acceptable salts can exist as single stereoisomers, racemates, and as mixtures of enantiomers and diastereomers. The compounds can also exist as geometric isomers. All such single

stereoisomers, racemates and mixtures thereof, and geometric isomers are intended to be within the scope of this invention.

[0741] It is assumed that when considering generic descriptions of JAK-2 compounds for the purpose of constructing a compound, such construction results in the creation of a stable structure. That is, one of ordinary skill in the art would recognize that theoretically some constructs which would not normally be considered as stable compounds (that is, sterically practical and/or synthetically feasible).

[0742] Methods for the preparation and/or separation and isolation of single stereoisomers from racemic mixtures or non-racemic mixtures of stereoisomers are well known in the art. For example, optically active (R)- and (S)- isomers can be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. Enantiomers (R- and S-isomers) can be resolved by methods known to one of ordinary skill in the art, for example by: formation of diastereoisomeric salts or complexes which can be separated, for example, by crystallization; via formation of diastereoisomeric derivatives which can be separated, for example, by crystallization, selective reaction of one enantiomer with an enantiomer-specific reagent, for example enzymatic oxidation or reduction, followed by separation of the modified and unmodified enantiomers; or gas-liquid or liquid chromatography in a chiral environment, for example on a chiral support, such as silica with a bound chiral ligand or in the presence of a chiral solvent. It will be appreciated that where a desired enantiomer is converted into another chemical entity by one of the separation procedures described above, a further step can be required to liberate the desired enantiomeric form. Alternatively, specific enantiomer can be synthesized by asymmetric synthesis using optically active reagents, substrates, catalysts or solvents or by converting on enantiomer to the other by asymmetric transformation. For a mixture of enantiomers, enriched in a particular enantiomer, the major component enantiomer can be further enriched (with concomitant loss in yield) by recrystallization.

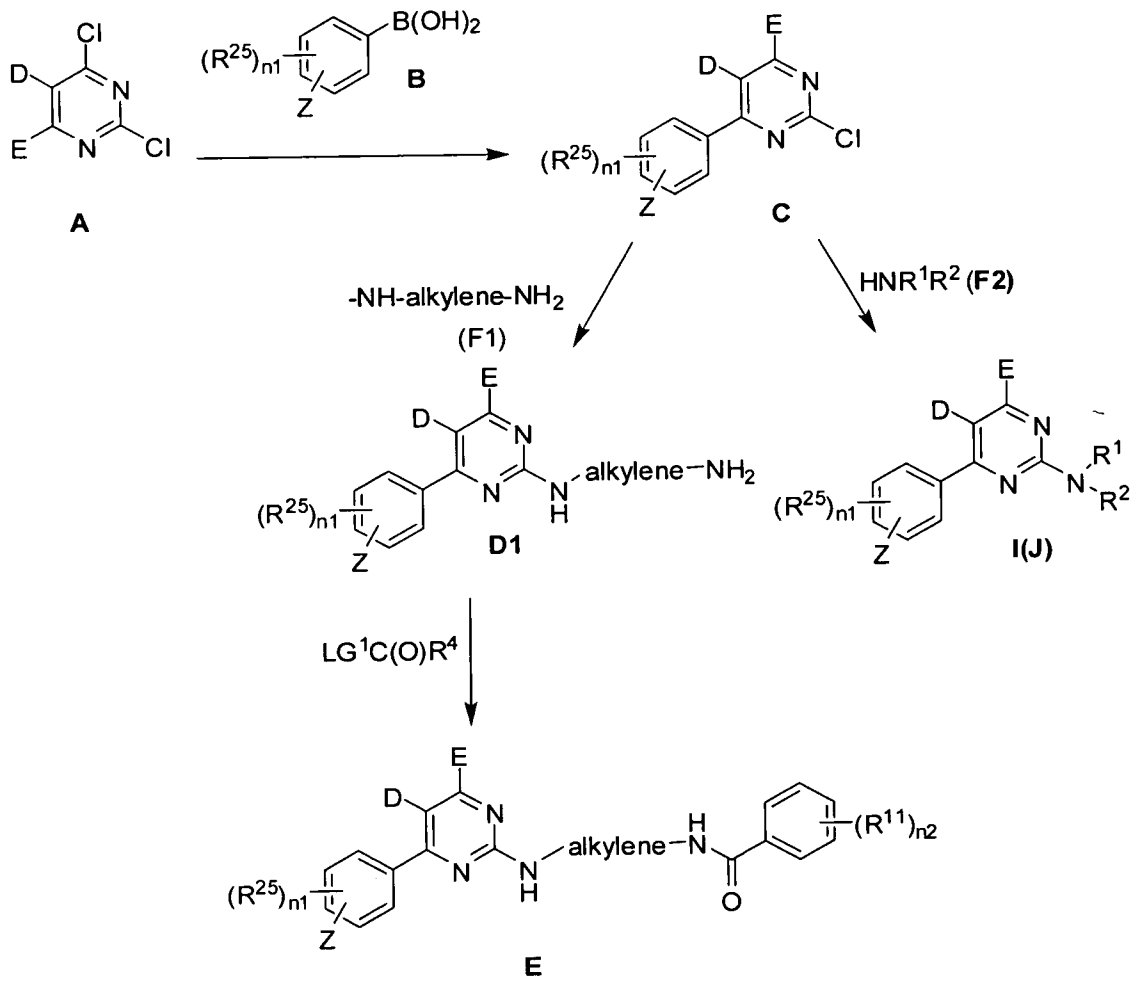
[0743] In addition, the JAK-2 compounds can exist in unsolvated as well as solvated forms with pharmaceutically acceptable solvents such as water, ethanol, and the like. In general, the solvated forms are considered equivalent to the unsolvated forms for the purposes of the present invention.

[0744] In addition, it is intended that the JAK-2 compounds are made either using standard organic synthetic techniques, including combinatorial chemistry or by biological methods, such as bacterial digestion, metabolism, enzymatic conversion, and the like.

[0745] Scheme 1 for the JAK-2 compounds below depicts the general synthetic procedure for the JAK-2 compounds. Synthesis of the JAK-2 compounds is not limited by the procedure of Scheme 1. One skilled in the art will know that other procedures can be used to synthesize the JAK-2 compounds, and that the procedure described in Scheme 1 is only one such procedure. In the descriptions below, one of ordinary skill in the art would recognize that specific reaction conditions, added reagents, solvents, and reaction temperatures can be modified for the synthesis of the JAK-2 compounds described herein. Thus, the general synthetic procedure depicted in Scheme 1 in conjunction with the specific examples that follow provide sufficient information and guidance to allow one of ordinary skill in the art to synthesize the JAK-2 compounds.

[0746] Compounds of formula I(J) can be prepared according to Scheme 1:

Scheme 1



[0747] The synthesis of compounds of Formula **I(J)** proceeds from commercially available reagents and employs standard techniques. Standard Suzuki coupling reactions

conditions can be used to convert dichloropyrimindines of formula **A** (commercially available from Sigma Aldrich) and boronic acids of formula **B** (commercially available from Sigma Aldrich, Fisher Scientific, or Combi-Blocks Inc.), where R^{25}, Z and and n1 are as defined in the Detailed Description of the Invention, to 4-substituted-2-chloropyrimindes of formula **C**. Compounds of Formula **D1** and **I** can be generated by reaction of **C** with the corresponding amines (**F1**, available from Fluka) or anilines (**F2**, available from Sigma Aldrich). Compounds of formula **D1** can be further transformed to amides of formula **E** using standard peptide coupling conditions with carboxylic acids or reaction with acid chlorides. For instance, **D1** ca be reacted with an intermediate of formula $LG^1C(O)R^4$ where LG^1 is a leaving group under acylation conditions and R^4 is phenyl optionally substituted with 1, 2, 3, 4, or 5 R^{11} groups, wherein R^{11} is as defined in the Detailed Description of the Invention to yield a compound of formula **E**.

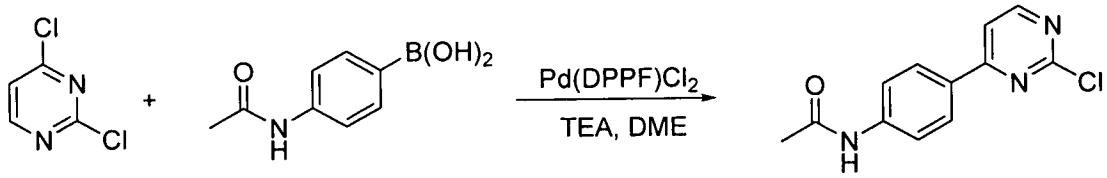
Synthetic Examples for JAK-2 Compounds

[0748] The following examples serve to more fully describe the manner of making the JAK-2 compounds described herein. These examples in no way serve to limit the scope of the JAK-2 compounds or the JAK-2 inhibitors, but rather are presented for illustrative purposes. All references cited herein are incorporated by reference in their entirety. Generally, each example is set out below with a corresponding multi-step synthesis procedure. Following the specific examples is a list of compounds that were made in a similar way.

Example 1

N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)acetamide (Compound 58)

a) N-(4-(2-chloropyrimidin-4-yl)phenyl)acetamide (C_1)

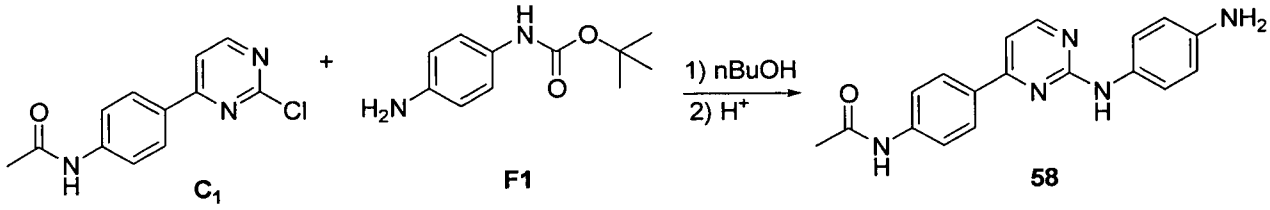


A_1 B_1 C_1

[0749] A flask was charged with 2,4-dichloropyrimindine A_1 (650 mg, 4.4 mmol), 4-acetoamidophenylboronic acid B_1 (820 mg, 4.6 mmol), dicholor[1,1'-bis(diphenyl-phosphino)ferrocenepalladium (480 mg, 0.56 mmol, 15 mol %), and triethylamine (1.5 mL, 11 mmol). Ethyleneglycoldimethylether (30 mL) was added to the flask and the mixture was purged with N_2 for 5 minutes. The reaction mixture was stirred under an N_2 atmosphere at 80

°C for 12 hours, after which time, ether was added and the reaction mixture was filtered. The product, C_1, was isolated by removal of the solvent with a rotary evaporator and used without further purification. LCMS: m/z 248 $(M+H)^+$.

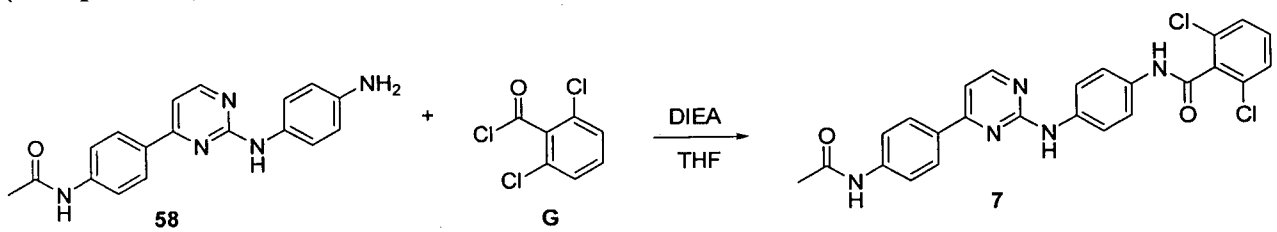
b) N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)acetamide (58)



[0750] A flask containing a solution of C_1 (500 mg, 2.0 mmol) and 3-boc-amino-aniline **F** (687 mg, 3.3 mmol) in nBuOH (5 mL) was immersed in an oil bath at 180 °C for 30 mins. The mixture was cooled to ambient temperature and to the black residue was added aqueous HCl and MeOH. The aqueous layer was twice washed with ethylacetate. The aqueous layer was then basified with NaOH and extracted twice with ethylacetate. The organic layer was washed with brine and dried with sodium sulfate. The solvent was removed on a rotary evaporator and the product was purified by HPLC with TFA/ACN as eluent. The TFA salt was removed by extraction with sodium hydroxide and ethylacetate to afford the title compound **58.**

Example 2

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide (Compound 7)



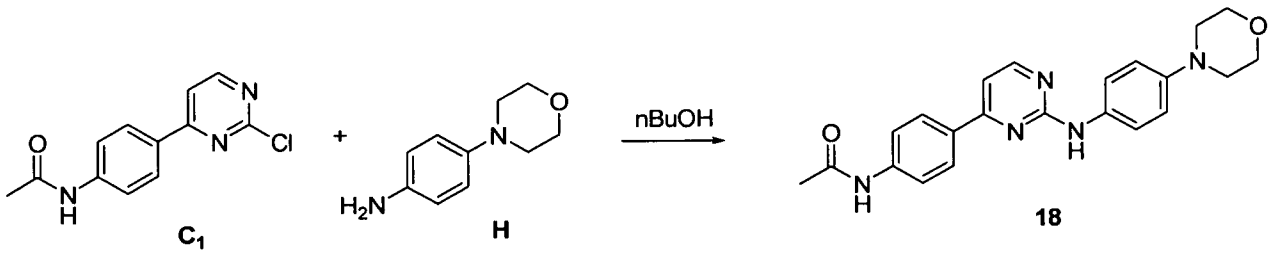
[0751] A flask was charged with **58** (638 mg, 2.0 mmol), 2,6-dichlorobenzoylchloride **G** (350 µL, 2.4 mmol), diispropylethylamine (1.1 mL, 6 mmol) and THF (50 mL). The reaction mixture was stirred at 70 °C for 6 hours. The crude mixture was concentrated on a rotary evaporator and the crude product was purified by HPLC with TFA/ACN as eluent. The title compound **7** was isolated by precipitation from ACN and washed with ether.

^{1}H-NMR (400MHz, d_6-DMSO): 10.718 ppm (s, 1H), 10.269 ppm (s, 1H), 9.678 ppm (s, 1H), 8.507 ppm (d, 1H), 8.419 ppm (s, 1H), 8.215 ppm (d, 2H), 7.758 ppm (d, 2H), 7.608 ppm (d,

2H), 7.532 ppm (t, 1H), 7.472 ppm (d, 1H), 7.380 ppm (d, 1H), 7.301 ppm (t, 1H), 7.216 ppm (d, 1H), 2.085 ppm (s, 3H); MS (EI) $C_{25}H_{19}Cl_2N_5O_2$: 492.2 (MH^+).

Example 3

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide (18)



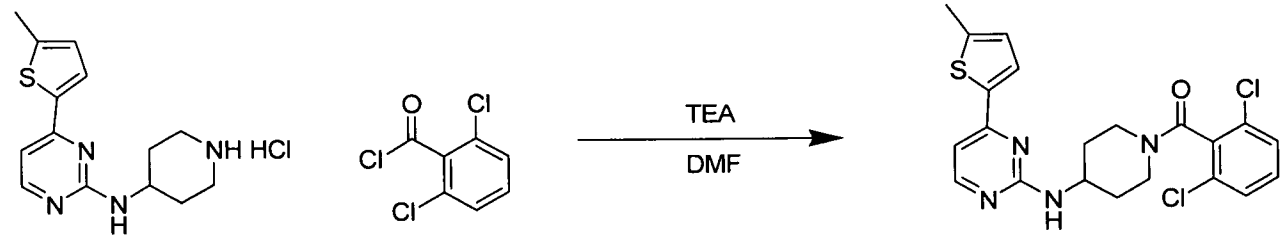
C_1 H 18

[0752] A flask was charged with C_1 (500 mg, 2.0 mmol), 4-morpholinoaniline **H** (540 mg, 3.0 mmol) and *n*BuOH (10 mL). The flask was immersed in a 180 °C oil bath for 30 minutes. The reaction mixture was cooled to ambient temperature and the black residue dissolved in DMF and MeOH. The product was purified by HPLC with TFA/ACN as eluent. The TFA salt was removed by extracting with sodium hydroxide and ethylacetate to afford the title compound (**18**).

^{1}H-NMR (400MHz, d_6-DMSO): 10.533 ppm (s, 1H), 9.408 ppm (s, 1H), 8.447 ppm (d, 1H), 8.114 ppm (d, 2H), 7.813 ppm (d, 2H), 7.705 ppm (d, 2H), 7.288 ppm (d, 1H), 6.982 ppm (br s, 2H), 4.65 ppm (br s, 4H), 3.072 ppm (br s, 2H), 2.108 ppm (s, 3H); MS (EI) $C_{22}H_{23}N_5O_2$: 390.3 (MH^+).

Example 4

N-{1-[(2,6-dichlorophenyl)carbonyl]piperidin-4-yl}-4-(4-methyl-2-thienyl)pyrimidin-2-amine



I G G2

[0753] To a solution of {4-[4-(5-Methyl-thiophen-2-yl)-phenyl]-pyrimidin-2-yl}-piperidin-4-yl-amine hydrochloride **I** (274mg, 1 mmoL) and TEA (0.69mL, 5 mmo) in DMF

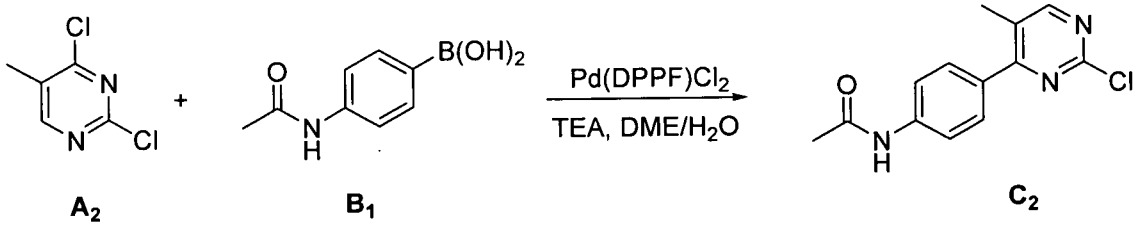
(5 mL) was added 2,6-dichlorobenzoyl chloride **G** (0.21mL, 1.5 mmol) and the solution was stirred for 4 h. To the resulting solution was added ethyl acetate (100mL) and the organic layer was washed with 5% LiCl (3 x 50mL), dried over anhydrous sodium sulfate, filtered, and concentrated to yield a residue. This residue was purified by reverse phase HPLC to yield the product **G2** (195mg, 38.9% yield, acetate salt) as a tan solid.

^{1}H NMR (400 MHz, d_6-DMSO): 8.28 (m, 1H), 7.73 (m, 1H), 7.58-7.54 (m, 2H), 7.48-7.46 (m, 1H), 7.32 (s, 1H), 7.27 (m, 1H), 7.01 (m, 1H), 4.47 (m, 1H), 4.03 (m, 1H), 3.30-3.05 (m, 2H), 2.25 (s, 3H), 2.03 (m, 1H), 1.88 (m, 1H), 1.58-1.48 (m, 3H); MS (EI) for $C_{21}H_{20}Cl_2N_4OS$: 447 (MH^+).

Example 5

N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide (Compound 574)

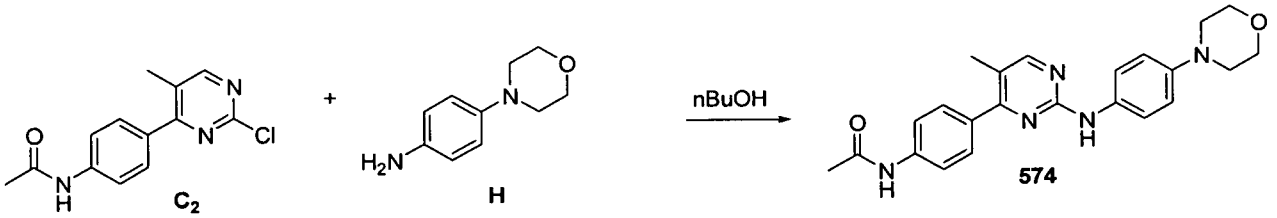
a) N-(4-(2-chloro-5-methylpyrimidin-4-yl)phenyl)acetamide (C_2)



A_2 B_1 C_2

[0754] A flask was charged with 5-methly-2,4-dichloropyrimindine C_2 (2.45g, 15.0mmol), 4-acetoamidophenylboronic acid (2.95g, 16.5mmol), dicholor[1,1'-bis(diphenyl-phosphino)ferrocenepalladium B_1 (1.22g, 1.5mmol, 10 mol %), and triethylamine (5.23mL, 37.5mmol). Ethyleneglycoldimethylether (20 mL) and H_2O (5ml) were added to the flask and the mixture was purged with N_2 for 5 minutes. The reaction mixture was stirred under an N_2 atmosphere at 90 °C for 2hours, after which time, ether was added and the reaction mixture was filtered. The product, C_2, was isolated by removal of the solvent with a rotary evaporator and used without further purification. LCMS: m/z 262 $(M+H)^+$.

b) N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide

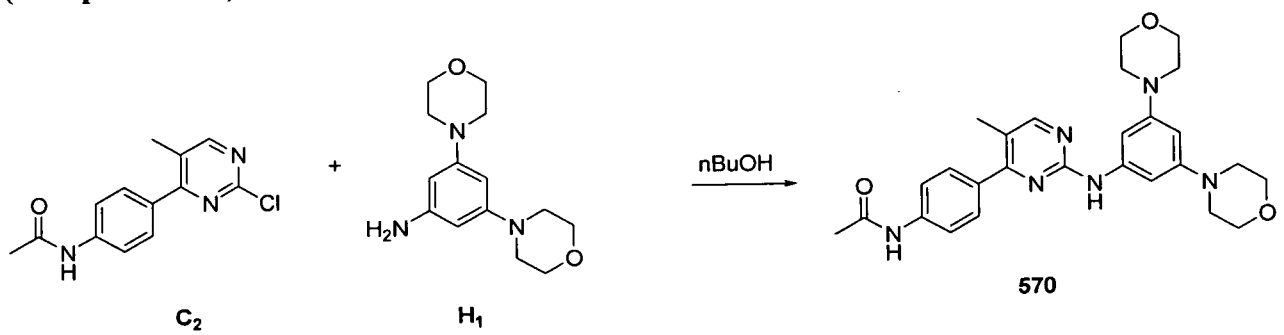


[0755] A flask containing a solution of C_2 (523 mg, 2.0 mmol) and **H** (392 mg, 2.2mmol) in *n*-BuOH (6 mL) was immersed in an oil bath at 180 °C for 3hr. The mixture was cooled to ambient temperature and concentrated in vacuo. The residue was purified by HPLC with Ammonium acetate/ACN as eluent to afford the title compound **574** (531mg, 66%).

^{1}H-NMR (400MHz, d_6-DMSO): 10.15 ppm (s, 1H), 9.27 ppm (s, 1H), 8.31 ppm (s, 1H), 7.72 ppm (d, J = 8.8Hz, 2H), 7.66-7.62 ppm (m, 4H), 6.88 ppm (d, J = 8.8Hz, 2H), 3.73 (t, J = 4.8Hz, 4H), 3.01 (t, J = 4.8Hz, 4H), 2.21 ppm (s, 3H), 2.09 (s, 3H); MS (EI) $C_{23}H_{25}N_5O_2$: 404 $(M+H)^+$.

Example 6

N-(4-(2-(3,5-dimorpholinophenylamino)-5-methylpyrimidin-4-yl)phenyl)acetamide (Compound 570)

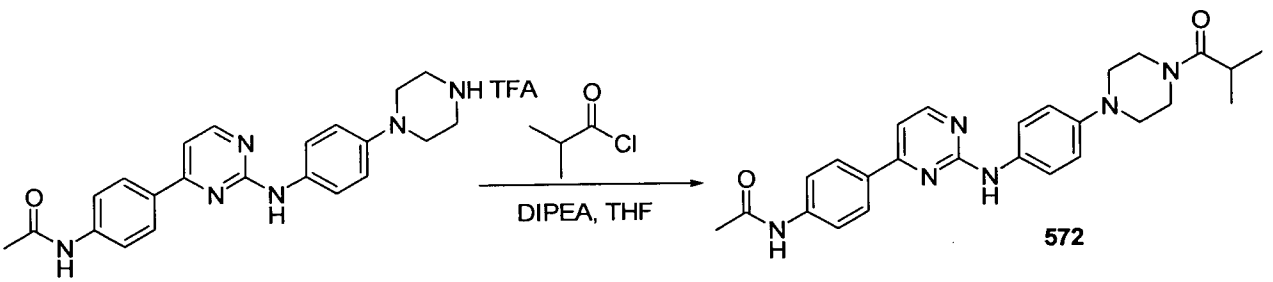


[0756] A flask containing a solution of C_2 (288 mg, 1.1 mmol) and H_1 (263 mg, 1.0mmol) in n-BuOH (3 mL) was immersed in an oil bath at 180 °C for 4hr. The mixture was cooled to ambient temperature and concentrated *in vacuo*. The residue was purified by HPLC with ammonium acetate/acetonitrile (ACN) as eluent to afford the title compound **570** (205mg, 42%).

^{1}H-NMR (400MHz, d_6-DMSO): 10.15 ppm (s, 1H), 9.22 ppm (s, 1H), 8.34 ppm (s, 1H), 7.72 ppm (d, J = 9.2Hz, 2H), 7.69 ppm (d, J = 8.8Hz, 2H), 7.10 ppm (d, J = 2.0Hz, 2H), 6.09 ppm (s, 1H), 3.71 (t, J = 4.8Hz, 8H), 3.03 (t, J = 4.8Hz, 8H), 2.26 ppm (s, 3H), 2.07 (s, 3H); MS (EI) $C_{27}H_{32}N_6O_3$: 489 $(M+H)^+$.

Example 7

'N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide

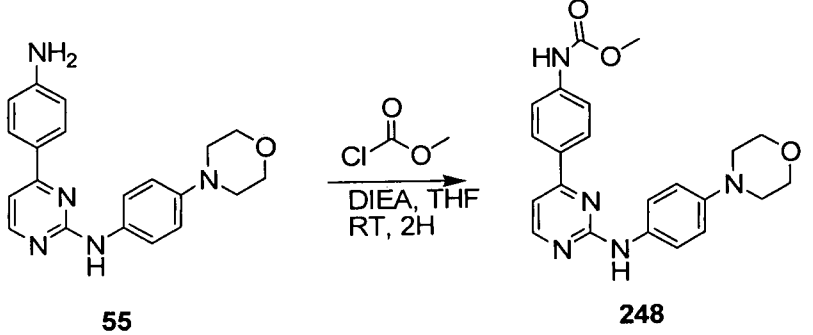


[0757] A solution of N-(4-(2-(4-(piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl) acetamide (300mg, 0.6mmol) and DIPEA (261ul, 1.50mmol) was treated with isobutyryl chloride at room temperature. After stirring for 10 minutes, the reaction mixture was directly concentrated *in vacuo* and the residue was purified by HPLC TFA/ACN as eluent. TFA salt was removed by using basic resin to afford 111mg (40%) of the title compound **572**.

^{1}H-NMR (400MHz, d_6-DMSO): 10.21 ppm (s, 1H), 9.40 ppm (s, 1H), 8.44 ppm (d, J = 4.8Hz, 1H), 8.11 ppm (d, J = 9.2Hz, 2H), 8.10 ppm (s, 1H), 7.74 ppm (d, J = 8.8Hz, 2H), 7.68 ppm (d, J = 8.8Hz, 1H), 7.28 ppm (d, J = 5.6Hz, 1H), 6.97 (d, J = 9.6Hz, 2H), 3.65-3.61 (m, 4H), 3.08-3.02 (m, 4H), 2.92 ppm (penth, J = 6.8Hz, 1H), 2.09 ppm (s, 3H), 1.03 ppm (s, 3H), 1.01 ppm (s, 3H); MS (EI) $C_{26}H_{30}N_6O_2$: 459 $(M+H)^+$.

Example 8

Methyl (4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)carbamate (Compound 248)



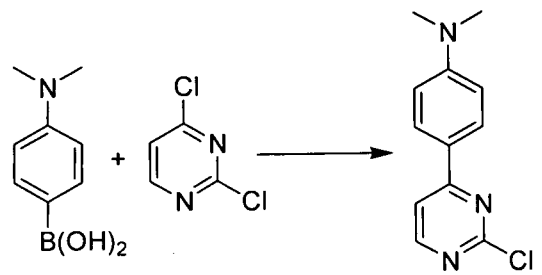
[0758] To a solution of 4-(4-aminophenyl)-N-(4-morpholinophenyl)pyrimidin-2-amine **55** (100 mg, 0.29 mmol) and DIEA (0.435 mmol, 75 µl) in THF (50 mL) was added methyl chloroformate (0.348 mmol, 27 µl) and the solution was stirred at room temperature for 2 hours. The solution mixture was concentrated, redissolved with MeOH and purified using reverse phase HPLC. The product obtained from the reverse phase HPLC was free base **248**, converted to HCl salt using 3 N HCl and lyophilized to yield the product **248** (60mg, 47% yield) as a yellow solid.

^{1}H-NMR (400MHz, d_6-DMSO): 10.063 ppm (s, 1H), 9.976 ppm (s, 1H), 8.521 ppm (d, 1H), 8.153 ppm (d, 2H), 7.878 ppm (d, 2H), 7.661 ppm (d, 2H), 7.554 ppm (bs, 2H), 7.432 ppm (d, 1H), 3.983 ppm (bs, 4H), 3.707 ppm (s, 3H), 4.435 ppm (bs, 4H); MS (EI) $C_{22}H_{23}N_5O_3HCl$: 475.4 (MH^+).

Example 9

4-[4-(dimethylamino)phenyl]-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine (67)

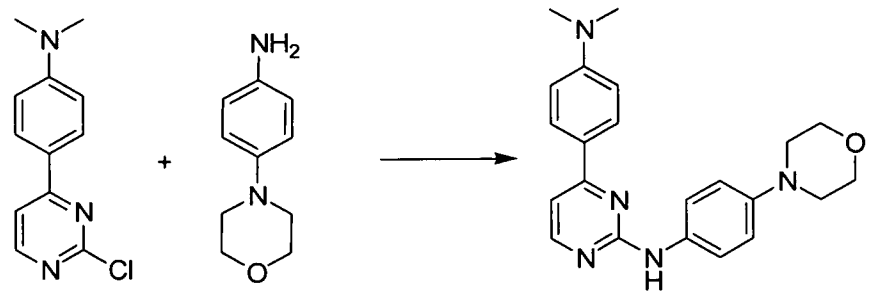
a) 4-(2-chloropyrimidin-4-yl)-N,N-dimethylaniline (C_3)



B_2 A_1 C_3

[0759] A flask was charged with A_1 (650 mg, 4.4 mmol), 4-(dimethylamino)phenylboronic acid B_2 (797 mg, 4.8 mmol), dicholor[1,1'-bis(diphenylphosphino)ferrocenepalladium (480 mg, 0.56 mmol, 15 mol %), and triethylamine (1.5 mL, 11 mmol). Ethyleneglycoldimethylether (30 mL) was added to the flask and the mixture was purged with N_2 for 5 minutes. The reaction mixture was stirred under an N_2 atmosphere at 80 °C for 12 hours, after which time, ether was added and the reaction mixture was filtered. The product, C_3, was isolated by removal of the solvent with a rotary evaporator and used without further purification. LCMS: m/z 234 $(M+H)^+$.

b) 4-[4-(dimethylamino)phenyl]-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine (67)



C_3 67

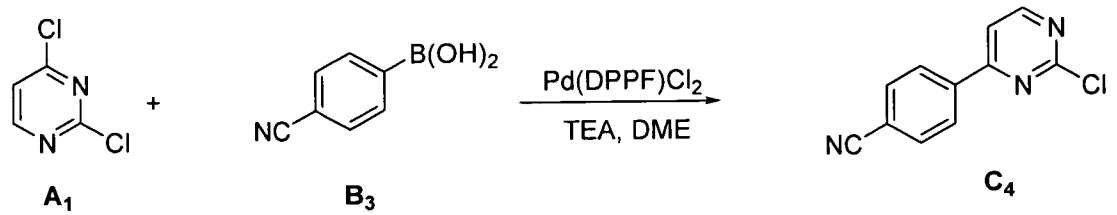
[0760] A flask was charged with C_3 (500 mg, 2.1 mmol), 4-morpholinoaniline (573 mg, 3.2 mmol) and nBuOH (10 mL). The flask was immersed in a 180 °C oil bath for 30 minutes. The reaction mixture was cooled to ambient temperature and the black residue dissolved in DMF and MeOH. The product **67** was purified by HPLC with TFA/ACN as eluent. The TFA salt was removed by extracting with sodium hydroxide and ethylacetate to afford the free base of **67**.

^{1}H-NMR (400MHz, d_6-DMSO): 9.24 ppm (s, 1H), 8.33 (d, 1H), 8.03 (d, 2H), 7.68 (d, 2H), 7.18 (d, 1H), 6.92 (d, 2H), 6.81 (d, 2H), 3.72-3.77 (m, 4H), 3.04-3.08 (m, 4H), 3.00 (s, 6H). MS (EI) $C_{22}H_{25}N_5O$: 376.1 (MH^+).

Example 10

4-[4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine (Compound 319)

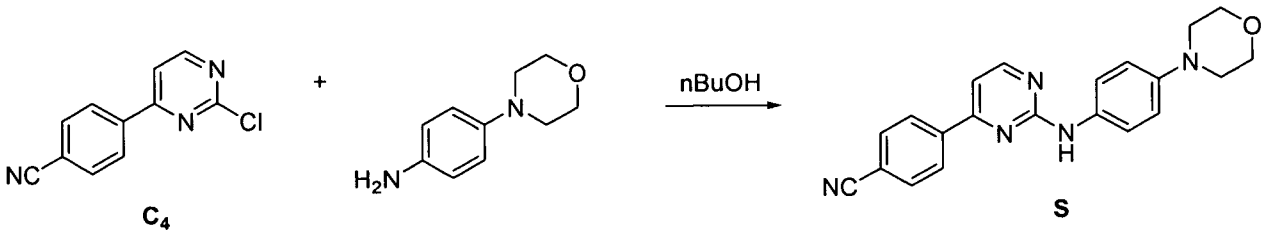
a) 4-(2-chloropyrimidin-4-yl)benzonitrile



A_1 B_3 C_4

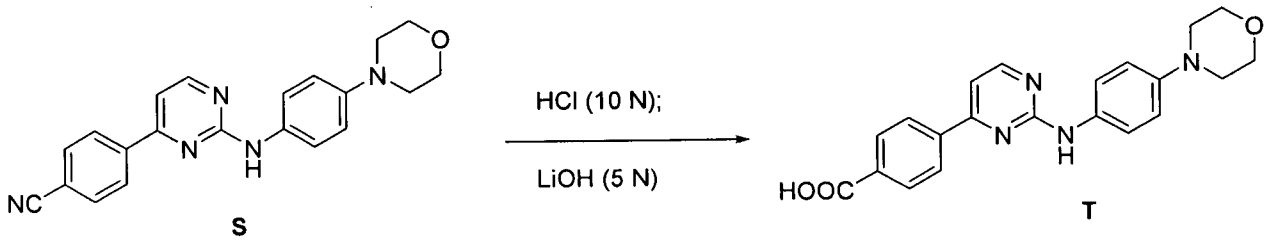
[0761] A flask was charged with A_1 (763 mg, 5.16 mmol), 4-cyanophenylboronic acid B_3 (848 mg, 5.77 mmol), dicholoro[1,1'-bis(diphenylphosphino)ferrocenepalladium (375 mg, 0.437 mmol, 10 mol %), and triethylamine (1.76 mL, 12.9 mmol). Ethylene glycol dimethyl ether (5.0 mL) was added to the flask and the mixture was purged with N_2. The reaction mixture was stirred under an N_2 atmosphere at 90 °C for 1 hour, after which time, it was cooled to ambient temperature and filtered. The product, C_4, was isolated by removal of the solvent with a rotary evaporator and used without further purification. LCMS: m/z 216 $(M+H)^+$.

b) 4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)benzonitrile (S)



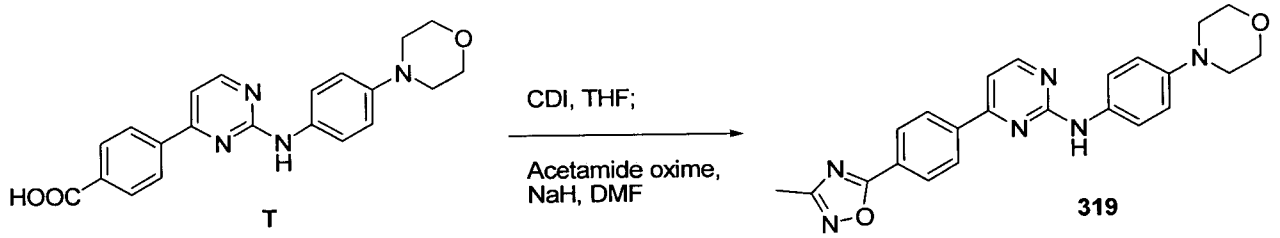
[0762] A flask containing a solution of C_4 (400 mg, 1.85 mmol) and 4-morphilinoaniline (362 mg, 2.04 mmol) in 1-butanol (10 mL) was immersed in an oil bath at 180 °C for 2 h. The mixture was cooled to ambient temperature, concentrated, and the crude product **S** was used without further purification. LCMS: m/z 358 $(M+H)^+$.

c) 4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)benzoic acid



[0763] A flask containing a solution of **S** (600 mg, 1.68 mmol) and 10 N HCl (aq., 20 mL) was immersed in an oil bath at 100 °C for 5 hours. The mixture was cooled to ambient temperature, after which time, 5 N LiOH was added until the reaction mixture was pH 6. The white precipitate was filtered and dried to give the product **T**, which was used without further purification. LCMS: m/z 377 $(M+H)^+$.

d) 4-[4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine (323)



[0764] To a flask containing a solution of **T** (570 mg, 1.47 mmol) and THF (10 mL) was added 1,1'-carbonyldiimidazole (475 mg, 2.93 mmol). The reaction mixture was immersed in an oil bath at 60 °C for 2 h, after which time, it was cooled to ambient temperature. A mixture of acetamide oxime (120 mg, 1.62 mmol) and NaH (39 mg, 1.6 mmol) in DMF (5 mL) was added to the reaction mixture, after which time, the reaction mixture was immersed in an oil bath at 80 °C for 2 hours. The reaction mixture was then cooled to ambient

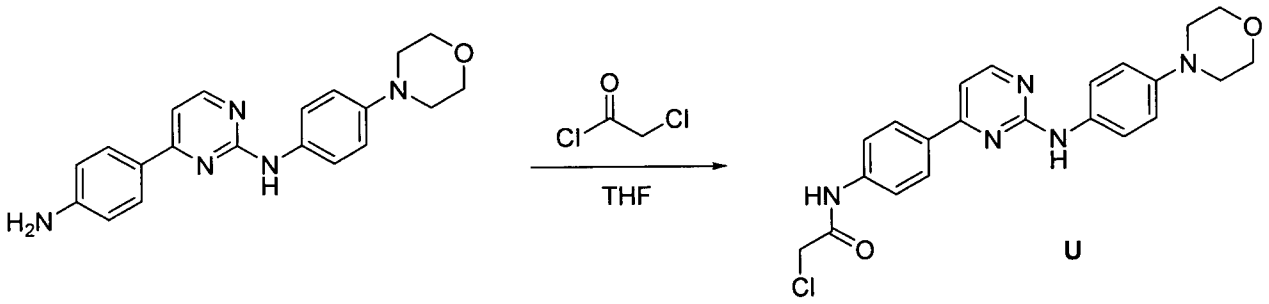
temperature, quenched with saturated NH_4Cl (aq., 10 mL), extracted with ethyl acetate (50 mL), dried over anhydrous sodium sulfate, filtered, and concentrated to yield a residue. The residue was purified by reverse phase HPLC to yield the product **319** (49.6 mg, 8.10% yield) as a light brown solid.

^{1}H-NMR (400MHz, d_6-DMSO): 9.57 ppm (s, 1H), 8.57 ppm (d, 1H), 8.38 ppm (d, 2H), 8.25 ppm (d, 2H), 7.67 ppm (d, 2H), 7.44 ppm (d, 1H), 6.95 ppm (d, 2H), 3.75 ppm (t, 4H), 3.06 ppm (t, 4H), 2.46 ppm (s, 3H); MS (EI) $C_{23}H_{22}N_6O_2$: 415.0 (MH^+).

Example 11

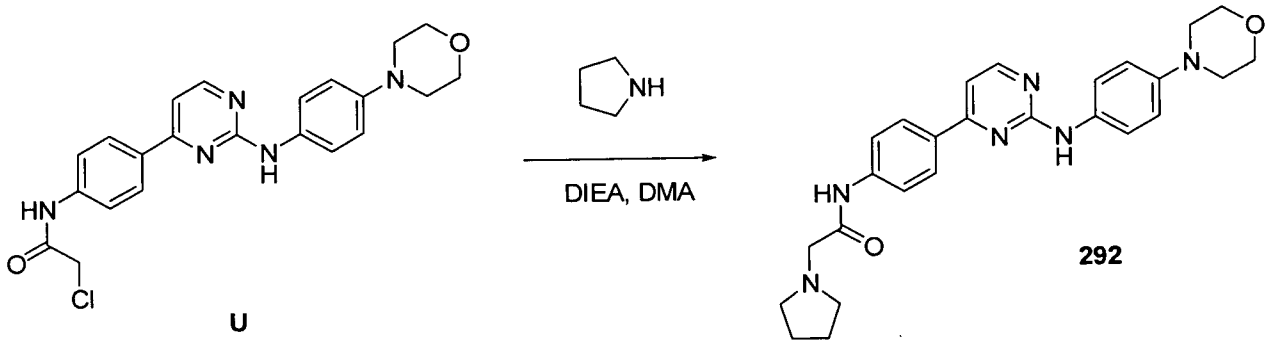
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-pyrrolidin-1-ylacetamide (Compound 292)

a) 2-chloro-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide



[0765] To a flask charged with 4-(4-aminophenyl)-N-(4-morpholinophenyl)pyrimidin-2-amine (100 mg, 0.286 mmol) and THF (1 mL) was added chloroacetyl chloride (0.0230 mL, 0.286 mmol). The solution was stirred at ambient temperature for 1 hour. The crude mixture was then concentrated and used without further purification. LCMS: m/z 424 $(M+H)^+$.

b) N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-pyrrolidin-1-ylacetamide (292)

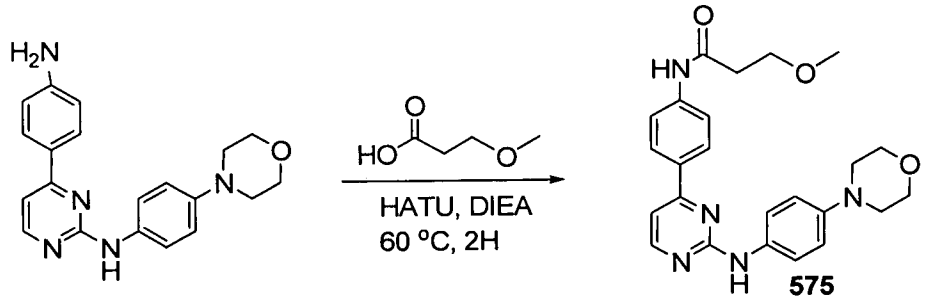


[0766] To a flask charged with **U** (100 mg, 0.236 mmol), diisopropylethylamine (0.2 mL, 1 mmol), and dimethylacetimide (1 mL) was added pyrrolidine (0.021 mL, 1.3 mmol). The reaction mixture was stirred at 80 °C for 1 hour. The crude mixture was concentrated on a rotary evaporator and the product **292** was purified by reverse phase HPLC.

^{1}H-NMR (400MHz, d_6-DMSO): 10.90 ppm (s, 1H), 10.20 ppm (br. s, 1H), 9.64 ppm (s, 1H), 8.50 ppm (d, 1H), 8.19 ppm (d, 2H), 7.78 ppm (d, 2H), 7.74 ppm (d, 2H), 7.36 ppm (d, 1H), 7.11 ppm (d, 2H), 4.32 ppm (s, 2H), 3.80 ppm (t, 4H), 3.70-3.65 ppm (m, 2H), 3.19-3.06 ppm (m, 6H), 2.10-1.86 (m, 4H); MS (EI) $C_{26}H_{30}N_6O_2$: 459.4 (MH^+).

Example 12

3-methoxy-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide (Compound 575)

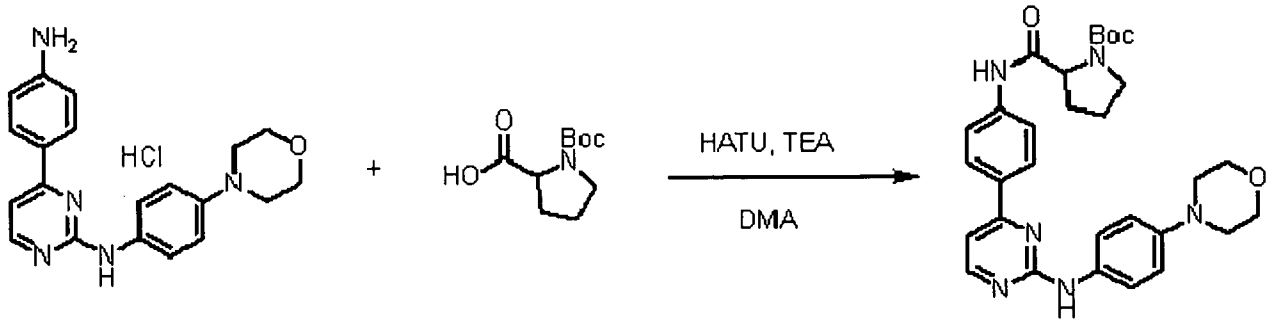


249(a)

[0767] To a solution of **249(a)** (0.18 g, 0.05 mmol), HATU (0.4 g, 1.1 mmol), and DIEA (0.5 mL, 4.0 mmol) in DMA (5 mL) was added 3-methoxypropanoic acid (0.1 mL, 1.05 mmol) and the solution was stirred at 60 °C for 2 hours. The solution mixture was diluted with ethyl acetate and the mixture was extracted with 10% LiCL (3X) and brine (1X). The resulting organic layer was dried with sodium sulfate and concentrated *in vacuo*. The product was purified by silica column chromatography (5% MeOH/DCM as eluent) to afford 0.1 g of the title compound **575** (49% yield) as a white solid.

^{1}H-NMR (400MHz, d_6-DMSO): 10.20 ppm (s, 1H), 9.37 ppm (s, 1H), 8.42 ppm (d, 1H), 8.10 ppm (d, 2H), 7.74 ppm (d, 2H), 7.65 ppm (d, 2H), 7.25pm (d, 1H), 6.91 ppm (d, 2H), 3.72 ppm (m, 4H), 3.61 ppm (t, 2H), 3.23 ppm (s, 3H), 3.03 ppm (m, 4H), 2.57 ppm (t, 2H); MS (EI) $C_{22}H_{23}N_5O_3HCl$: 434.3 (MH^+).

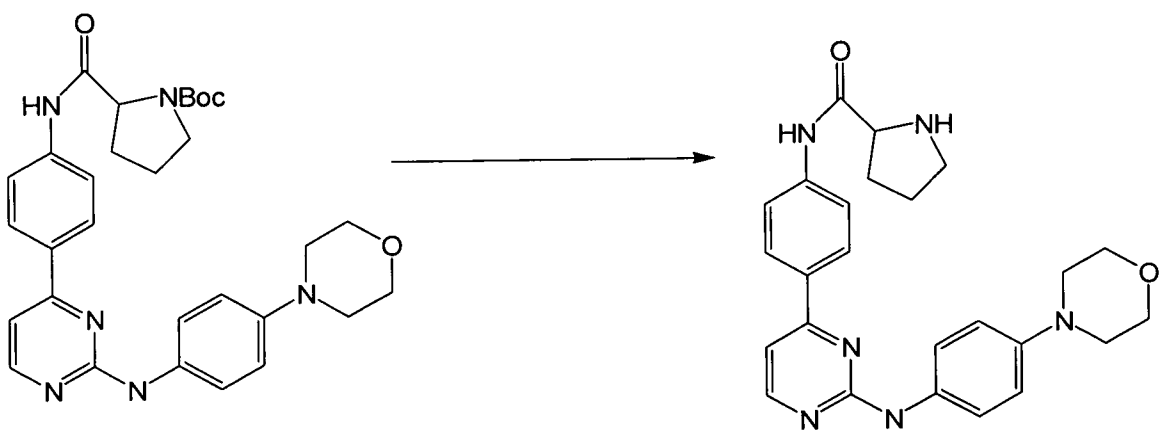
Example 13
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)prolinamide (576)



249(a) Z

[0768] To a solution of **249(a) (5HCl)** (0.2 g, 0.37 mmol) in DMA (5 mL) was added a solution of 1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid, (*d,l*-boc-proline) (0.1 g, 0.46 mmol), Hunigs base (0.5 mL, 2.5 mmol), HATU (0.2 g, 0.52 mmol) and the solution was stirred at RT for 14 hours. The resulting solution was loaded on the silica gel and was purified by silica gel column chromatography (10-100% gradient of ethyl acetate/hexanes) to yield **Z** (160 mg) in 79% yield as yellow solid. LCMS: m/z 545 $(M+H)^+$.

*d) **N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide (Compound 585)***



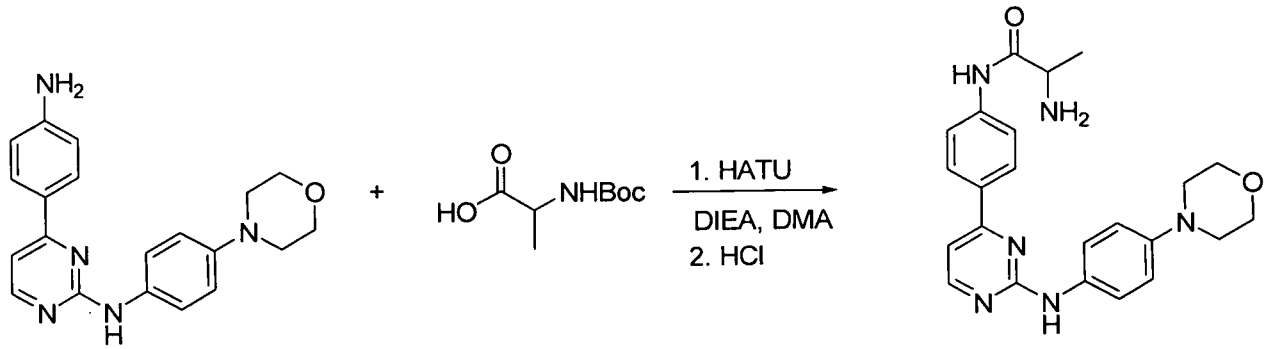
Z 576

[0769] A flask containing a solution of **Z** (160 mg, 0.29 mmol) in 4M HCl in 1,4-dioxane (5 mL) and MeOH (5 mL) was stirred at 50 C for 1 hour. Concentration of the solvent gave a yellow solid that was purified by reverse phase HPLC using an ammonium acetate buffer to yield 105 mg (68%) of **576** as a yellow solid.

^{1}H NMR (400 MHz, d_4-MeOD): 8.36 (m, 1H), 8.14 (m, 2H), 7.78 (m, 2H), 7.62 (m, 2H), 7.22 (m, 1H), 6.98 (m, 2H), 4.15 (m, 1H), 3.83 (m, 4H), 3.21 (m, 2H), 3.13 (m, 4H), 2.41 (m, 1H), 2.06-1.91 (m, 3H); LCMS: for $C_{25}H_{28}N_6O_2$: 445 $(M + H)^+$.

Example 14

2-amino-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide (Compound 208)



249(a) **208**

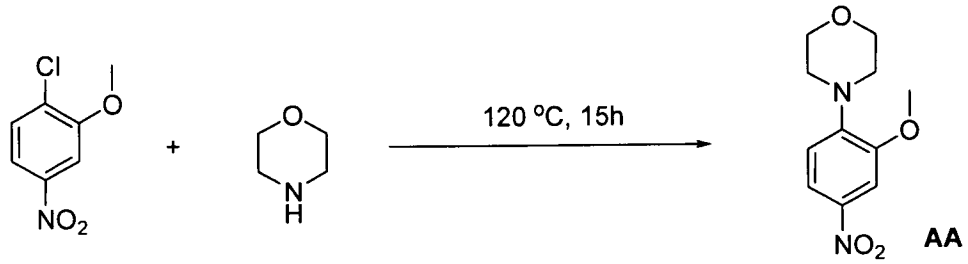
[0770] A flask was charged with **249(a)** (140 mg, 0.3 mmol), *N*-(*tert*-butoxycarbonyl)-alanine (57 mg, 0.3 mmol, purchased from Chem-Impex International), HATU (140 mg, 0.37 mmol), diispropylethylamine (0.6 mL, 3.0 mmol) and DMA (5 mL). The reaction mixture was stirred at RT for 12 hours. The crude mixture was concentrated on a rotary evaporator and the residue was dissolved in 10 mL of MeOH and 5 mL of 4N HCl in dioxane. The reaction mixture was stirred at 70 °C for 1 hour. The crude mixture was concentrated on a rotary evaporator and the product was purified by HPLC with NH_4OAc/ACN as eluent. The resulting solution was concentrated on a rotary evaporator and the final product, **208**, was dried by lyophilization.

^{1}H-NMR (400MHz, d_6-DMSO): 9.387 ppm (s, 1H), 8.443 ppm (d, 1H), 8.127 ppm (d, 2H), 7.825 ppm (d, 2H), 7.676 ppm (d, 2H), 7.287 ppm (d, 1H), 6.939 ppm (d, 2H), 3.747 ppm (m, 4H), 3.457 ppm (q, 1H), 3.050 ppm (m, 4H), 1.896 ppm (s, 3H (AcOH)) 1.243 ppm (d, 3H); MS (EI) $C_{23}H_{26}N_6O_2$: 419.1 (MH^+).

Example 15

N-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide (Compound 341)

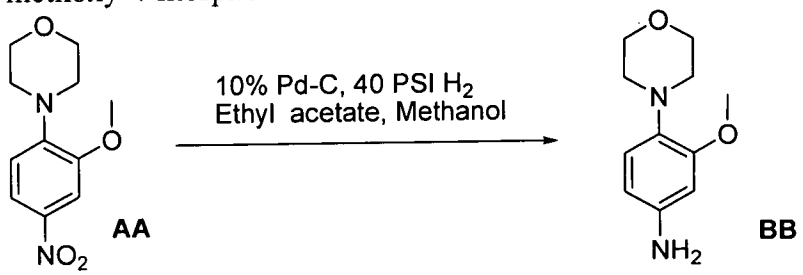
a) 4-(2-methoxy-4-nitrophenyl)morpholine (AA)



AA

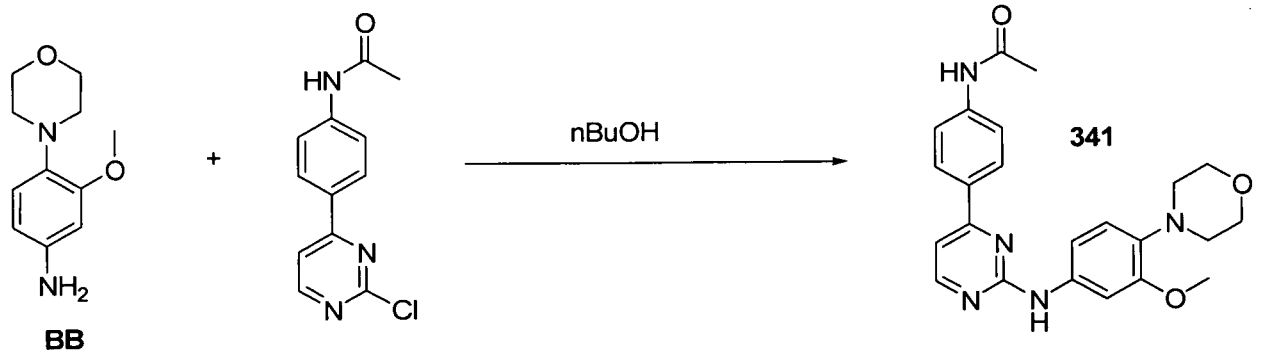
[0771] A pressure bottle was charged with 1-chloro-2-methoxy-4-nitrobenzene (10.0 g mg, 53.3 mmol, purchased from TCI America) and morpholine (15 mL, 172.0 mmol). The reaction mixture was stirred at 120 °C for 15 hours and it was allowed to cool to room temperature by itself. The resulting solid was suspended in 20 mL of ethyl acetate, filtered, and washed with 20 mL of *tert*-butyl methyl ether. 8.8 g of yellow solid as the desired product **AA** was collected (69% yield). ^{1}H-NMR (400MHz, d_6-DMSO): 7.83 (dd, 1H), 7.67 (d, 1H), 6.98 (d, 1H), 3.88 (s, 3H), 3.71 (m, 4H), 3.16 (m, 4H). MS (EI) $C_{11}H_{14}N_2O_4$: 239 $(M+H)^+$.

b) 3-methoxy-4-morpholinoaniline



[0772] To a solution of **AA** (8.8 g, 37.0 mmol) in ethyl acetate (30 mL) and methanol (10 mL) in a Parr bottle was added 1 g 10% palladium on carbon. The reaction mixture was hydrogenated at 40 PSI H_2 for 1 hour, filtered and concentrated. 8.0 g of a pink solid as the product **BB** was obtained as a crude product and used without further purification. MS (EI) $C_{11}H_{16}N_2O_2$: 209 $(M+H)^+$.

c) *N-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide*

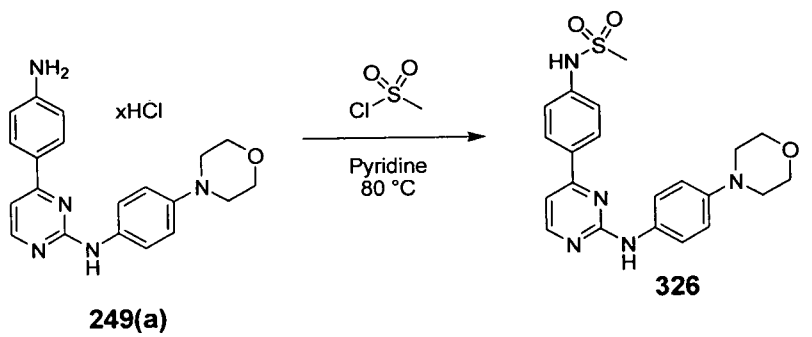


[0773] A flask was charged with **BB** (51 mg, 0.24 mmol), N-(4-(2-chloropyrimidin-4-yl)phenyl)acetamide (50 mg, 0.2 mmol) and nBuOH (2 mL). The flask was immersed in a 180 °C oil bath for 30 minutes, and then cooled to ambient temperature. The residue was suspended in 5 mL of ethyl acetate, stirred for 1 hour, filtered, and washed with 10 mL of ethyl acetate. 50 mg of an off-white powder was obtained as the title compound (**341**) (60% yield).

^{1}H-NMR (400MHz, d_6-DMSO): 10.33 (s, 1H), 9.50 (br, 1H), 8.54 (d, 1H), 8.15 (d, 2H), 7.95 (br, 1H), 7.77 (d, 2H), 7.42 (m, 2H), 3.94 (s, 3H), 3.77 (br, 4H), 3.40 (br, 2H), 2.15 (s, 2H). MS (EI) $C_{23}H_{25}N_5O_3$: 420 $(M+H)^+$.

Example 16

N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)methanesulfonamide (Compound 326)



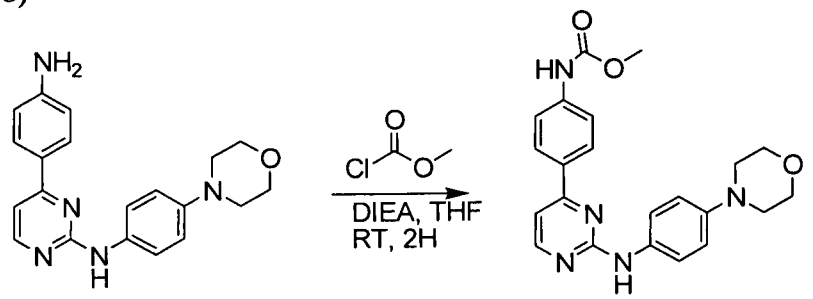
[0774] **82** (500 mg, 0.94 mmol) was dissolved in 4 mL of pyridine. Methanesulfonyl chloride (730 □L, 9.4 mmol) was added dropwise to the vigorously stirred pyridine solution. The addition of the sulfonyl chloride was exothermic and caused a significant increase in the temperature of the reaction. The reaction was maintained at 80 °C for several hours. After

cooling, the solvent was removed under vacuum and the residue was purified by reverse phase HPLC to afford 200 mg (52% yield) of the title compound (**326**).

^{1}H-NMR (400MHz, d_6-DMSO): 10.16 ppm (s, 1H), 9.41 ppm (s, 1H), 8.45 ppm (d, 1H), 8.13 ppm (d, 2H), 7.67 ppm (d, 2H), 7.33 ppm (d, 2H), 7.28 ppm (d, 1H), 6.94 ppm (d, 2H), 3.74 ppm (br s, 4H), 3.09 ppm (s, 3H), 3.05 ppm (br s, 4H); MS (EI) $C_{21}H_{23}N_5O_3S$: 426 (MH^+).

Example 17

Methyl (4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)carbamate (Compound 248)



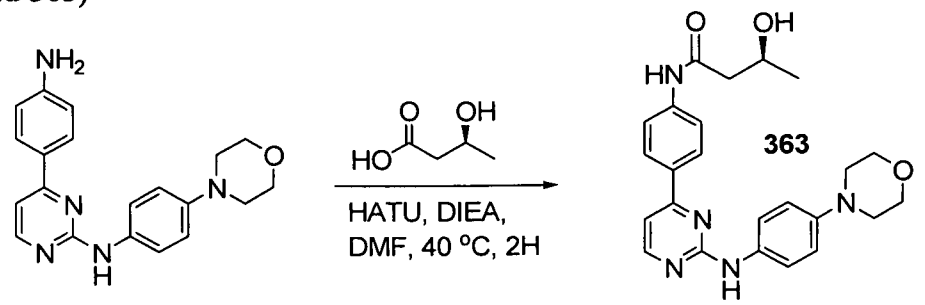
249(a) **248**

[0775] To a solution of 4-(4-aminophenyl)-N-(4-morpholinophenyl)pyrimidin-2-amine **249(a)** (100 mg, 0.29 mmol) and DIEA (0.435 mmol, 75 µl) in THF (50 mL) was added methyl chloroformate (0.348 mmol, 27 µl) and the solution was stirred at room temperature for 2 hours. The solution mixture was concentrated, redissolved with MeOH and purified using reverse phase HPLC. The product obtained from the reverse phase HPLC was free base **248**, converted to HCl salt using 3 N HCl and lyophilized to yield the product **248** (60mg, 47% yield) as a yellow solid.

^{1}H-NMR (400MHz, d_6-DMSO): 10.063 ppm (s, 1H), 9.976 ppm (s, 1H), 8.521 ppm (d, 1H), 8.153 ppm (d, 2H), 7.878 ppm (d, 2H), 7.661 ppm (d, 2H), 7.554 ppm (bs, 2H), 7.432 ppm (d, 1H), 3.983 ppm (bs, 4H), 3.707 ppm (s, 3H), 4.435 ppm (bs, 4H); MS (EI) $C_{22}H_{23}N_5O_3HCl$: 475.4 (MH^+).

Example 18

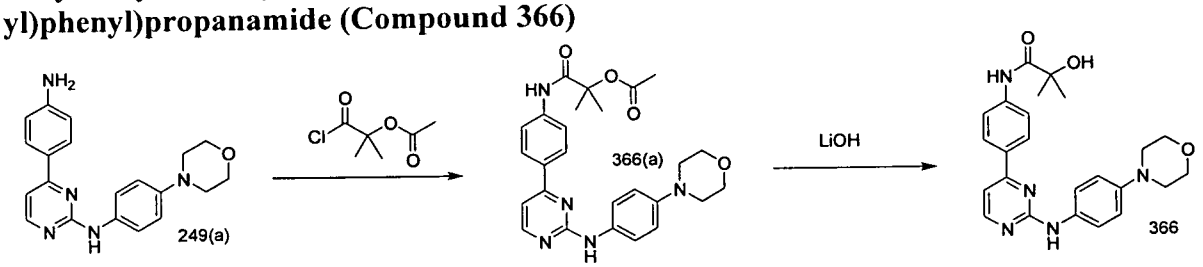
(*S*)-3-hydroxy-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide (Compound 363)



[0776] To a solution of (*S*)-3-hydroxybutyrate (0.180 g, 1.73 mmol), HATU (0.602 g, 1.58 mmol), DIEA (1.0 mL, 5.4 mmol) in DMF (3.0 mL) was added a solution of 4-(4-aminophenyl)-*N*-(4-morpholinophenyyl)pyrimidin-2-amine (0.500 g, 1.44 mmol) in DMF (1.0 mL). The reaction mixture was stirred at rt for 2 hours, at which time it was quenched with saturated $NaHCO_3$ (10 mL, aq.), extracted into DCM (3X), and washed with brine (1X). The organic layers were dried with sodium sulfate and concentrated. The product was purified by reverse phase HPLC to afford (*S*)-3-hydroxy-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide (0.136 g, 22% yield) as a light brown solid. (**363**) ^{1}H-NMR (400MHz, DMSO-d_6): 10.14 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.27 (d, 1H), 6.94 (d, 2H), 4.79 (d, 1H), 4.11 (m, 1H), 3.74 (m, 4H), 3.05 (m, 4H), 2.47 (dd, 1H), 2.35 (dd, 1H)), 1.15 (d, 3H); MS (EI) m/z for $C_{24}H_{28}N_5O_3$: 434.3 (MH^+).

Example 19

2-Hydroxy-2-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide (Compound 366)

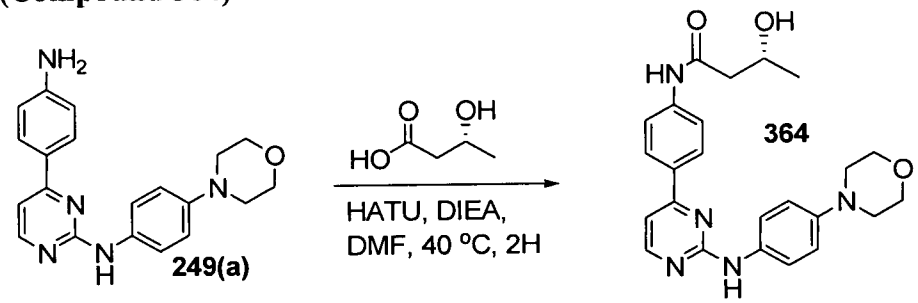


[0777] To a solution of 4-(4-aminophenyl)-*N*-(4-morpholinophenyyl)pyrimidin-2-amine (1.0 g, 2.8 mol) **249(a)** and DIPEA (0.5 mL, 1 eq.) in anhydrous DMA (5 mL) was added dropwise 2-acetoxy-2-methylpropionyl chloride (3 mol, 1.05 eq., 0.44 mL) at 0 °C. The mixture was stirred for 20 min at room temperature. The solution was diluted with water and EtOAc. The organic layer was concentrated in vacuo. The residue **366(a)** was suspended in MeOH (10 mL) and a solution of LiOH-H_2O (8.3 mmol, 3 eq. 0.35 g) in water (3 mL) was

added. The reaction was complete within 20 min and then was neutralized. The organic solvent was removed *in vacuo*. The residue was purified to afford 2-hydroxy-2-methyl-*N*-(4-(2-(4-morpholino-phenylamino)pyrimidin-4-yl)phenyl)propanamide (**366**) (1.0 g, 85% yield) as a pale yellow solid. ^{1}H-NMR (400MHz, DMSO-d_6): 9.86 (s, 1H), 9.41 (s, 1H), 8.47 (d, 1H), 8.12 (d, 2H), 7.94 (d, 2H), 7.68 (d, 2H), 7.30 pm (d, 1H), 6.94 (d, 2H), 5.82 (s, 1H), 3.75 (m, 4H), 3.08 (m, 4H), 1.38 (s, 6H); MS (EI) m/z for $C_{22}H_{23}N_5O_3HCl$: 434.2 (MH^+).

Example 20

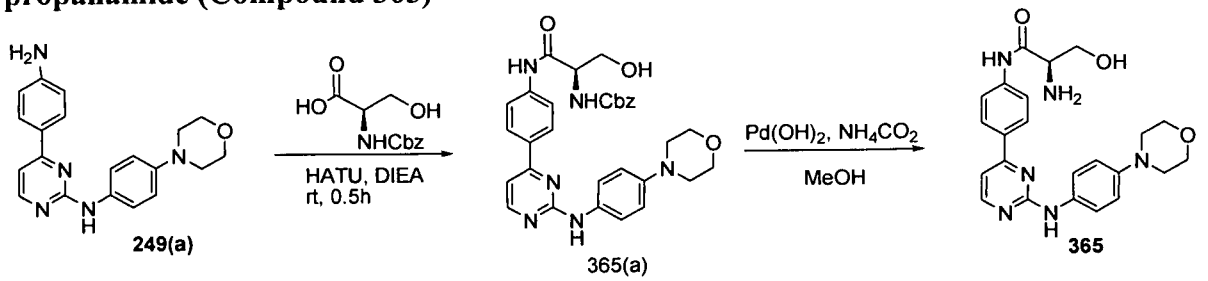
(*R*)-3-hydroxy-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide (Compound 364)



[0778] To a solution of (*R*)-3-hydroxybutyrate (0.180 g, 1.73 mmol), HATU (0.602 g, 1.58 mmol), DIEA (1.0 mL, 5.4 mmol) in DMF (3.0 mL) was added and a solution of 4-(4-aminophenyl)-*N*-(4-morpholinophenyyl)pyrimidin-2-amine (**249(a)**) (0.500 g, 1.44 mmol) in DMF (1.0 mL). The reaction mixture was stirred at room temperature for 2 hours, at which time it was quenched with saturated $NaHCO_3$ (10 mL, aq.), extracted into DCM (3X), washed with brine (1X), and the organic layers were dried with sodium sulfate. The solution was concentrated and the product was purified by reverse phase HPLC to afford (*R*)-3-hydroxy-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide (**364**) (0.129 g, 21% yield) as a light brown solid. ^{1}H-NMR (400MHz, DMSO)-d_6: 10.14 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.27 (d, 1H), 6.94 (d, 2H), 4.79 (d, 1H), 4.11 (m, 1H), 3.74 (m, 4H), 3.05 (m, 4H), 2.47 (dd, 1H), 2.35 (dd, 1H), 1.15 (d, 3H); MS (EI) m/z for $C_{24}H_{28}N_5O_3$: 434.3 (MH^+).

Example 21

(*R*)-2-amino-3-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-propanamide (Compound 365)

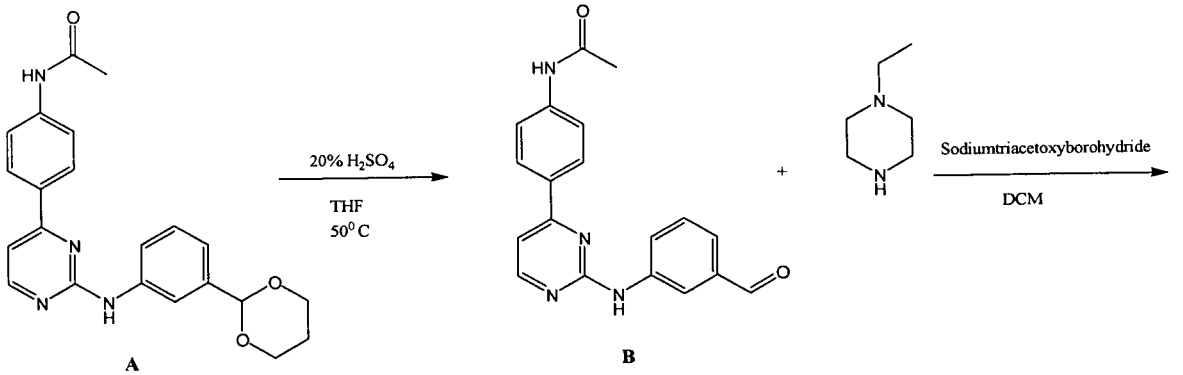


[0779] To a solution of 4-(4-aminophenyl)-*N*-(4-morpholinophenyyl)pyrimidin-2-amine **249(a)** (521mg, 1.5 mmol), N-CBZ-D-Serine (359mg, 1.5mmol), and DIEA (0.653mL, 3.75mol) in DMA (4mL) was added HATU (855mg, 2.25mmol) and the solution was stirred at room temperature for 0.5 hour. Excess H_2O was added to the reaction mixture. The precipitate was collected and were redissolved in CH_2Cl_2, washed with $NaHCO_3$ (aq) (2X), brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica column chromatography (1% MeOH/DCM as eluent) to afford (*R*)-benzyl 3-hydroxy-1-(4-(2-(4-morpholino-phenylamino)pyrimidin-4-yl)phenylamino)-1-oxopropan-2-ylcarbamate **365(a)** (668 mg, 78% yield).

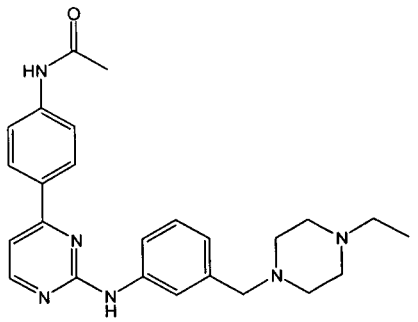
[0780] To a stirred solution of (*R*)-benzyl 3-hydroxy-1-(4-(2-(4-morpholinophenylamino)-pyrimidin-4-yl)phenylamino)-1-oxopropan-2-ylcarbamate from the step above in MeOH (10 mL) was added $Pd(OH)_2$ (134 mg) and ammonium formate (369 mg, 5.85). The mixture was heated at 60 °C for 2 hours, cooled down to room temperature, and filtered on Celite by eluting with MeOH. The filtrate was concentrated *in vacuo* and the residue was purified by prepatory HPLC (TFA). The TFA salt was removed by using basic resin to afford (*R*)-2-amino-3-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide **365** (346 mg, 68%). ^{1}H-NMR (400MHz, DMSO-d_6): 9.39 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.83 (d, 2H), 7.67 (d, 2H), 7.29 (d, 1H), 6.94pm (d, 2H), 4.94 (m, 1H), 3.75 (m, 4H), 3.60 (m, 2H), 3.46 (m, 1H), 3.05 (m, 4H); MS (EI) m/z for $C_{23}H_{26}N_6O_3$: 435.4 (MH^+).

Example 22

N-{4-[2-({3-[(4-ethylpiperazin-1-yl)methyl]phenyl}amino)pyrimidin-4-yl]phenyl}-acetamide (Compound 122)



A B



122

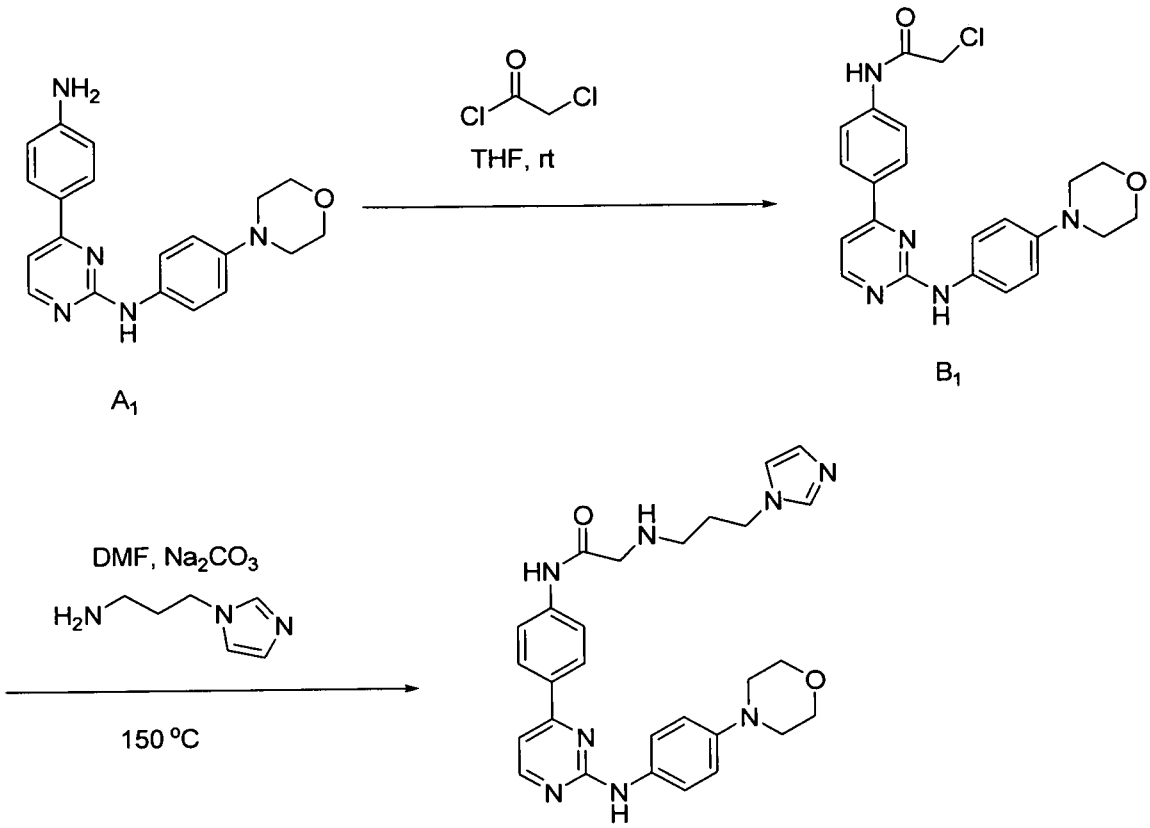
[0781] Intermediate **A** (0.5g) was dissolved in THF (5 ml), 20% aqueous H_2SO_4 solution (5ml) was then added to the solution. The mixture was stirred at 50^0 C for 2 hours and monitored by LC/MS (MH+, 333). The solution was then neutralized with 2N NaOH solution and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to afford 0.38g of the aldehyde **B**. (90% yield)

[0782] A flask was charged with aldehyde **B** (0.1g, 0.3 mmol), dichloromethane (10 ml), sodiumtriacetoxyborohydride (0.32g, 1.5mmol), and 1-ethylpiperazine (0.19 ml, 1.5mmol). The reaction mixture was stirred at room temperature overnight and checked with LC/MS. The product **122** was isolated by removal of the solvent with a rotary evaporator and then purified with a preparative HPLC.

^{1}H NMR (400 MHz, d_6-DMSO): 10.23 (s, 1H), 9.6 (s, 1H), 8.5 (d, 1H), 8.14 (d, 2H), 7.9 (s, 1H), 7.76 (d, 2H), 7.65 (d, 1H), 7.36 (d, 1H), 7.24 (t, 1H), 6.89 (d, 1H), 3.43 (s, 2H), 2.4 (br, 6H), 2.3 (q, 2H), 2.1 (s, 3H), 0.96 (t, 3H). MS (EI) for $C_{25}H_{30}N_6O$: 431 (MH^+).

Example 23

2-(3-(1H-imidazol-1-yl)propylamino)-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide (Compound 143)



143

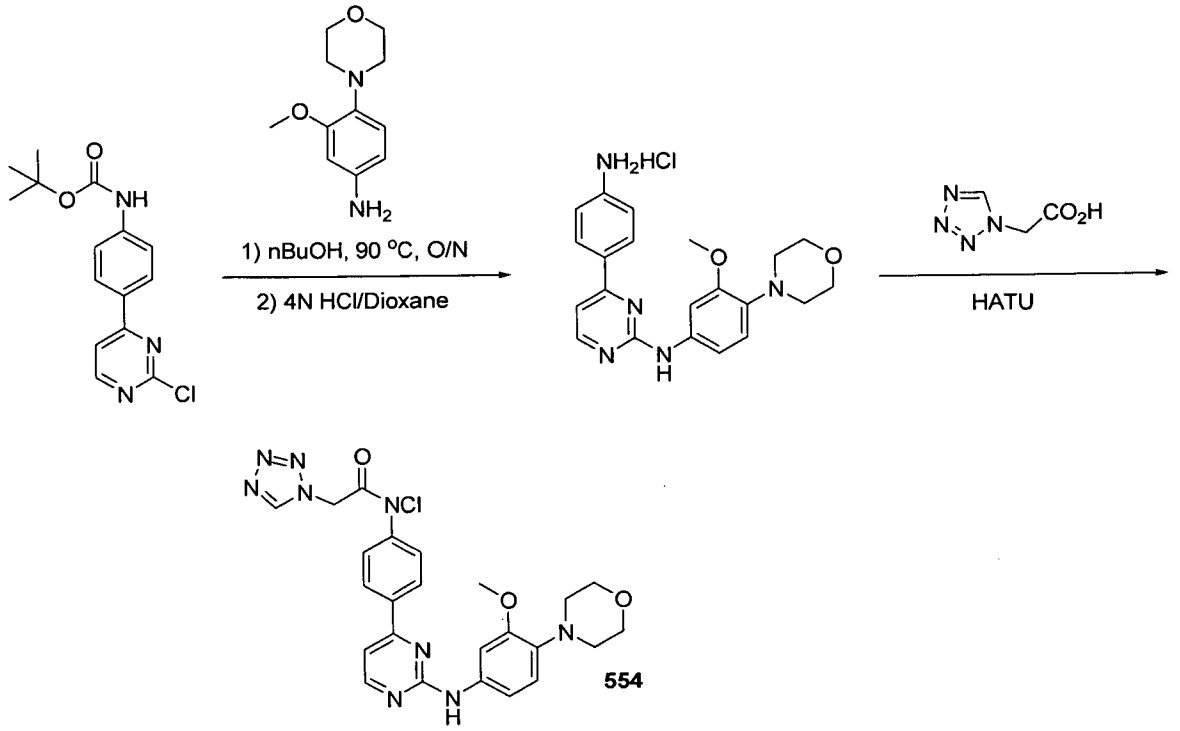
[0783] A flask was charged with aniline A_1 (100 mg, 0.29 mmol), and THF (1.0 mL). Chloroacetylchloride (23 μL, 0.29 mmol) was added and the mixture was stirred at ambient temperature for 1 hr, after which time it was concentrated. The product, B_1, was isolated by removal of the solvent with a rotary evaporator and used without further purification.

[0784] A flask was charged with alkyl chloride B_1 (20 mg, 0.047 mmol), Na_2CO_3 (30 mg, 0.28 mmol), 1-(3-Aminopropyl)imidazole (5.6 μL, 0.047 mmol), and DMF (1.0 mL). The mixture was stirred at 150 °C for 1 hr, after which time it was concentrated. The product **143** was purified by reverse phase HPLC to afford 9.7 mg (40% yield from B_1) as a white solid.

^{1}H-NMR (400MHz, d6-DMSO): 8.35 (d, 1H), 8.13 (d, 2H), 7.78-7.63 (m, 3H), 7.61 (d, 2H), 7.22 (d, 1H), 7.17 (s, 1H), 7.05-6.95 (m, 2H), 4.62 (s, br, 1H), 4.16 (t, 2H), 3.87-3.77 (m, 4H), 3.49 (s, 1H), 3.34 (s, 1H), 3.15-3.07 (m, 4H), 2.67 (t, 2H), 2.11-2.01 (m, 2H), 1.95 (s, 2H). MS (EI) $C_{28}H_{32}N_8O_2$: 513.1 (MH+).

Example 24

N-chloro-N-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(1H-tetrazol-1-yl)acetamide (Compound 554)



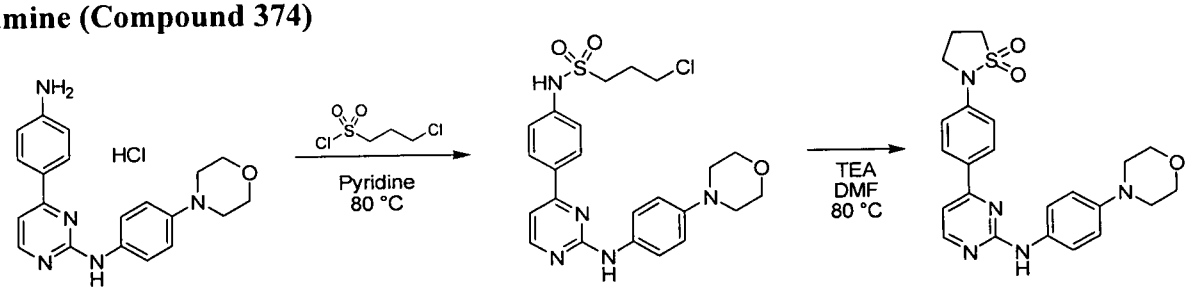
[0785] 4-(4-aminophenyl)-N-(3-methoxy-4-morpholinophenyl)pyrimidin-2-amine hydrochloride: A flask was charged with tert-butyl 4-(2-chloropyrimidin-4-yl)phenylcarbamate **A** (12.2 g, 40.0 mmol), 3-Methoxy-4-morpholinoaniline (9.7 g, 40.76 mmol) and 50 mL n-butanol. The reaction mixture was stirred under an N_2 atmosphere at 100 °C for 12 hours, after which time, then, cooled to room temperature. 25 mL of 4N HCl in dioxane was added, the reaction mixture was stirred at 50 °C for 5 hours. After cooled to room temperature, it was filtered, washed with ethyl acetate, dried in the air to collect 16 g of yellow-green solid as the desired product. NMR (400 MHz, d6-DMSO): 10.40 (s, 1H), 8.60 (d, 1H), 8.20 (s, 2H), 7.94 (s, 1H), 7.84 (d, 1H), 7.54 (d, 1H), 7.41 (d, 1H), 7.30 (m, 2H), 4.10 (m, 2H), 3.99 (s, 3H), 3.60 (br, 2H), 3.39 (m, 2H), 1.25 – 1.42 (m, 4H). MS (EI) for $C_{21}H_{23}N_5O_2$: 378 (MH+).

[0786] A flask was charged with 4-(4-aminophenyl)-N-(3-methoxy-4-morpholinophenyl)pyrimidin-2-amine hydrochloride **B** (471.0 mg, 0.84 mmol), 2-(1H-tetrazol-1-yl)acetic acid (216.0 mg, 1.69 mmol), HATU (1276.0 mg, 3.38 mmol) and 2 mL of DMA. The reaction mixture was stirred at room temperature for 24 hours, and then quenched with 50 mL of water, extracted with ethyl acetate (3X50 mL). The combined

organics were washed with water and then brine (50 mL each), dried over anhydrous sodium sulfate, and then concentrated. The crude product was purified with a silica gel column (ethyl acetate to 10% methanol in ethyl acetate), 345.0 mg of the desired product **554** was obtained as yellowish powder. NMR (400 MHz, d6-DMSO): 10.85 (s, 1H), 9.50 (s, 1H), 9.43 (s, 1H), 8.47 (s, 1H), 8.19 (d, 2H), 7.75 (d, 2H), 7.63 (s, 1H), 7.20 (m, 3H), 6.84 (d, 1H), 5.56 (s, 2H), 3.80 (s, 3H), 3.74 (m, 4H), 2.94 (m, 4H). MS (EI) for $C_{24}H_{25}N_9O_3$: 488 (MH+).

Example 25

4-[4-(1,1-Dioxidoisothiazolidin-2-yl)phenyl]-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine (Compound 374)



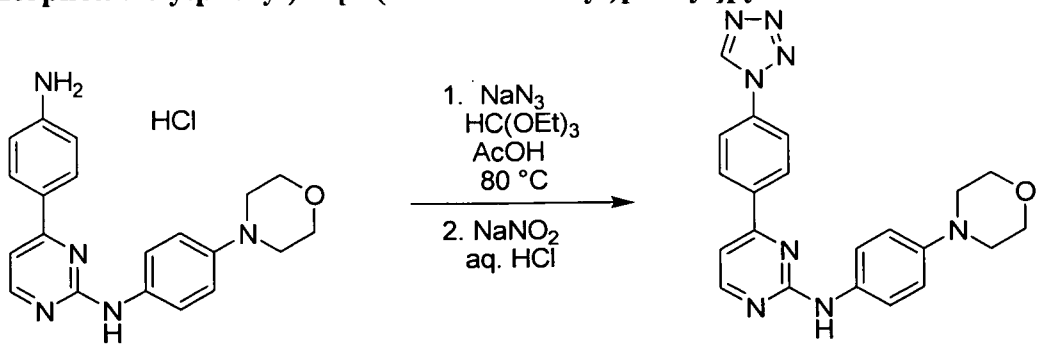
A 374

[0787] Aniline **A** (300 mg, 0.78 mmol) was dissolved in 4 mL of dry pyridine. 3-Chloropropanesulfonyl chloride (950 uL, 7.8 mmol) was added dropwise. The reaction mixture was heated to 80 °C and stirred overnight under a nitrogen atmosphere. The solvent was removed under vacuum and the residue was re-dissolved in 25 mL of ethyl acetate. The reaction mixture was washed one time each with 10 mL portions of water, 0.1 M HCl, and saturated aqueous NaCl. The organic layer was dried with $MgSO_4$ and concentrated under vacuum. The residue was taken up in DMF (4 mL) and triethylamine (1100 uL, 7.9 mmol). The reaction mixture was heated to 80 °C and stirred overnight. The product was purified by preparative HPLC to give 85 mg of **374**. ^{1}H NMR (400 MHz, d_6-DMSO): 9.78 (s, 1H), 8.49 (d, 1H), 8.20 (d, 2H), 7.78 (d, 2H), 7.39 (d, 1H), 7.33 (d, 2H), 7.25 (br s, 2H), 3.84 (br s, 4H), 3.73 (t, 2H), 3.60 (t, 2H), 2.54 (m, 2H), 2.45 (m, 2H) 2.01 (m, 2H); MS (EI) for $C_{23}H_{25}N_5O_3S$: 452 (MH^+).

5

Example 26

N-(4-Morpholin-4-ylphenyl)-4-[4-(1H-tetrazol-1-yl)phenyl]pyrimidin-2-amine

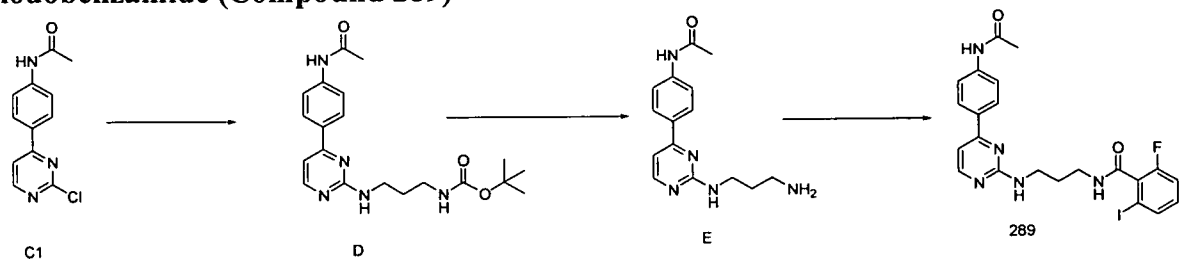


A **375**

10 **[0788]** Aniline **A** (200 mg, 0.52 mmol), sodium azide (45 mg, 0.69 mmol), triethylorthoformate (280 uL, 1.7 mmol) and acetic acid (480 uL, 8.4 mmol) were combined in a 25 mL round bottom flask. The reaction mixture was stirred for 2 hours at 80 °C. The reaction mixture was allowed to cool to room temperature and then it was cooled further in an ice bath. A solution of 670 uL of 6.0 M HCl in 1.25 mL of water was added to the
15 reaction mixture. After stirring in the ice bath for 5 minutes, another solution of sodium nitrite (50 mg, 0.72 mmol) in water (200 uL) was added slowly. The precipitate was filtered off and purified by reverse phase HPLC to give 24 mg of **375**. ^{1}H NMR (400 MHz, d_6-DMSO): 10.19 (s, 1H), 9.51 (s, 1H), 8.53 (d, 1H), 8.40 (dd, 2H), 8.10 (d, 2H), 7.65 (d, 2H), 7.43 (d, 1H), 6.92 (d, 2H), 3.73 (m, 4H), 3.03 (m, 4H); MS (EI) for $C_{21}H_{20}N_8O$: 401 (MH^+).

Example 27

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-fluoro-6-iodobenzamide (Compound 289)



[0789] A flask was charged with **C1** (5.0 g, 20.2388 mmol) and (3-aminopropyl)-carbamicacid-t-butyl ester (6 mL, 30.3582 mmol). n-butanol (40 mL) were added to the flask and heated to 175 °C for an hour. Solvent was evaporated and reaction mixture was checked with LC/MS. The reaction mixture was cooled to room temperature and ethyl acetate was added. The precipitate, **B**, was filtered and used without further purification. LC/MS: m/z 386 $(M+H)^+$.

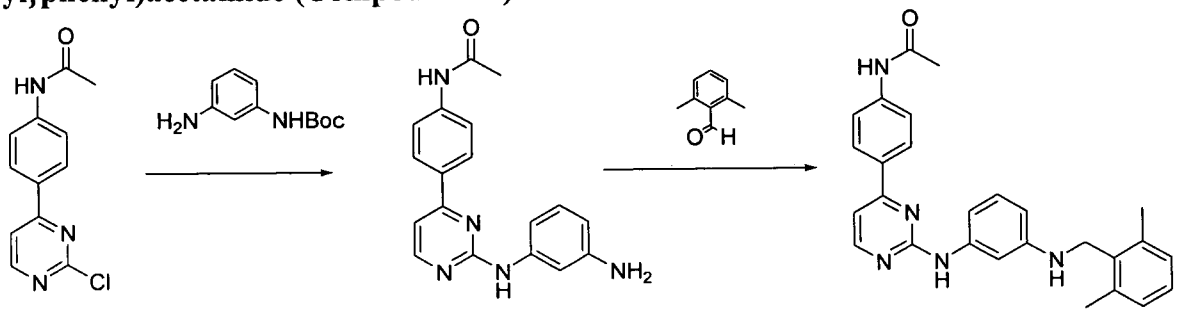
[0790] A flask was charged with **B**. 4 N HCl in dioxane was added and stirred at room temperature for 3 hours. The reaction mixture was checked with LC/MS. The product, **E**, was isolated by removal of the solvent with a rotary evaporation and used without further purification. LC/MS; m/z 286 $(M+H)^+$.

[0791] A flask was charged with **E** (254 mg, 0.8902 mmol), 2-fluoro-6-idobenzoyl chloride (90 μL, 0.6231 mmol), tetrahydrofuran (25 mL), and n-ethyldiisopropylamine (108 μL, 0.6231 mmol). The reaction mixture was stirred at room temperature for 12 hours. The reaction mixture was monitored with LC/MS. The product, **289**, was isolated by removal of the solvent with a rotary evaporator and purified with a TFA preparative HPLC (10:90, 11 min run).

^{1}H-NMR (400MHz, d_6-DMSO): 10.16 ppm (s, 1H), 8.64 ppm (t, 1H), 8.30 ppm (d, 1H), 8.06 ppm (d, 2H), 7.70 ppm (m, 3H), 7.30 ppm (m, 1H), 7.20 ppm (m, 1H), 7.13 ppm (m, 1H), 7.07 ppm (m, 1H), 3.34 ppm (m, 4H), 2.08 ppm (s, 3H), 1.83 ppm (m, 2H); MS (EI) $C_{22}H_{21}FIN_5O_2$: 533.9 (MH^+).

Example 28

N-(4-{2-[(3-{[(2,6-dimethylphenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide (Compound 51)



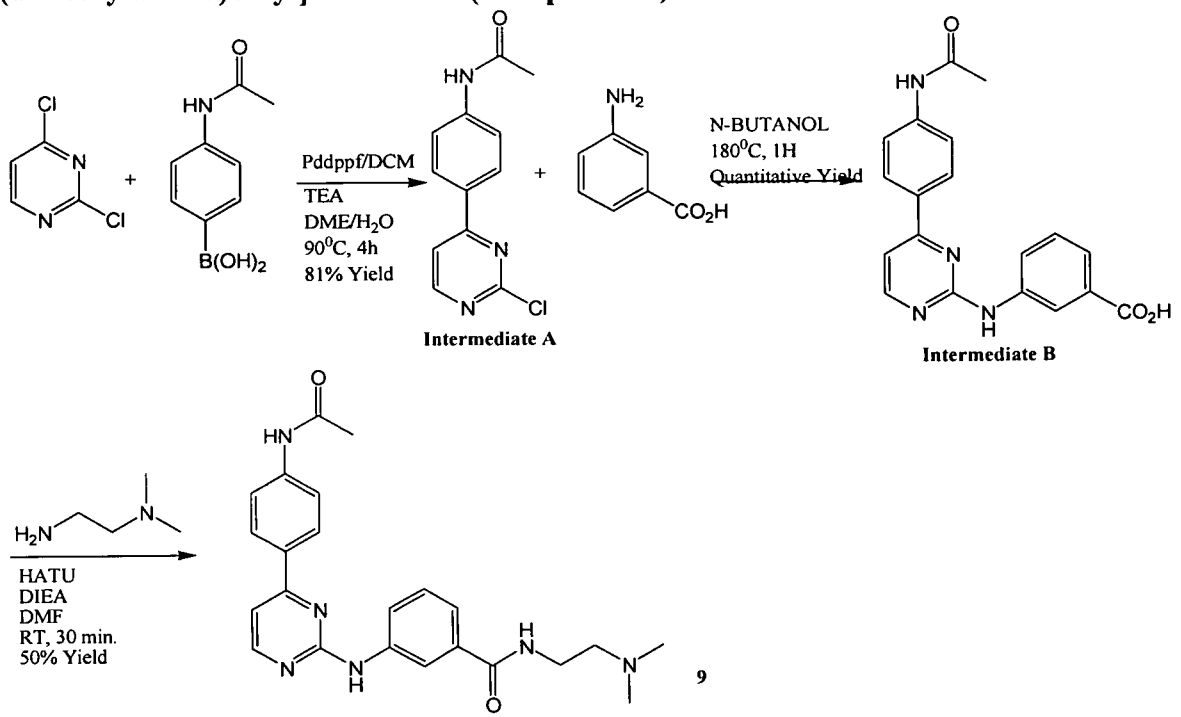
C1 D 51

[0792] A flask was charged with **C1** (5.0 g, 20.2388 mmol) and tert-butyl 3-aminophenylcarbamate (4.6 g, 22.2627 mmol). n-butanol (40 mL) were added to the flask and heated to 175 °C for 4 hours. Solvent was evaporated and reaction mixture was checked with LC/MS. The reaction mixture was cooled to room temperature and ethyl acetate was added. The precipitate, **D**, was filtered and used without further purification. LC/MS: m/z 320 $(M+H)^+$.

[0793] A flask was charged with **D** (463 mg, 1.4514 mmol), dichloromethane/tetrahydrofuran (2;1, 15 mL), sodium triacetoxyborohydride (615 mg, 2.9028 mmol), and 2,6-dimethylbenzaldehyde (196 µL, 1.4514 mmol) The reaction mixture was stirred at room temperature for 12 hours and monitored with LC/MS. The product, **51**, was isolated by removal of the solvent with a rotary evaporator and purified with a TFA preparative HPLC (10:90, 11 min run). ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 ppm (s, 1H), 9.36 ppm (s, 1H), 8.47 ppm (d, 1H), 8.16 ppm (d, 2H), 7.72 ppm (d, 2H), 7.35 ppm (s, 1H), 7.31 ppm (d, 1H), 7.12 ppm (m, 1H), 7.07 ppm (m, 2H), 6.99 ppm (m, 3H), 6.38 ppm (d, 1H), 5.46 ppm (t, 1H), 4.14 ppm (d, 2H), 2.36 ppm (s, 6H), 2.08 ppm (s, 3H); MS (EI) $C_{27}H_{27}N_5O$: 438.1 (MH^+).

Example 29

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(dimethylamino)ethyl]benzamide (Compound 9)



[0794] A flask was charged with 2,4-dichloropyrimidine (22.7 g, 152.38 mmol), 4-acetoamidophenylboronic acid (30.0 g, 167.62 mmol), dicholor[1,1'-bis(diphenylphosphino)-ferrocenepalladium (16.726 g, 22.86 mmol, 15 mol %), and triethylamine (53 mL, 380.95 mmol). Ethyleneglycoldimethylether (500 mL) and H_2O (20 mL) was added to the flask. The reaction mixture was stirred at 80 °C for 4 hours. The product, Intermediate **A**, was isolated by removal of the solvent with a rotary evaporator and purified using glass column chromatography and eluted with ethyl acetate to afford 30.5 g (123.14 mmol, 81% yield) of intermediate **A** as a yellow solid.

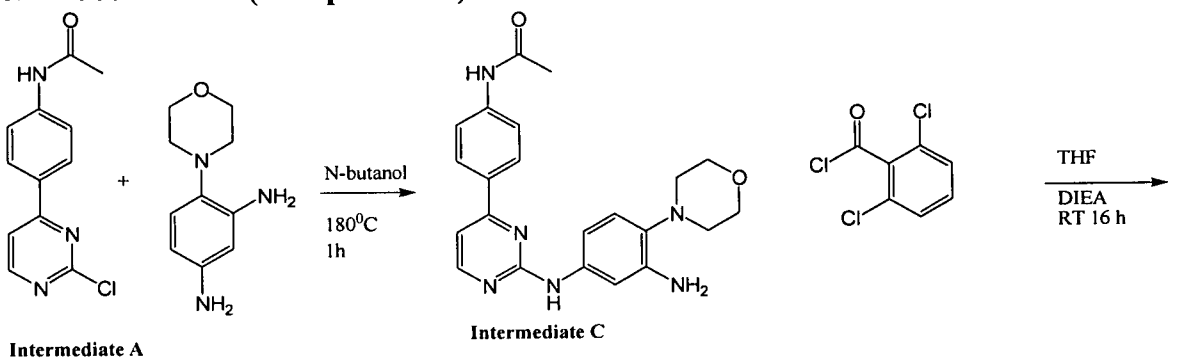
[0795] A seal tube was charged with intermediate **A** (400 mg, 1.62 mmol) and 3-aminobenzoic acid (222 mg, 1.62 mmol). N-butanol (15 mL) was added to the seal tube and stirred at 180°C. The reaction was done in 1hour according to LCMS to afford intermediate **B** as a yellow solid. Intermediate **B** was placed on a rotary evaporator to remove excess n-butanol. Intermediate **B** was carried on to the next step without further purification.

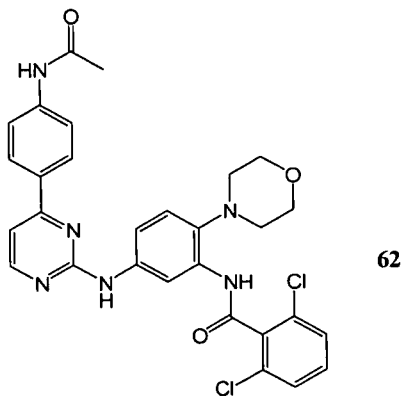
[0796] A flask was charged with intermediate **B** (282 mg, 0.81 mmol), HATU (464 mg, 1.22 mmol), DMF (15 mL) and DIEA (212 µL, 1.22 mmol). The reaction mixture was stirred at rt and completed in 30 min. to afford the final product (**9**). The final product was purified using Preperative HPLC and ammonium acetate buffer and lyophilized to afford the product as ACE salt (170 mg, 0.41 mmol). ^{1}H-NMR (400MHz, d_6-CD_3OD): 8.523 ppm (t,

1H), 8.45 ppm (d, 1H), 8.176 ppm (m, 2H), 7.828 ppm (m, 1H), 7.2 ppm (d, 2H), 7.475-7.404 ppm (m, 2H), 7.326 ppm (d, 1H), 3.738 ppm (t, 2H), 3.244 ppm (t, 2H), 2.877 ppm (s, 6H), 2.162 ppm (s, 3H), 1.955 (s, 3H, ACE). MS (EI) $C_{23}H_{26}N_6O_2$: 419.1 (MH^+).

Example 30

N-[5-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-2-morpholin-4-ylphenyl]-2,6-dichlorobenzamide (Compound 62)





62

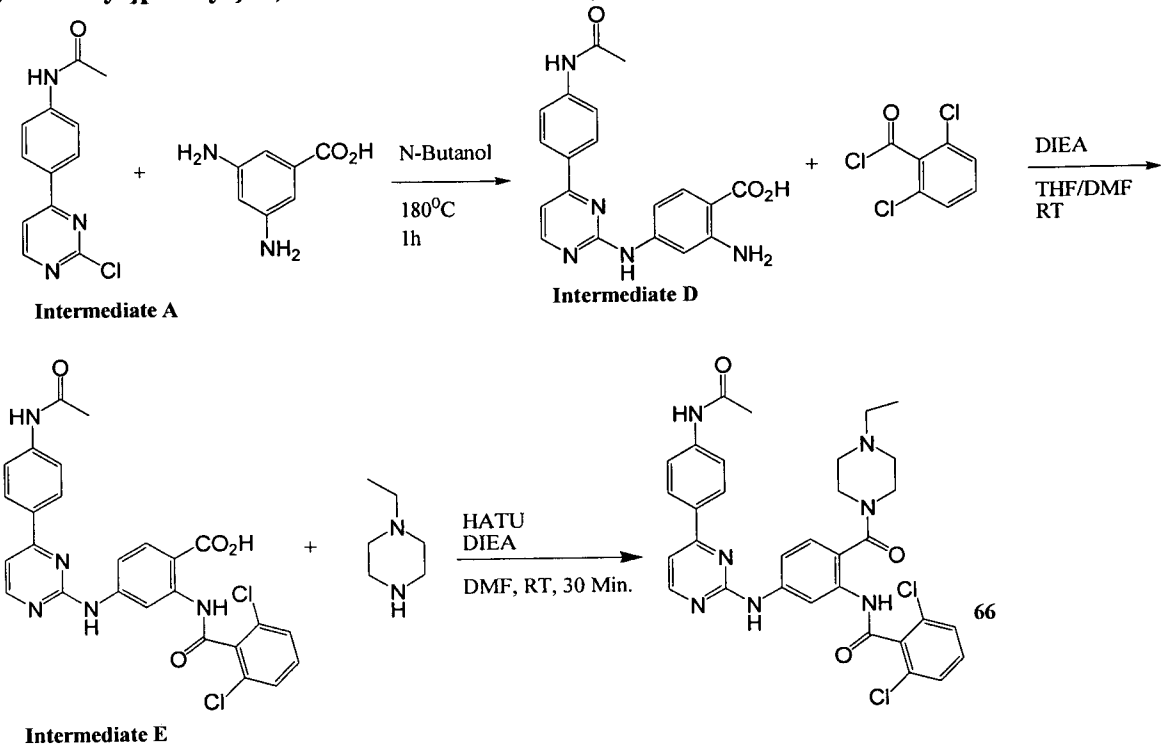
[0797] A seal tube was charged with intermediate **A** (500 mg, 2.02 mmol) and 4-morpholinobenzene-1,3-diamine (400 mg, 2.02 mmol, Zerenex Limited). N-butanol (15 mL) was added to the seal tube and stirred at 180°C. The reaction was done in 1h according to LCMS to afford intermediate **C** as a yellow solid. Intermediate **C** was placed on a rotary evaporator to remove excess n-butanol. Intermediate **C** was carried on to the next step without further purification.

[0798] A flask was charged with intermediate **C** (816 mg, 2.02 mmol), THF (100 mL), DIEA (705 μL, 4.04mmol), and 2,6-dichlorobenzoyl chloride (290 μL, 2.02 mmol). The reaction mixture was stirred at rt over night to afford the final product **62**. The final product was purified using Preperative HPLC and TFA buffer, then was free-based and lyophilized (165 mg, 0.28 mmol, 14% Yield).

^{1}H NMR (400 MHz, DMSO): 10.194 (s, 1H), 9.8 (s, 1H), 9.607 (s, 1H), 8.585 (s, 1H), 8.484 (d, 1H), 8.235 (d, 2H), 7.711 (d, 2H), 7.592 (d, 2H), 7.496 (m, 2H), 7.356 (d, 1H), 7.183 (d, 1H), 3.74 (t, 4H)), 2.89 (t, 4H), 2.07 (s, 3H). MS (EI) for $C_{29}H_{26}Cl_2N_6O_3$: 579.1 (MH^+).

Example 31

N-{3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-5-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-2,6-dichlorobenzamide (Compound 66)



Intermediate A

Intermediate D

Intermediate E

[0799] A seal tube was charged with intermediate **A** (300 mg, 1.21mmol) and 3,5-diaminobenzoic acid (204 mg, 1.34 mmol). N-butanol (15 mL) was added to the seal tube and stirred at 180°C. The reaction was done in 1h according to LCMS to afford intermediate **D** as a yellow solid. Intermediate **D** was placed on a rotary evaporator to remove excess n-butanol. Intermediate **D** was carried on to the next step without further purification.

[0800] A flask was charged with intermediate **D** (439 mg, 1.21 mmol), THF (30 mL), DMF(5 mL), DIEA (632 µL, 3.63 mmol), and 2,6-dichlorobenzoyl chloride (174 µL, 1.21 mmol). The reaction mixture was stirred at rt over night. The reaction mixture was quenched with 2 M NaOH (100 mL) and extracted with ethyl acetate (3x) and the organic layer was discarded. The aqueous NaOH layer was neutralized with conc. HCl. The solid formed was collected via filtration and washed with excess water to afford intermediate **E** (274 mg, 0.51 mmol, 62% yield) as a yellow solid. Intermediate **E** was carried on to the next step without further purification.

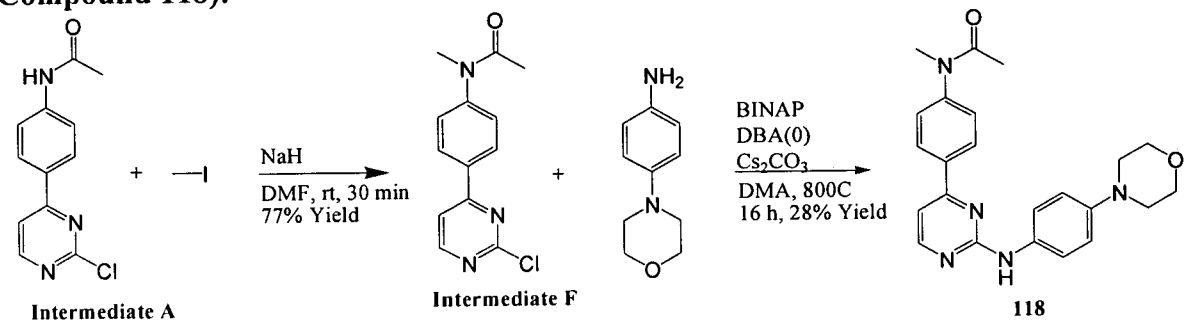
[0801] A flask was charged with intermediate **E** (274 mg, 0.51 mmol), HATU (291 mg, 0.765 mmol), DMF (25 mL), ethylpiperazine (78 µL, 0.61 mmol) and DIEA (133 µL, 0.765 mmol). The reaction was stirred at rt and completed in 15 min. The final product **66** was

purified using Preperative HPLC and TFA buffer, free-based and lyophilized to afford the product (166 mg, 52% yield).

^{1}H NMR (400 MHz, DMSO): 10.896 (s, 1H), 10.33 (s, 1H), 9.881 (s, 1H), 8.533 (d, 1H), 8.374 (s, 1H), 8.202 (d, 2H), 7.776 (d, 2H), 7.636-7.6 (m, 3H), 7.529 (m, 1H), 7.419 (d, 1H), 7.296 (s, 1H), 3.628 (br s, 2H), 3.415 (br s, 2H), 2.427-2.314 (m, 6H), 2.091 (s, 3H), 0.996 (t, 3H). MS (EI) for $C_{32}H_{31}Cl_2N_7O_3$: 634.1(MH^+).

Example 32

***N*-methyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide (Compound 118):**



Intermediate A Intermediate F 118

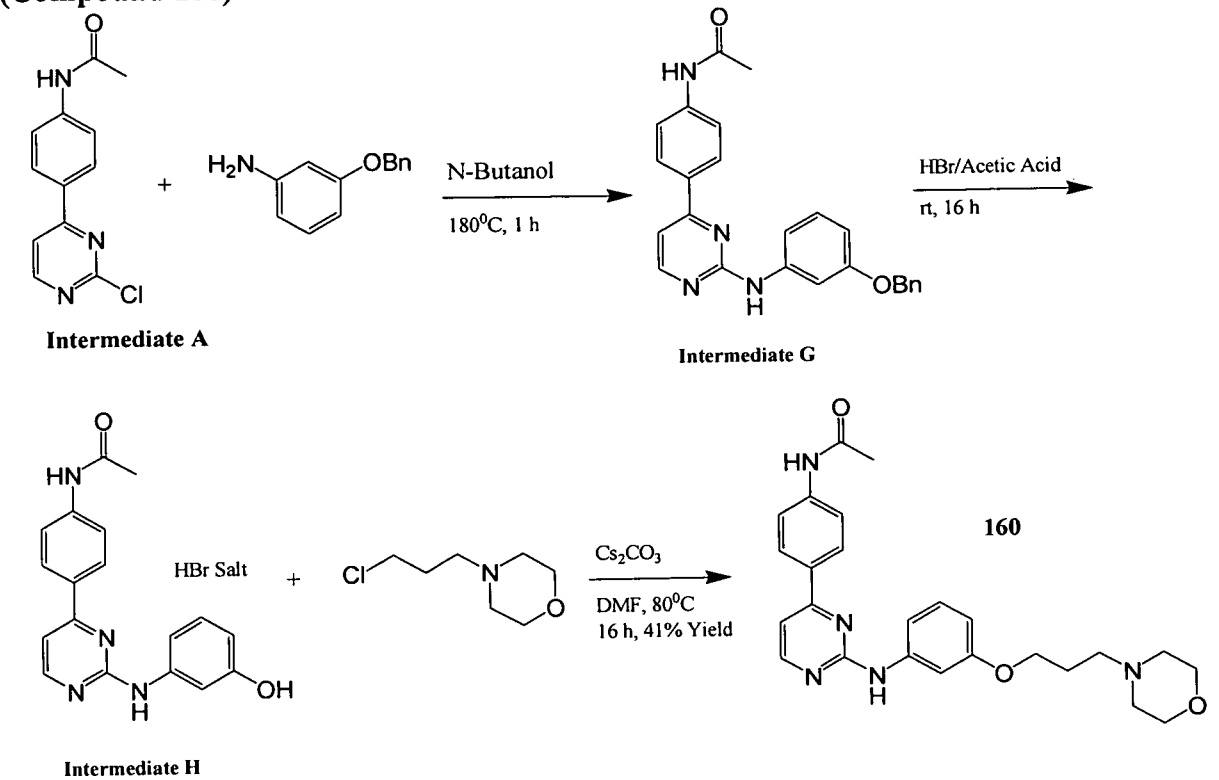
[0802] A flask was charged with intermediate **A** (250 mg, 1.01 mmol), DMF (10 mL), NaH (30.0 g, 167.62 mmol), dicholor[1,1'-bis(diphenylphosphino)ferrocenepalladium (60 mg, 1.5 mmol), and methyl iodide (94 μL, 1.5 mmol). The reaction mixture was stirred at rt and completed in 30 min. The reaction mixture was quenched with H_2O and extracted with ethyl acetate (3X) and washed with 10% LiCl solution (1X), brine (1X), dried over sodium sulfate, and filtered. The organic layer was removed with a rotary evaporator to afford intermediate **F** (200 mg, 0.766 mmol) as a yellow gelatin. Intermediate **F** was carried on to the next step without further purification.

[0803] A seal tube was charged with intermediate **F** (200 mg, 0.766 mmol), anhydrous DMA (15 mL), cesium carbonate (374 mg, 1.15 mmol), racemic-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl (70 mg, 0.115 mmol), and tris(dibenzylideneacetone)dipalladium(0). The reaction was flushed with N_2 gas for five minutes and the seal tube was sealed and stirred at 80^{0}C over night. The reaction was filtered and washed with ethyl acetate and the solid was discarded. The organic solvent was removed using the rotary evaporator. The final product **66** was purified using Preperative HPLC and TFA buffer, free-based and lyophilized to afford the product (95 mg, 0.235 mmol, 28% Yield).

^{1}H-NMR (400MHz, d_6-DMSO): 9.464 ppm (s, 1H), 8.511 ppm (d, 1H), 8.209 ppm (d, 2H), 7.67 ppm (m , 2H), 7.516 ppm (d, 2H), 7.366 ppm (d, 1H), 6.926 ppm (m, 2H), 3.743 ppm (t, 4H), 3.22 ppm (s, 3H), 3.048 ppm (t, 4H). MS (EI) $C_{23}H_{25}N_5O_2$: 404.3 (MH^+).

Example 33

N-(4-(2-(3-(3-morpholinopropoxy)phenylamino)pyrimidin-4-yl)phenyl)acetamide (Compound 160)



[0804] A seal tube was charged with intermediate **A** (500 mg, 2.02 mmol) and 3-benzyloxyaniline (404 mg, 2.02 mmol). N-butanol (15 mL) was added to the seal tube and stirred at 180^{0}C. The reaction was done in 1h according to LCMS to afford intermediate **G** as a yellow solid. Intermediate **G** was placed on a rotary evaporator to remove excess n-butanol. Intermediate **G** was carried on to the next step without further purification. A flask was charged with intermediate **G** and HBr/Acetic acid (33%, 10 mL) and stirred at rt over night. The reaction was done and the solid was collected via filtration and washed with ether to afford intermediate **H** as a yellow and HBr salt solid (800 mg, 1.66 mmol, 82% yield).

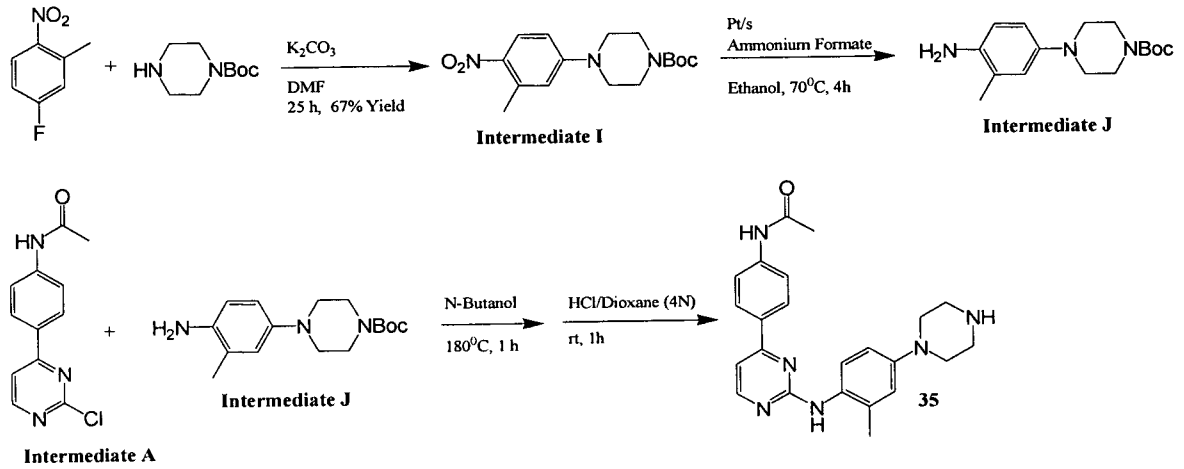
[0805] A flask was charged with intermediate **H** (250 mg, 0.52 mmol), DMF (15mL), Cs_2CO_3 (847mg, 2.6 mmol) and 4-(3-chloropropyl)morpholine HCl salt (135 mg, 0.676 mmol, purchased from Apin Chemicals, Ltd.) and stirred at 80^{0}C over night. The reaction mixture had approximately 85% desired product and 15% bis-alkylated by-product. The solid was filtered and washed with ethyl acetate and discarded. The filtrate was concentrated

using the rotary evaporator. The final product was purified using Preperative HPLC and TFA buffer, free-based, converted to HCl salt and lyophilized to afford the product (115mg, 0.237 mmol, 46% Yield).

^{1}H NMR (400 MHz, DMSO): 11.058 (s, 1H), 10.403 (s, 1H), 9.761 (s, 1H), 8.532 (d, 1H), 8.158 (d, 2H), 7.81 (d, 2H), 7.677 (s, 1H), 7.4-7.345 (m, 2H), 7.231 (t, 1H), 6.569 (m, 1H), 4.081 (t, 2H), 3.962 (m, 2H), 3.82 (t, 2H), 3.46 (m, 2H), 3.267 (m, 2H), 3.123 (m, 2H), 2.254 (m, 2H), 2.104 (s, 3H). MS (EI) for $C_{25}H_{29}N_5O_3$: 448.3 (MH^+).

Example 34

N-(4-{2-[(2-methyl-4-piperazin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide (Compound 35):

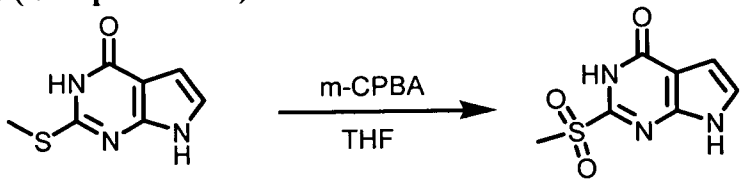


[0806] A flask was charged with 5-fluoro-2-nitrotoluene (1 mL, 8.2 mmol), DMF (15 mL), Bocpiperazine (1.68 g, 9.02 mmol), and K_2CO_3 (2.27 g, 16.4 mmol). The reaction mixture was stirred at 50 ^{0}C for about 25 h. The reaction was quenched with H_2O and the solid precipitated out of the solution and collected via filtration and washed with excess H_2O to obtain intermediate **I** (1.765g, 5.4 mmol). Intermediate **I** was carried on to the next step without further purification. A flask was charged with intermediate **I** (290 mg, 0.9 mmol), ethanol (18 mL), ammonium formate (340 mg, 5.4 mmol) and Pt/S (10.2 mg, 0.04 mmol). The reaction mixture was stirred at 70^{0}C for 3 h and 78^{0}C for 4 h. The reaction mixture was filtered through celite and washed with ethanol. The filtrate was removed using the rotary evaporator and then treated with ethyl acetate and washed with H_2O, dried over sodium sulfate, and filtered. The ethyl acetate layer was concentrated using rotary evaporator to afford intermediate **J**.

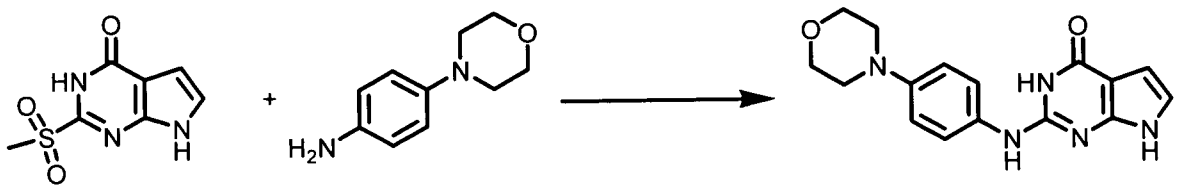
[0807] A seal tube was charged with intermediate **A** (200 mg, 0.81 mmol), and intermediate **J** (235 mg, 0.81 mmol). N-butanol (15 mL) was added to the seal tube and stirred at 180^{0}C. The reaction was done in 1h and concentrated to remove excess n-butanol and then treated with 4N HCl/dioxane. The reaction mixture was stirred at rt for 1h to afford the final product **35**. The final product was purified using Preperative HPLC and ammonium acetate buffer, then free-based and lyophilized (90 mg, 0.22 mmol, 27% Yield). ^{1}H-NMR (400MHz, d_6-DMSO): 10.31 ppm (s, 1H), 8.569 ppm (s, 1H), 8.323 ppm (d, 1H), 8.022 ppm (d, 2H), 7.715 ppm (d, 2H), 7.271 ppm (d, 1H), 7.186 ppm (d, 1H), 6.8 ppm (m, 2H), 3.023 ppm (t, 4H), 2.844 ppm (t, 4H), 2.175 ppm (s, 3H), 2.077 ppm (s, 3H), 1.605 ppm (s, 2H); MS (EI) $C_{23}H_{26}N_60$: 403.1 (MH^+).

Example 35

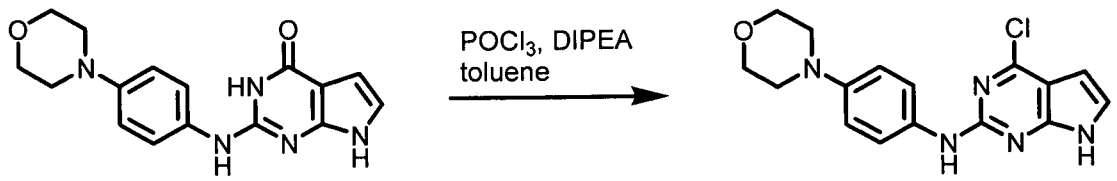
***N*-[4-({2-[(4-morpholin-4-ylphenyl)amino]-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-yl}amino)-phenyl]acetamide (Compound 306)**



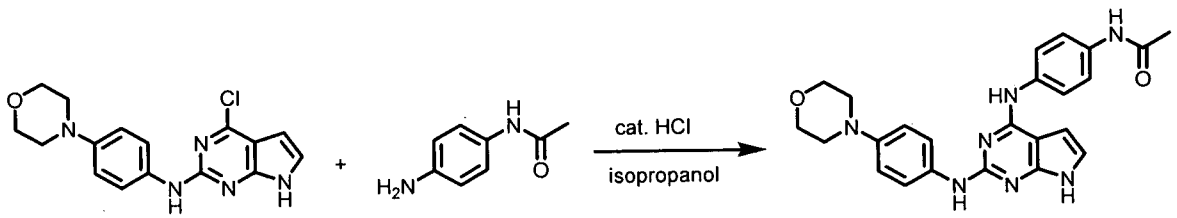
[0808] A flask was charged with methylsulfide (2.1g, 11.6mmol) and THF (50mL). To this, m-CPBA (7.9g, 46mmol) was added and the mixture was stirred at ambient temperature for 20 hours. Volatiles were removed under *vacuo*. The crude mixture was partitioned between EtOAc and DI H_2O. The aqueous layer was extracted with EtOAc (3x15mL). The combined organics were washed with 1N $NaHCO_3$ (x2), DI H_2O (x2), brine, (x1), dried over sodium sulfate, filtered and concentrated under *vacuo*. The product (1.8g, 75%) was used without further purification. LCMS: m/z 214$(M+H)^+$.



[0809] A pressure tube was charged with methylsulfone (1.15g, 5.4mmol) and aniline (2.8g, 16.2mmol). The tube was sealed and the mixture heated at 140°C for 30 minutes. The mixture was cooled. Methanol was added and the resulting solid collected via filtration then washed with methanol. The product (270mg, 8.7%) was used without further purification. LCMS: 312 $(M+H)^+$.



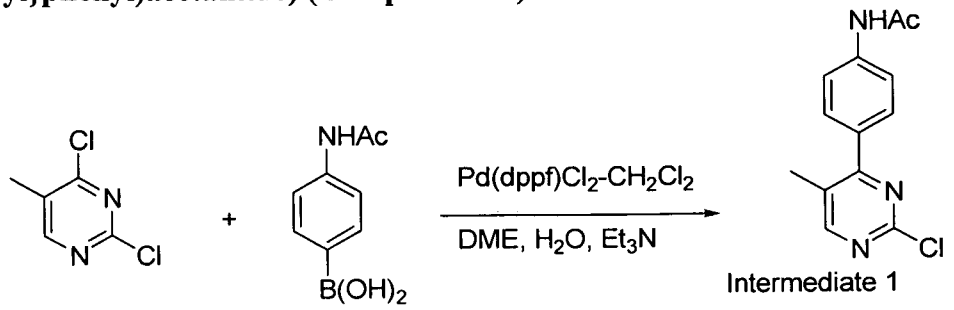
[0810] A flask was charged with pyrrolopyrimidinone (250mg, 0.8mmol) and toluene (5mL). Phosphorous oxychloride (218μL, 2.41mmol) and DIPEA (165μL, 0.96mmol) were added and the mixture stirred at 110°C for 6 hours. The volatiles were removed under *vacuo* and the product used without further purification. LCMS: 330 $(M+H)^+$.



[0811] A flask was charged with pyrrolopyrimidine (100mg, 0.3mmol) and isopropanaol (1mL). Aniline (55mg, .036mmol) and two drops of conc. HCl were added and the mixture heated to reflux for 6 hours. Volatiles were removed under *vacuo*. The product was purified by preparative HPLC to afford the title compound (**306**) (12.8mg, 9.6%).
^{1}H NMR (400MHz, d6-DMSO): 11.13 (s, 1H), 9.95 (s, 1H), 9.04 (s, 1H), 8.56 (s, 1H), 7.86 (d, 2H), 7.66 (d, 2H), 7.54 (d, 2H), 6.88-6.82 (m, 3H), 6.65-6.61 (m, 1H), 3.78-3.71 (m, 4H), 3.05-2.99 (m, 4H), 2.04 (s, 3H). MS (EI) for $C_{24}H_{25}N_7O_2$: 444 (MH+).

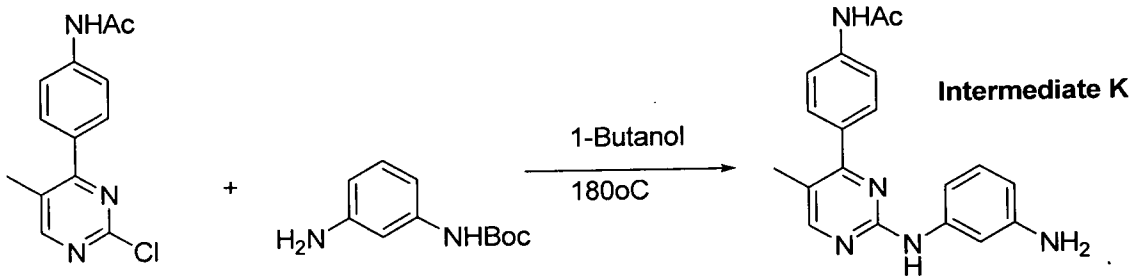
Example 36

(N-(4-{2-[(3-{[(2,6-dichlorophenyl)sulfonyl]amino}phenyl)amino]-5-methylpyrimidin-4-yl}phenyl)acetamide) (Compound 26)

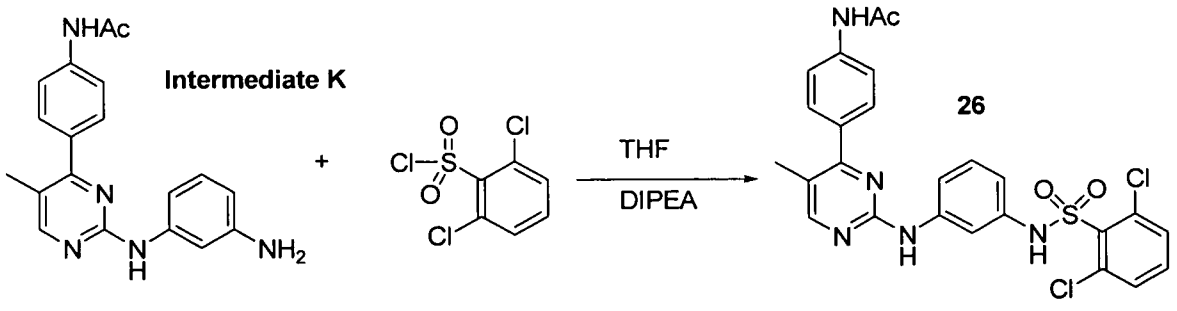


Intermediate 1

[0812] To a mixture of 2,4-dichloro-5-methylpyrimidine (4.17g, 25.6mmol) and 4-acetamidophenylboronic acid (5.0g, 27.9mmol) in DME (40ml) was added Et_3N (8.92ml, 64.0mmol), H_2O (4ml), and dichloro[1,1'-bis(diphenylphosphino)ferrocenepalladium (2.81g, 3.44mmol, 13%). The mixture was allowed to stir at reflux for 5hours. After the mixture was cooled down to rt, the crude mixture was directly filtered on silica gel and eluted with EtOAc. The filtrate was concentrated in vacuo. Further purification was conducted by flash chromatography to afford Intermediate 1 (5.94g, 89%) as a white solid. LCMS: m/z 262 $(M+H)^+$.



[0813] To a stirred solution of chloropyrimidine (1.05g, 4.0mmol) in 1-butanol (10ml) was added N-Boc-amino-3-aniline (920mg, 4.4mmol) and the mixture was heated in the sealed tube at 180°C for 1.5 hours. The mixture was cooled down to rt and acidified with 1N HCl (20ml). The aqueous layer was washed with EtOAc (50ml). The separated aqueous layer was basified with 2N NaOH to pH 8-9 and extracted with EtOAc (50ml*3). The combined organic layer was dried over Na_2SO_4, concentrated in vacuo, and purified by flash chromatography to afford product **Intermediate K** (943mg, 71% as a light yellow solid. LCMS: m/z 334 $(M+H)^+$.

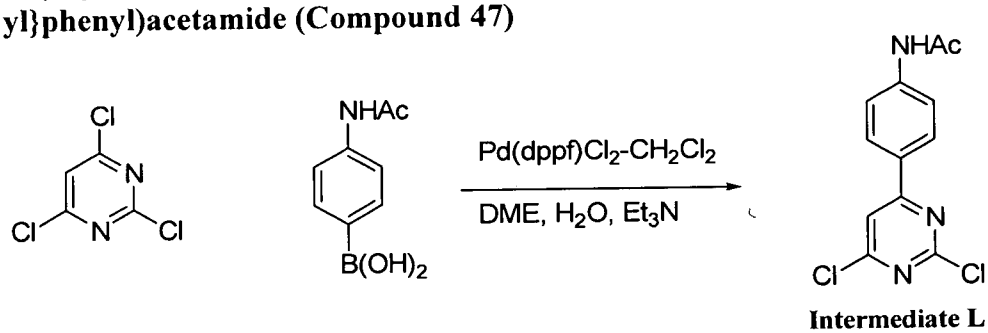


[0814] To a stirred suspension of aniline (250mg, 0.75mmol) in THF (5ml) was added DIPEA (157ml, 0.90mmol) and 2,6-dichlorobenzenesulfonyl chloride (203mg, 0.83mmol) and the mixture containing intermediate K was stirred at reflux for 2hrs. After cooling down to rt, the mixture was diluted with EtOAc, washed with H_2O, brine, and dried over Na_2SO_4. After concentrated in vacuo, the residue was purified by flash chromatography to give product **26** (299mg, 73%) as a light pink solid.

^{1}H-NMR (400MHz, d_6-DMSO): 10.71 (s, 1H), 10.16 (s, 1H), 9.54 (s, 1H), 8.34 (s, 1H), 7.75-7.69 (m, 5H), 7.60 (dd, 2H), 7.51 (dd, 1H), 7.31 (dd, 1H), 7.09 (t, 1H), 6.66 (dd, 1H), 2.25 (s, 3H), 2.08 (s, 3H); MS (EI) $C_{25}H_{21}Cl_2N_5O_3S$: 542.2 $(M+H)^+$.

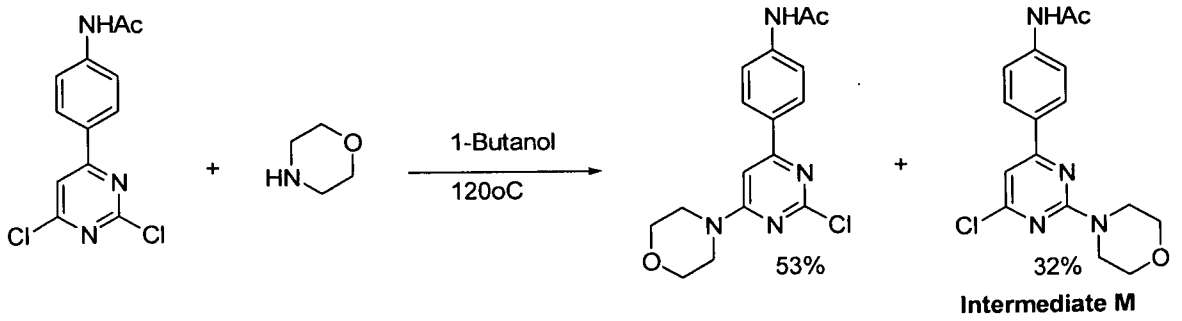
Example 37

N-(4-{6-morpholin-4-yl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide (Compound 47)



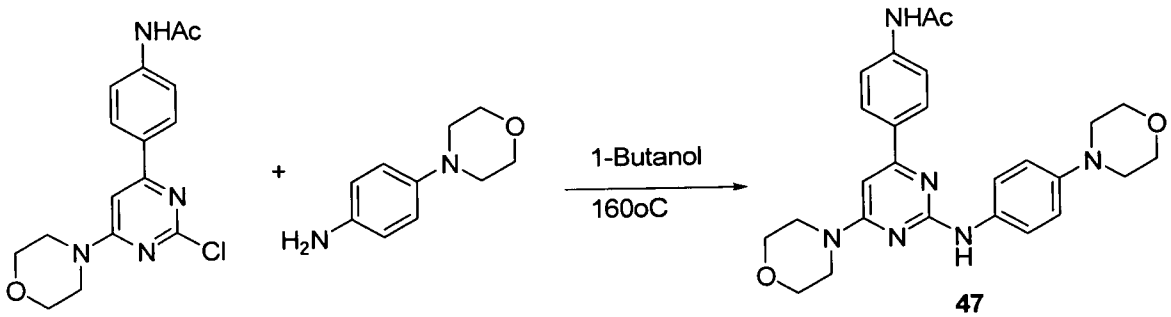
Intermediate L

[0815] The mixture of 2,4,6-trichloropyrimidine (1.72ml, 15mmol) 4-acetamidophenyl-boronic acid (1.79g, 10mmol) in DME (20ml) was added Et_3N (3.5ml, 25.0mmol), H_2O (2ml), and dichloro[1,1'-bis(diphenylphosphino)ferrocenepalladium (1.22g, 1.5mmol, 15%). The mixture was allowed to stir at reflux for 2hrs. After the mixture was cooled down to rt, the crude mixture was directly filtered on silica gel and eluted with EtOAc. The filtrate was concentrated in vacuo. Further purification was conducted by flash chromatography to afford intermediate L (1.91g, 68%) as a white solid. LCMS: m/z 282 $(M+H)^+$.



Intermediate M

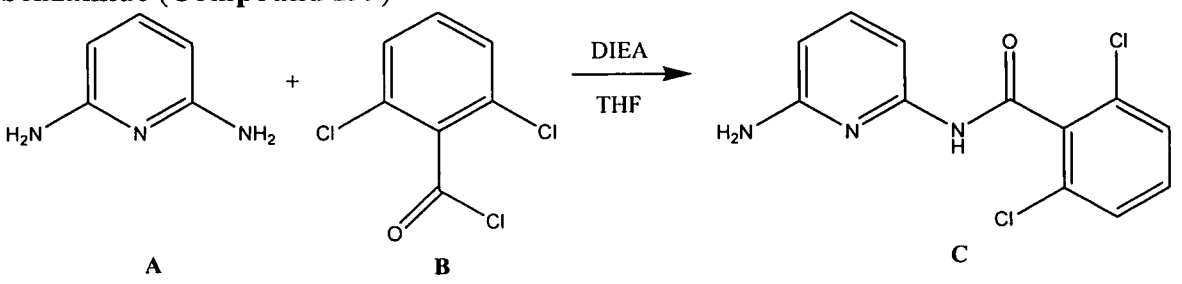
[0816] To a stirred suspension of pyrimidine (282mg, 1.0mmol) in 1-butanol (5ml) was added morpholine (96ml, 1.10mmol) and DIPEA (209µl, 1.2mmol). The mixture was heated at 120°C for 1hr, cooled down to rt, and concentrated in vacuo. The residue was purified by flash chromatography to afford intermediate M (176mg, 53%) as well as isomer (108mg, 32%). LCMS: m/z 333 $(M+H)^+$.



[0817] The mixture of chloropyrimidine (176mg, 0.53mmol) and 4-morpholinoaniline (104mg, 0.58mmol) in 1-butanol (5ml) was heated in the sealed tube at 160°C for 3hrs. The reaction mixture was cooled down to rt and the crude mixture was directly subjected on silica gel to afford product **47** (122mg, 49%) as a pale pink solid. LCMS: m/z 475 $(M+H)^+$. ^{1}H-NMR (400MHz, d_6-DMSO): 10.13 (s, 1H), 8.87 (s, 1H), 8.07 (d, 2H), 7.70-7,64 (m, 4H), 6.90 (d, 2H), 6.71 (d, 1H), 3.74-3.68 (m, 12H), 3.03 (t, 4H), 2.08 (s, 3H); MS (EI) $C_{26}H_{30}N_6O_3$: 475 (MH+).

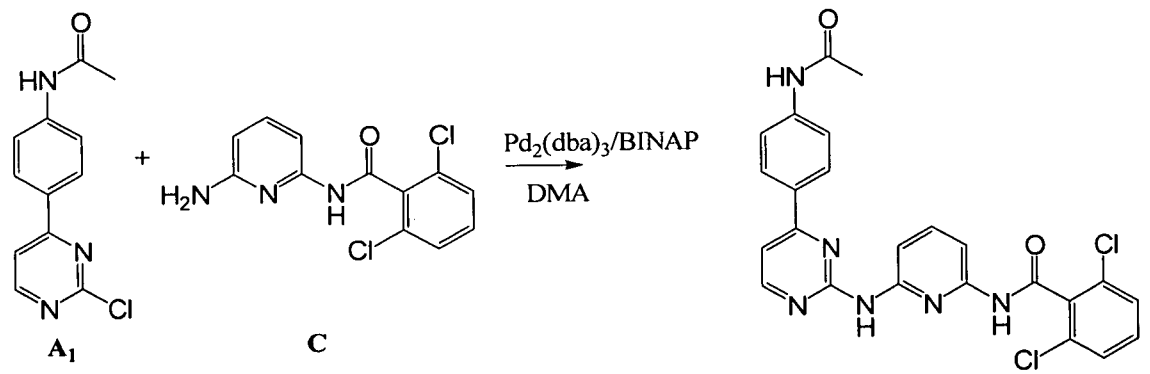
Example 38

N-[6-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)pyridin-2-yl]-2,6-dichlorobenzamide (Compound 299)



A B C

[0818] To a mixture of 2,6-diaminopyridine **A** (9.2 mmol, 1.0 g), and diisopropylethylamine (6.9mmol, 1.2ml) in 20ml of THF, was added 2,6-dichlorobenzoylchloride **B** (4.6mmol, 0.67ml) dropwise. The mixture was stirred at room temperature for 1 hour and LCMS indicated it was done (M+H: 283). THF was removed and replaced with ethyl acetate. The reaction mixture was then extracted with water, brine, and dried over sodium sulfate. The product, **C** , was isolated by removal of the solvent with a rotary evaporator and used without further purification. LCMS: 283 (M+H).



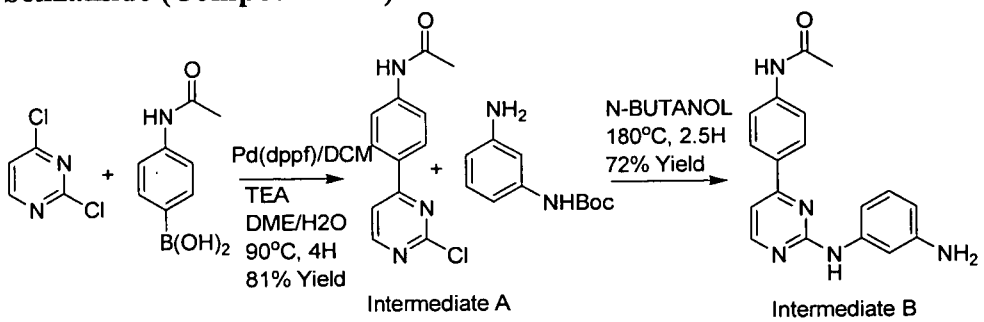
A_1 C 299

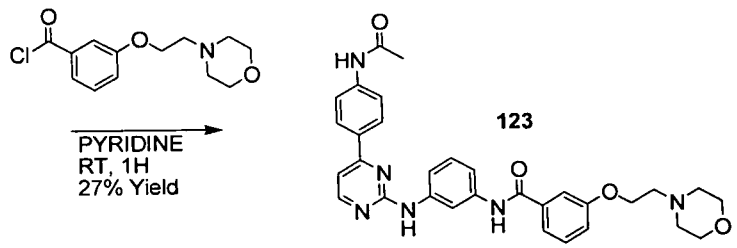
[0819] A seal tube was charged with intermediate A_1 (0.2g, 0.81 mmol), compound **C** from the previous step (0.56g, 2.0mmol), tris(dibenzylideneacetone)dipalladium(0) (0.15g, 0.16 mmol), racemic-2,2'-bis(diphenylphosphino)-1,1'binaphthyl (0.12g, 0.2mmol), cesium carbonate (0.4g, 1.22mmol). Dimethylacetamide (10ml) was added and the mixture was purged with N_2 for 5 minutes. The tube was sealed and the reaction mixture was stirred at 80^0C overnight. LCMS showed the reaction was done (M+H: 493). The reaction mixture was partitioned between ethyl acetate and water, the organic layer extracted with 10% LiCl solution, followed by brine, dried over Na_2SO_4, and then evaporated. The crude product 299 was then purified via prep HPLC.

^{1}H NMR (400 MHz, d_6-DMSO): 11.12 (s, 1H), 10.25 (s, 1H), 9.43 (s, 1H), 8.58 (d, 1H), 8.2-8.13 (m, 3H), 7.9 (t, 1H), 7.83 (d, 1H), 7.78 (d, 2H), 7.55 (d, 2H), 7.52-7.45 (m, 2H), 2.1 (s, 3H). MS (EI) for $C_{24}H_{18}Cl_2N_6O_2$: 493 (MH^+).

Example 39

N-(3-(4-(4-acetamidophenyl)pyrimidin-2-ylamino)phenyl)-3-(2-morpholinoethoxy)-benzamide (Compound 123)





[0820] A flask was charged with 2,4-dichloropyrimindine (22.7 g, 152.38 mmol), 4-acetoamido-phenylboronic acid (30.0 g, 167.62 mmol), dicholor[1,1'-bis(diphenylphosphino)-ferrocene-palladium (16.726 g, 22.86 mmol, 15 mol %), and triethylamine (53 mL, 380.95 mmol). Ethyleneglycoldimethylether (500 mL) and H_2O (20 mL) were added to the flask. The reaction mixture was stirred at 80 °C for 4 hours. The product, Intermediate **A**, was isolated by removal of the solvent with a rotary evaporator and purified using glass column chromatography and eluted with ethyl acetate to afford 30.5 g (123.14 mmol, 81% yield) of intermediate **A** as a yellow solid.

[0821] A seal tube was charged with intermediate **A** (400 mg, 1.62 mmol) and 3-(tert-butoxycarbonylamino)aniline (1.99g, 9.57 mmol). N-butanol (50 mL) was added to the seal tube and stirred at 180^{0}C. The reaction was stopped after 2.5h, monitored by LCMS. The reaction mixture was diluted with methanol and the solid precipitate was filtered to afford intermediate **B** as a yellow solid. The filter pad was washed with ethyl-acetate, 72% yield. Intermediate **B** was carried on to the next step without further purification.

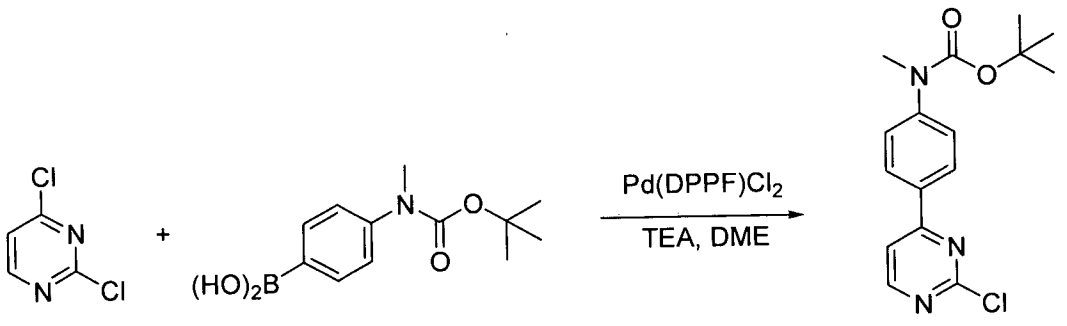
[0822] A flask was charged with intermediate **B** (159mg, 0.5 mmol), 3-(2-morpholinoethoxy)benzoyl chloride (169mg, 0.63 mmol), and Pyridine (8 mL). The reaction mixture was stirred at RT under nitrogen. Reaction was complete after 1hour. The final product **123** was purified using Preperative HPLC and trifluoroacetic acid buffer then free based with hydroxide resin in methanol. The filtrate was then concentrated, the yellow oil was then freezed and lyophilized.

1H-NMR (400MHz, d6-DMSO): 10.206(s, br, 2H), 9.665(s, br, 1H), 8.512(d, 1H), 8.502(s, 1H), 8.440(d, 2H), 7.755(d, 2H), 7.582(m, 2H), 7.483(m, 2H), 7.375(d, 1H), 7.287(m, 2H), 7.163(d, 1H), 4.188(m, 2H), 3.595 (m, 4H), 3.174(m, 4H), 2.732(m, 2H), 2.083(s, 3H).

MS(EI) for $C_{31}H_{32}N_6O_4$: 553 (MH+).

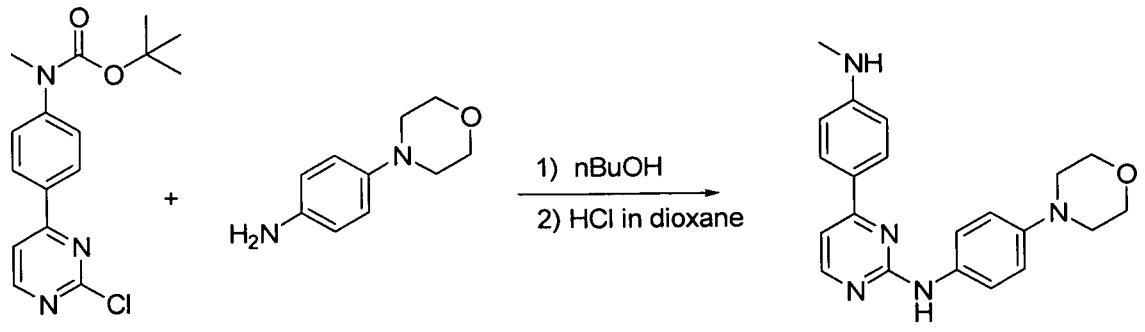
Example 40

4-[4-(methylamino)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine (Compound 124)



A_1 B C

[0823] A flask was charged with 2,4-dichloropyrimidine (810 mg, 5.5 mmol), 4-(tert-butoxycarbonyl(methyl)amino)phenylboronic acid **B** (4.93 g, 15 mmol), dicholoro[1,1'-bis(diphenylphosphino)ferrocenepalladium (590 mg, 0.81 mmol, 15 mol %), triethylamine (1.8 mL, 13 mmol), and water (2 mL). Ethylene glycol dimethyl ether (5.0 mL) was added to the flask and the mixture was purged with N_2. The reaction mixture was stirred under an N_2 atmosphere at 90 °C for 1 hour, after which time, it was cooled to ambient temperature and filtered. The product, **C**, was isolated by removal of the solvent with a rotary evaporator and used without further purification. LCMS: m/z 319 $(M+H)^+$.



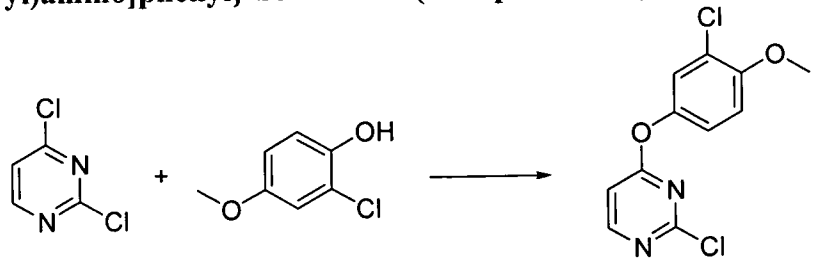
C 124

[0824] A flask containing a solution of **C** (1.9 g, 5.8 mmol) and 4-morphilinoaniline (1.5 g, 8.2 mmol) in 1-butanol (10 mL) was immersed in an oil bath at 180 °C for 4 h. The mixture was cooled to ambient temperature, concentrated, and the residue was dissolved in dichloromethane (10 mL) and 4N HCl in dioxane (10 mL). A portion of this crude product (200 mg) was purified by reverse phase HPLC to yield the product **124** (20 mg) in > 99% purity.

^{1}H-NMR (400MHz, d_6-DMSO): 9.92-9.99 ppm (bs, 1H), 8.20-8.29 (bs, 1H), 8.02 (d, 2H), 7.52-7.68 (bs, 2H), 7.33 (d, 1H), 7.04-7.17 (bs, 1H), 6.67 (d, 2H), 3.71-3.82 (bs, 4H), 3.14-3.24 (bs, 4H), 2.78 (s, 3H). MS (EI) $C_{21}H_{23}N_5O$: 362.1 (MH^+).

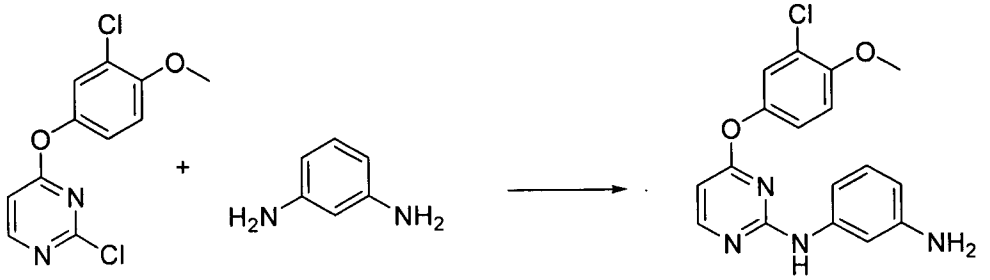
Example 41

2,6-dichloro-N-{3-[(4-{[3-chloro-4-(methyloxy)phenyl]oxy}pyrimidin-2-yl)amino]phenyl}-benzamide (Compound 304)



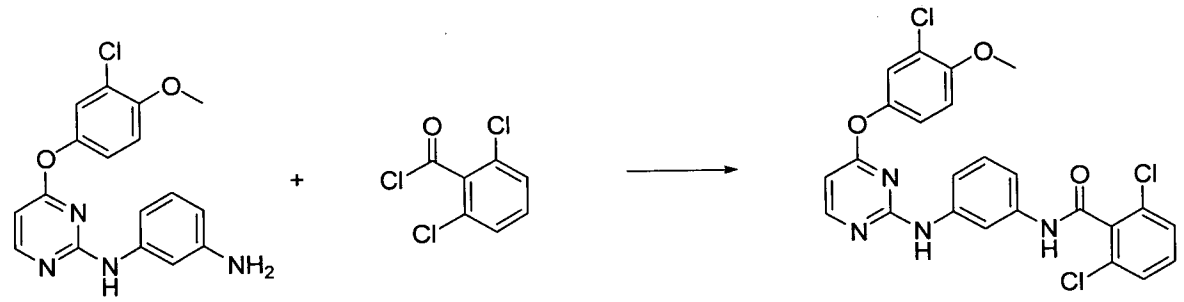
A B

[0825] A flask was charged with 2,4-dichloropyrimidine (500 mg, 3.4 mmol), 2-chloro-4-methoxyphenol (580 mg, 3.7 mmol), and diisopropylethylamine (1.2 mL, 6.9 mmol). Dimethylformamide (20 mL) was added to the flask and the mixture was stirred at 70 °C for 15 hours. The reaction mixture was diluted with water and the mixture was extracted with dichloromethane 2X and 5% LiCL 3X. The crude product, **B**, was isolated by removal of the solvent with a rotary evaporator and the resultant brown oil was used without further purification. LCMS: m/z 272 $(M+H)^+$.



B C

[0826] A flask containing a solution of intermediate **B** (910 mg, 3.4 mmol) and benzene-1,3-diamine (540 mg, 5.0 mmol) in nBuOH (5 mL) was immersed in an oil bath at 180 °C for 30 mins. The intermediate, **C**, was isolated by removal of the solvent with a rotary evaporator and used without further purification. LCMS: m/z 343 $(M+H)^+$.



C 304

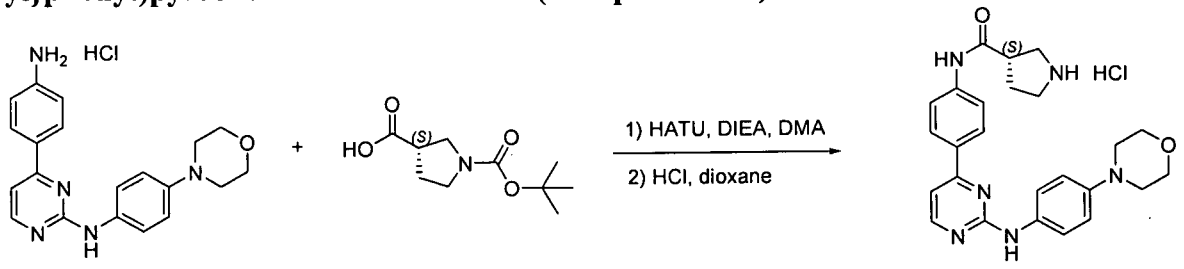
[0827] A flask was charged with intermediate **C** (1.1 g, 3.4 mmol), 2,6-dichlorobenzoylchloride (1.2 mL, 8.3 mmol), diispropylethylamine (1.8 mL, 10 mmol) and THF (50 mL). The reaction mixture was stirred at 60 °C for 15 hours. The reaction mixture was diluted with ethylacetate, extracted with 5% LiCl 3X, and the organic fraction was concentrated on a rotary evaporator. The crude product was purified by silica column chromatography (1:1 ethylacetate:hexanes as eluent) followed by reverse phase HPLC (TFA/ACN as eluent) to yield the product, **304** (24 mg, 1% yield).

^{1}H-NMR (400MHz, d6-DMSO): 10.7 (s, 1H), 9.65 (s, 1H), 8.36 (d, 1H), 7.77 (s, 1H), 7.58-7.47 (m, 3H), 7.36-7.28 (m, 3H), 7.23 (d, 1H), 7.04-6.98 (m, 2H), 6.47 (d, 1H), 3.83 (s, 3H).

MS (EI) $C_{24}H_{17}Cl_3N_4O_3$: 514.8 (MH-).

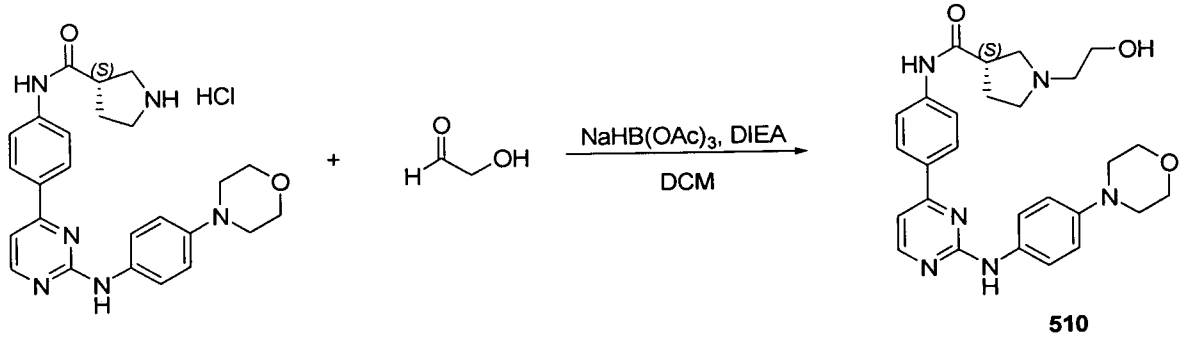
Example 42

(3S)-1-(2-hydroxyethyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyrrolidine-3-carboxamide (Compound 510)



249 (a) B C

[0828] To a solution of **249(a)** (300 mg, 0.78 mmol) in DMA (10 mL) was added a solution of (S)-1-(tert-butoxycarbonyl)pyrrolidine-3-carboxylic acid (350 g, 1.6 mmol) diisopropyl-ethylamine (0.5 mL, 2.7 mmol), and HATU (600 mg, 1.6 mmol) in DMA (10 mL) and the solution was stirred at room temperature 15 hours. The solution was diluted with ethyl acetate (100 mL), washed with 10% LiCl (2X) and brine. The resultant solution was dried over Na_2SO_4, filtered and concentrated to yield a residue that was purified by silica gel column chromatography (3:1 ethyl acetate/hexanes). The Boc intermediate was isolated as a solid (340 mg, 78% yield). LC/MS: m/z 545 $(M+H)^+$. A flask containing the Boc-intermediate was dissolved in 4N HCl in dioxane (10 mL) and dichloromethane (10 mL) and the mixture was stirred at room temperature for 15 hours. Intermediate **C** was isolated as a yellow solid after filtration and used without purification.



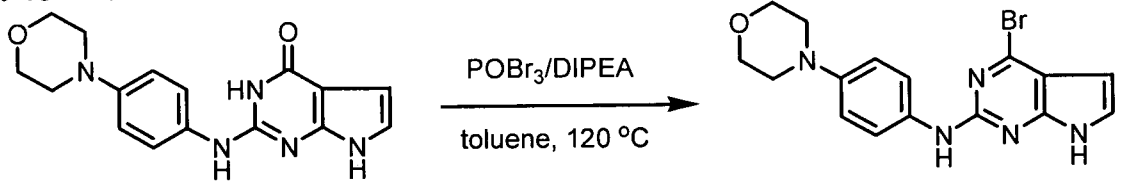
C 510

[0829] A flask was charged with intermediate C (450 mg, 0.78 mmol), 2-hydroxy-acetaldehyde (45 mg, 0.75 mmol), sodium triacetoxyborohydride (150 mg, 0.71 mmol), diisopropylethylamine (0.7 mL, 3.8 mmol) and dichloromethane (20 mL) and the mixture was stirred at room temperature for 4 hours. The reaction mixture was diluted with water and the solution was extracted with saturated $NaHCO_3$ (2X) and brine. The residue was purified by reverse phase HPLC (ammonium acetate/ACN as eluent) to afford the product **510** (120 mg, 31% yield).

^{1}H-NMR (400MHz, d6-DMSO): 10.2 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.75 (d, 2H), 7.67 (d, 2H), 7.28-7.27 (m, 1H), 6.93 (d, 2H), 4.47 (br 1H), 3.76-3.73 (m, 4H), 3.49 (t, 2H), 3.06-3.03 (m, 4H), 2.91 (t, 1H), 2.70-2.65 (m, 1H), 2.58-2.56 (m, 1H), 2.54-2.49 (m, 4H), 1.99 (t, 2H). MS (EI) $C_{27}H_{32}N_6O_3$: 489.2 (MH+).

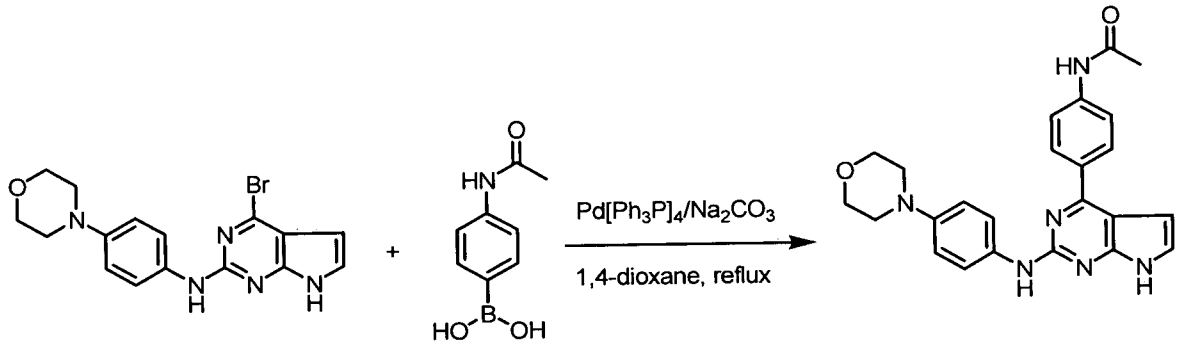
Example 43

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}phenyl)acetamide (Compound 329)



A B

[0830] A mixture of 2-[(4-morpholin-4-ylphenyl)amino]-3,7-dihydro-4H-pyrrolo[2,3-d]pyrimidin-4-one A (312 mg, 1 mmol), phosphorous oxybromide (717 mg, 2.5 mmol), and diisopropylethylamine (130 mg, 1 mmol) in anhydrous toluene (15 ml) was heated at reflux under N_2 overnight. The mixture was cooled down to room temperature, and the solid was filtered, washed with sat. $NaHCO_3$, water, and dried over $MgSO_4$. The solvent was removed in vacuo to give the product 4-bromo-N-(4-morpholin-4-ylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-2-amine B (284 mg, 76%) as a black solid. This was clean and used as such without further purification.



B C 329

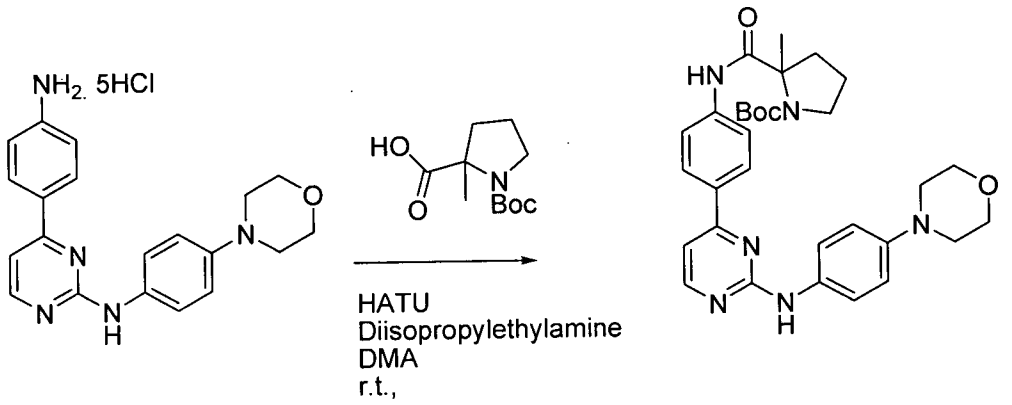
[0831] A mixture of 4-bromo-N-(4-morpholin-4-ylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-2-amine B (284 mg, 0.76 mmol), 4-acetoamidophenylboronic acid C (340 mg, 2.5 eq), tetrakis(triphenyl-phosphine)palladium(0) (120 mg, 0.1 mmol), and 1M Na_2CO_3 (1ml, 1 mmol) in 1,4-dioxane (15 ml) was heated at reflux overnight. The mixture was cooled, extracted with 3N HCl. The aqueous layer was washed with ethylacetate, and then basified with 6N NaOH. The solid was filtered, and the crude product was purified by

preparative HPLC to give the product N-(4-{2-[(4-morpholin-4-ylphenyl)amino]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}phenyl)acetamide D (0.8 mg, 0.25%) as a yellow solid. ^{1}H NMR (400 MHz, CD_3OD): 8.10 (d, 2H), 7.75 (d, 2H), 7.68 (d, 2H), 7.12 (d, 1H), 6.98 (d, 2H), 6.70 (d, 1H), 3.85 (t, 4H), 3.09 (t, 4H), 2.17 (s, 3H). MS (EI) for $C_{24}H_{24}N_6O_2$: 429 (MH^+).

Example 44

2-Methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)prolinamide (Compound 367)

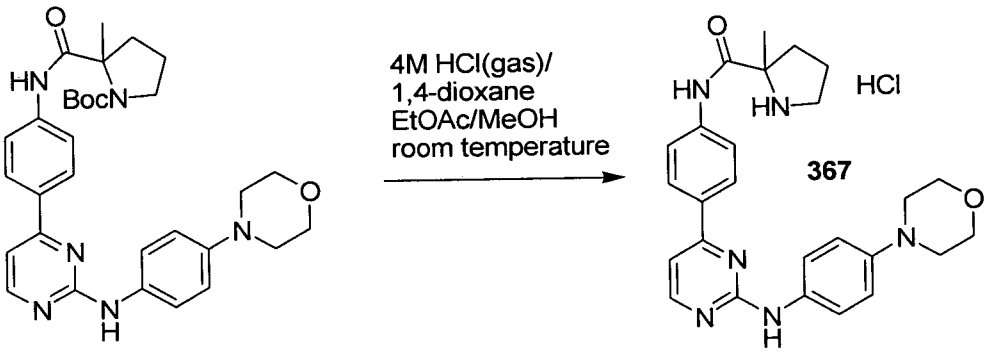
Preparation of *tert*-butyl 2-methyl-2-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenylcarbamoyl)pyrrolidine-1-carboxylate



[0832] An oven dried 50 ml round bottomed flask fitted with a Teflon stirrer and gas inlet was flushed with dry nitrogen and allowed to cool to room temperature. The flask was charged with 4-(4-aminophenyl)-N-(4-morpholinophenyl)pyrimidin-2-amine pentahydrochloride (1 equiv., 0.52 g, 0.9631 mmoles) and anhydrous dimethylacetamide (15 ml). The mixture was stirred for 10 minutes to allow for the complete dissolution of the amine. Diisoproplyethylamine (10 equiv., 1.24 g, 1.67 ml, 9.631 mmoles) was added in one lot and the reaction mixture was stirred for 5 minutes. 1-(tert-Butoxycarbonyl)-2-methylpyrrolidine-2-carboxylic acid (4 equiv., 3.852 mmoles, 0.883 g, purchased from Fluka-Sigma Aldrich) was added to the reaction mixture in one lot, followed by 2-(7-aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU, 4 equiv., 3.852 mmoles, 1.464 g, purchased from Oakland Products). The reaction mixture was stirred at room temperature and the progress of the reaction was monitored by LC/MS. After 72 hours, the reaction mixture was quenched with ethyl acetate (20ml), and transferred to separatory funnel. The reaction flask was further rinsed with ethyl acetate (20 ml), transferred to the separatory funnel, shaken and the layered separated off. The aqueous layer was further

washed with ethyl acetate (3 x 50 ml). The combined ethyl acetate solutions were washed with cold water (2 x 50 ml) and saturated sodium chloride solution (2 x 50 ml). The ethyl acetate solution was dried over anhydrous sodium sulfate, filtered and evaporated under reduced pressure to give orange oil. The resulting crude material was purified by silica phase flash chromatography (45 mm x 250 mm) using 3:1 ethyl acetate -hexane to give 0.147 g of *tert*-butyl 2-methyl-2-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenylcarbamoyl)-pyrrolidine-1-carboxylate as a white solid (27% yield). 1H NMR (400 MHz, d6-DMSO) 10.01 (br s, 1H), 9.45 (br s 1H), 8.19 (d, 1H), 7.70 (d, 2H), 7.46 (d, 2H), 6.74 (d, 1H), 6.66 (d, 2H), 6.28 (d, 2H), 3.67 (m, 4H), 3.40 (m, 1H), 3.30 (m, 1H), 2.29 (m, 4H), 1.76 (m, 1H), 1.64 (m, 1H), 1.58 (s, 3H), 1.54 (m, 1H), 1.40 (s, 9H). MS (EI) for C31H38N6O4: 559 (M+).

Preparation of 2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)prolinamide

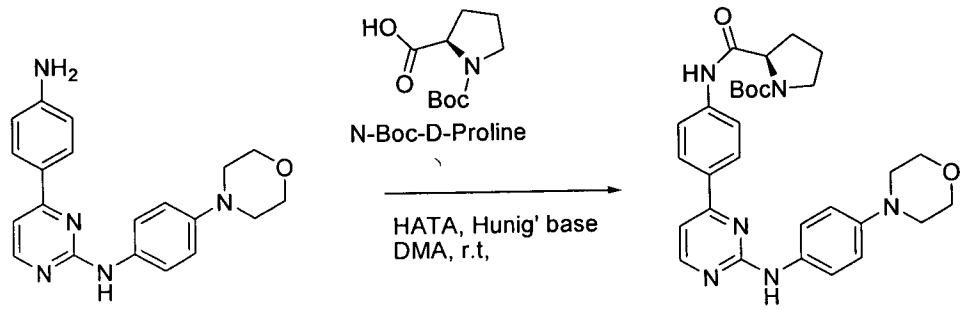


[0833] *tert*-Butyl 2-methyl-2-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl-carbamoyl)pyrrolidine-1-carboxylate (0.140 g, 0.250 mmoles), was dissolved in an ethyl acetate (5 ml) and methanol (1 ml) mixture. 4 M hydrogen chloride in 1,4-dioxane (0.625 ml, 2.5 mmoles, 10 equivalents, purchased from Sigma-Aldrich) was then added in a drop wise fashion over 5-10 minutes. Upon completion of addition, the reaction mixture was stirred at room temperature, and the progress of the reaction monitored by LC/MS. After 16 hours, additional 4M hydrogen chloride in 1,4-dioxane (0.312 ml, 1.25 mmoles, 5 equivalents) was added. After a total of 48 hours the reaction was complete and the resulting slurry was filtered off. The reaction flask was rinsed with ethyl acetate to ensure complete transfer of product. The resulting solid was washed with ethyl acetate (3 x 10 ml) and diethyl ether (2 x 25 ml) and dried under reduced pressure to give of 0.061 mg 2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)prolinamide **367** as its hydrochloride salt (53% yield).

1H NMR (400 MHz, d6-DMSO): 10.88 (s, 1H), 9.79 (br s, 1H), 8.47 (d, 1H), 8.12 (d, 1H), 8.10 (d, 1H), 7.80 (br d, 2H), 7.75 (d, 2H), 7.37 (d, 2H), 5.26 (br s, 3H), 3.72 (br s, 4H), 3.27 (br s, 4H), 2.80 (m , 1H), 2.70 (m, 1H), 2.01 (m, 1H), 1.76 (m, 1H), 1,64 (m, 1H), 1.54 (m, 1H), 1.38 (s, 3H). MS (EI) for $C_{26}H_{30}N_6O_2$: 459 (MH+).

Example 45

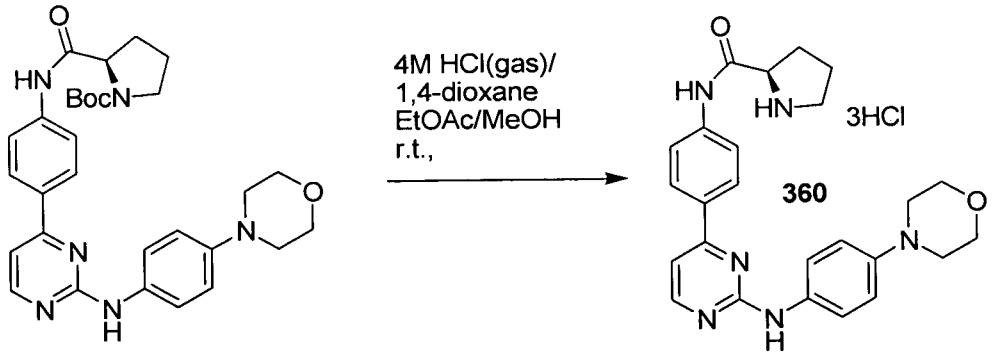
2-Methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]-pyrimidin-4-yl}phenyl)prolinamide (Compound 360)



[0834] An oven dried 50 ml round bottomed flask fitted with a Teflon stirrer and gas inlet was flushed with dry nitrogen and allowed to cool to room temperature. The flask was charged with 4-(4-aminophenyl)-N-(4-morpholinophenyl)pyrimidin-2-amine pentahydrochloride (1 equiv., 0.4 g, 0.756 mmoles) and anhydrous dimethylacetamide (15 ml). The mixture was stirred for 10 minutes to allow for the complete dissolution of the amine. Diisoproplyethylamine (10 equiv., 0.977 g, 1.31 ml, 7.561 mmoles) was added in one lot and the reaction mixture was stirred for 5 minutes. N-Boc-D-proline (4 equiv., 3.204 mmoles, 0.65 g, purchased from Fluka-Sigma Aldrich) was added to the reaction mixture in one lot, followed by 2-(7-aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU, 4 equiv., 3.024 mmoles, 1.149 g, purchased from Oakland Products). The reaction mixture was stirred at room temperature and the progress of the reaction was monitored by LC/MS. After 72 hours, the reaction mixture was quenched with ethyl acetate (20ml), and transferred to separatory funnel. The reaction flask was further rinsed with ethyl acetate (20 ml), transferred to the separatory funnel, shaken and the layer separated off. The aqueous layer was further washed with ethyl acetate (3 x 50 ml). The combined ethyl acetate solutions were washed with chloride solution (2 x 50 ml). The ethyl acetate solution was dried over anhydrous sodium sulfate, filtered and evaporated under reduced pressure to give an orange oil. The resulting crude material was purified by silica phase flash chromatography (45 mm x 250 mm) using 3:1 ethyl acetate -hexane to give 0.39

g of 1,1-dimethylethyl (2R)-2-{[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]carbonyl}pyrrolidine-1-carboxylate as a white solid (94 % yield).

1H NMR (400 MHz, d6-DMSO): 10.26 (br s ,1H), 9.38 (br s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.78 (d, 2H)< 7.68 (d, 2H), 7.28 (d, 1H), 6.94 (d, 2H), 4.22 (m, 1H), 3.74 (m, 4H), 3.43 (m, 1H), 3.34 (m, 1H), 3.04 (m, 4H), 2.20 (m, 1H), 1.90 (m, 1H), 1.81 (m, 1H)< 1.40 (s, 3H), 1.27 (s, 6H). MS (EI) for $C_{30}H_{36}N_6O_4$: 545 (MH+).

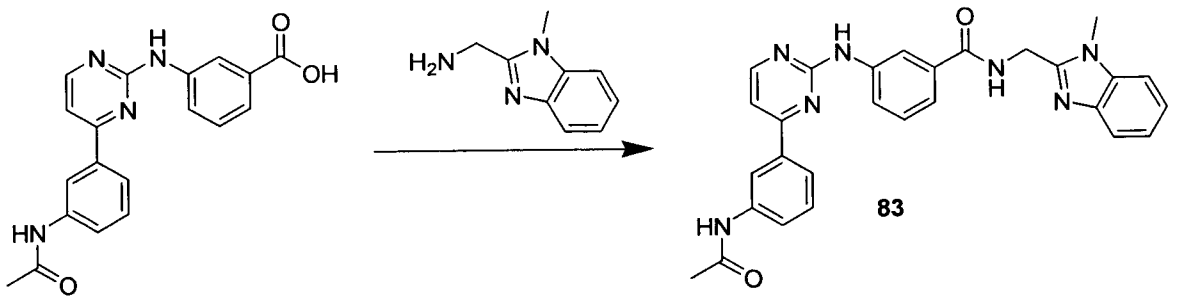


[0835] 1,1-Dimethylethyl (2R)-2-{[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)amino]carbonyl}pyrrolidine-1-carboxylate (0.38 g, 0.698 mmoles), was dissolved in an ethyl acetate (10 ml) and methanol (2 ml) mixture. 4 M hydrogen chloride in 1,4-dioxane (1.75 ml, 6.98 mmoles, 10 equivalents, purchased from Sigma-Aldrich) was then added in a drop wise fashion over 5-10 minutes. Upon completion of addition, the reaction mixture was stirred at room temperature, and the progress of the reaction monitored by LC/MS. After 16 hours, additional 4M hydrogen chloride in 1,4-dioxane (0.87, 1.25 mmoles, 5 equivalents) was added. After a total of 48 hours the reaction was complete and the resulting slurry was filtered off. The reaction flask was rinsed with ethyl acetate to ensure complete transfer of product. The resulting solid was washed with ethyl acetate (3 x 10 ml), followed by diethyl ether (3 x 25 ml) and dried under reduced pressure to give of 0.264 mg 2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]-pyrimidin-4-yl}phenyl)prolinamide (68 % yield).

1H NMR (400 MHz, d6-DMSO): 11.43 (br s, 1H), 10.07 (br s, 2H), 8.73 (d, 1H), 8.57 (d, 1H), 8.21 (d, 2H), 7.91 (d, 2H), 7.98 (d, 2H), 7.71 (br s, 2H), 7.48 (d, 1H), 4.48 (m, 1H), 4.08 (s, 4H), 3.74 (m, 4H), 3.42 (m, 1H), 3.36 (m, 1H), 3.04 (m, 4H), 2.22 (m 1H), 1.90 (m, 2H), 1.82 (m, 2H). MS (EI) for $C_{25}H_{28}N_6O_2$: 445 (MH+).

Example 46

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(1-methyl-1H-benzimidazol-2-yl)methyl]benzamide (Compound 83)



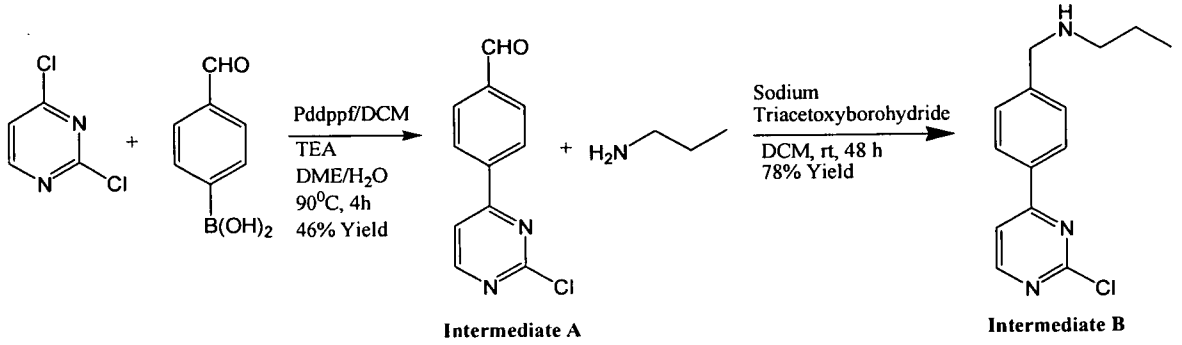
[0836] 7.9 grams (11.04 mmol, 1.9 eq) of PL-TFP Resin (source: *Polymer Laboratories*) was weighed into a pressure tube. 60 ml of DCM was added. 2 g (5.74 mmol) of 3-(4-(3-acetamidophenyl)pyrimidin-2-ylamino)benzoic acid was dissolved in 15 ml of DMF and After 10 min, this solution was added to the pressure tube. Dimethylaminopyridine (4.41 mmol, .6 eq, source: *Acros*) was added to the pressure tube as a solid, followed by 1,3-diisopropylcarbodiimide (33.08 mmol, 4.5 eq, source: *Acros*). The pressure tube was sealed and the reaction was placed on a vertical shaker overnight. The resin was filtered, and then washed 3 times with DMF, followed by three times with THF, followed by three times with DCM. The resin was then dried overnight by vaccum.

[0837] 300 mg of resin prepared above (loading = 0.6 mmol/g, .18 mmol) was added to a 1 dram vial. 2 ml of DMA were added. 1 ml of (1-methyl-1H-benzo[d]imidazol-2-yl)methanamine (0.12 mmol, 0.67 eq) dissolved in DMA was added to the vial. The reaction was stirred overnight at room temperature. The reaction was filtered and rinsed twice with 4 ml of MeOH. The solution was further purified by HPLC to yield (3-(4-(4-acetamidophenyl)pyrimidin-2-ylamino)-N-((1-methyl-1H-benzo[d]imidazol-2-yl)methyl) benzamide **83** (10.2 mg, 17%).

^{1}H-NMR (400MHz, d_6-DMSO): 10.23 (s, 1H), 9.80 (s, 1H), 9.01 (t, 1H), 8.52 (t, 2H), 8.17-8.19 (m, 2H), 7.91-7.93 (m, 1H), 7.75 (d, 2H), 7.50-7.59 (m, 3H), 7.39-7.43 (m, 2H), 7.16-7.26 (m, 2H), 4.80 (d, 2H), 3.86 (s, 3H), 2.10 (s, 3H). MS (EI) for $C_{28}H_{25}N_7O_2$: 492.4 (MH^+).

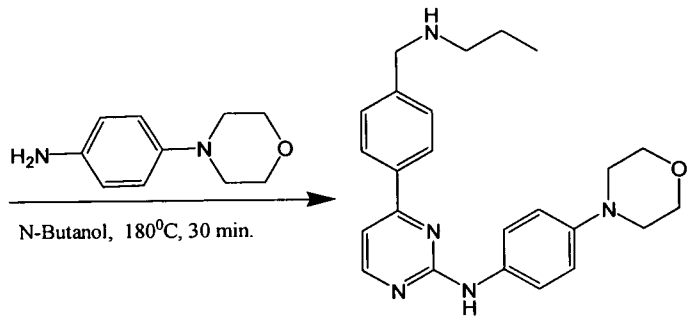
Example 47

N-(4-morpholin-4-ylphenyl)-4-{4-[(propylamino)methyl]phenyl} pyrimidin-2-amine (Compound 283)



Intermediate A

Intermediate B



283

[0838] A flask was charged with 2,4-dichloropyrimindine (1.5 g, 10 mmol), 4-formylphenyl boronic acid (1.65 g, 11 mmol), dicholor[1,1'-bis(diphenylphosphino)-ferrocenepalladium (731 mg, 1 mmol, 10 mol %), and triethylamine (2.6 mL, 15 mmol). Ethyleneglycoldimethylether (50 mL) and H_2O (2mL) was added to the flask. The reaction mixture was stirred at 80 °C for 4 hours. The product, Intermediate **A**, was isolated by removal of the solvent with a rotary evaporator and purified using glass column chromatography and eluted with ethyl acetate to afford 1.0 g (4.58 mmol, 46% yield) of intermediate **A** as a yellow solid.

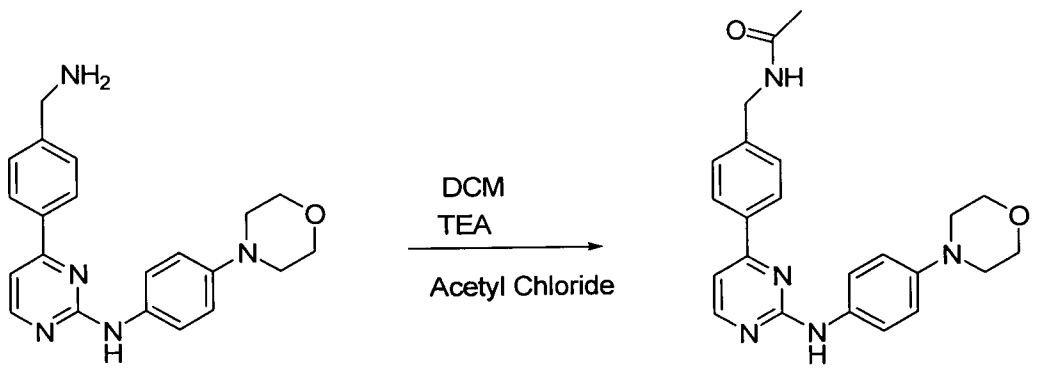
[0839] A flask was charged with intermediate **A** (150 mg, 0.668 mmol), sodium triacetoxy-borohydride (220 mg, 1.032 mmol), propylamine (63 µl, 0.756 mmol). Dichloromethane (50 mL) was added to the flask and the reaction mixture was stirred at room temperature for 48 h. The reaction was quenched with 2 N NaOH and extracted with ethyl acetate, washed with brine, dried over sodium sultate, and filtered. The solvent was removed using the rotary evaporator to afford intermediate **B** as a yellow solid (140 mg, 0.536 mmol, 80% Yield). Intermediate **B** was carried on without further purification.

[0840] A seal tube was charged with intermediate **B** (140 mg, 0.536 mmol) and 4-morpholinoaniline (95 mg, 0.536 mmol). N-butanol (15 mL) was added to the seal tube and stirred at 180^{0}C. The reaction was done in 1h according to LCMS to afford 283 as a yellow solid. **Compound 283** was purified using preperative HPLC and TFA buffer. **Compound 283** was free-based, converted to HCl salt, and lyophilized (20mg, 0.455 mmol).

^{1}H NMR (400 MHz, DMSO): 9.93 (br s, 1H), 9.396 (br s, 2H), 8.607 (d, 1H), 8.233 (d, 2H), 7.905 (d, 2H), 7.767 (d, 2H), 7.571-7.494 (m, 3H), 4.226 (br s, 2H), 3.998 (br s, 4H), 3.436 (br s, 4H), 2.865 (m, 2H), 1.708 (m, 2H), 0.914 (t, 3H). MS (EI) for $C_{24}H_{29}N_5O$: 404.4 (MH^+).

Example 48

N-[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)methyl]acetamide (Compound 282)



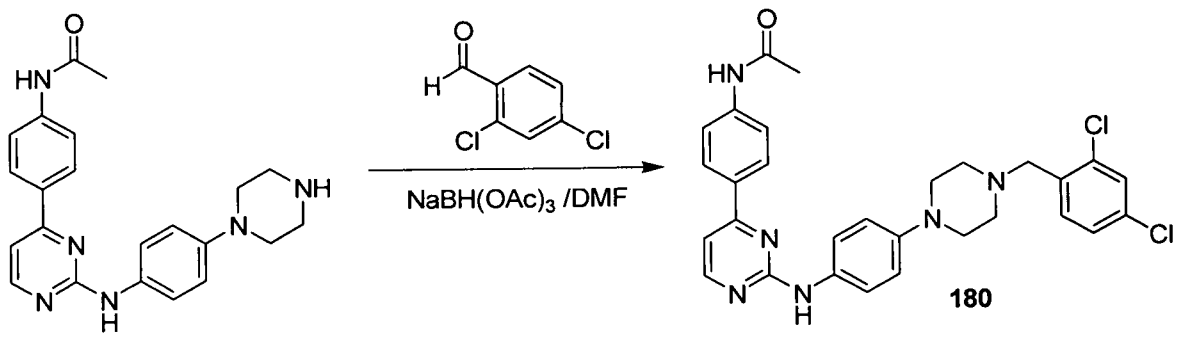
Compound A **282**

[0841] In a 20 ml round bottomed flask, 36 mg (1 mmol) of compound A was dissolved in 5 ml of dichloromethane and 0.5 ml of triethylamine was added. It was cooled in ice bath and 10 mg (1.2 mmol) of acetyl chloride was added and stirred for 30 min. Compound **282** precipitated out and purified in a Waters prep column. Yield 40 mg (90%).

^{1}H NMR (400MHz, CD_3CN):11.20-11.22(b,1H), 8.40 (d, 2H), 8.05(d,2H), 7.80(d,2H), 7.50 (d, 2H), 7.45 (s, 1H), 7.20 (d, 1H), 7.05-7.10 (b, 1H), 4.40-4.44 (b, 2H), 3.90 (t, 4H), 3.40 (t, 4H),2.01(s,3H); MS (EI) for $C_{23}H_{25}N_5O_2$: 404 (MH^+).

Example 49

N-(4-{2-[(4-{4-[(2,4-dichlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide (Compound 180)



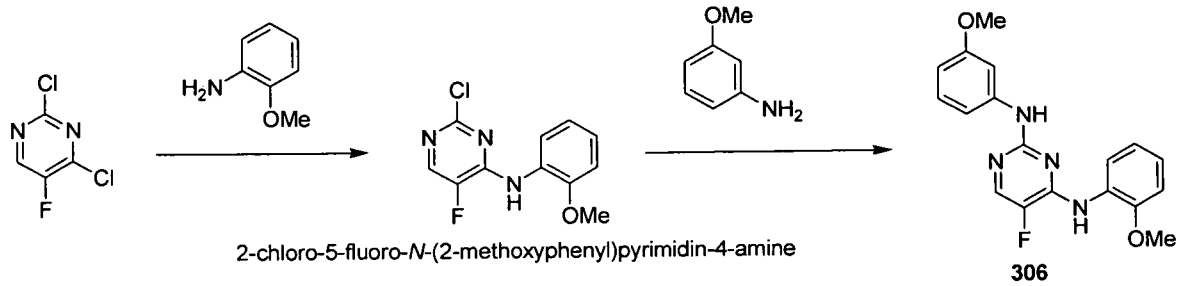
180

[0842] To a 1 ml vial was added N-(4-{2-[(4-piperazin-1-ylphenyl)amino]pyrimidin-4-yl}-phenyl)acetamide (38.85 mg, 0.1 mmol), 2,4-dichlorobenzaldehyde (350 mg, 2.0 mmol, 20 eq, source: Aldrich) and 1 ml of DMF. To this mixture was added sodium triacetoxyborohydride (106 mg, 0.5 mmol, 5 eq). The mixture was stirred over night at room temperature. Upon completion of the reaction as determined by LC/MS, 0.1 ml of 2M HCl was added. The residue was purified via reverse phase HPLC (ammonium acetate/ACN) to yield N-(4-{2-[(4-{4-[(2,4-dichlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide **180** (20.2 mg, 37 %) .

^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.80 (s, 1H), 9.10 (t, 1H), 8.53 (d, 2H), 8.18 (d, 2H), 7.94-7.91 (m, 1H), 7.75 (d, 1H), 7.69-7.57 (m, 4H), 7.48-7.39 (m, 2H), 4.58 (d, 6H), 2.50 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{28}Cl_2N_6O$: 548.5 (MH+).

Example 50

5-fluoro-N^4-[2-(methyloxy)phenyl]-N^2-[3-(methyloxy)phenyl] pyrimidine-2,4-diamine (Compound 306)



2-chloro-5-fluoro-*N*-(2-methoxyphenyl)pyrimidin-4-amine

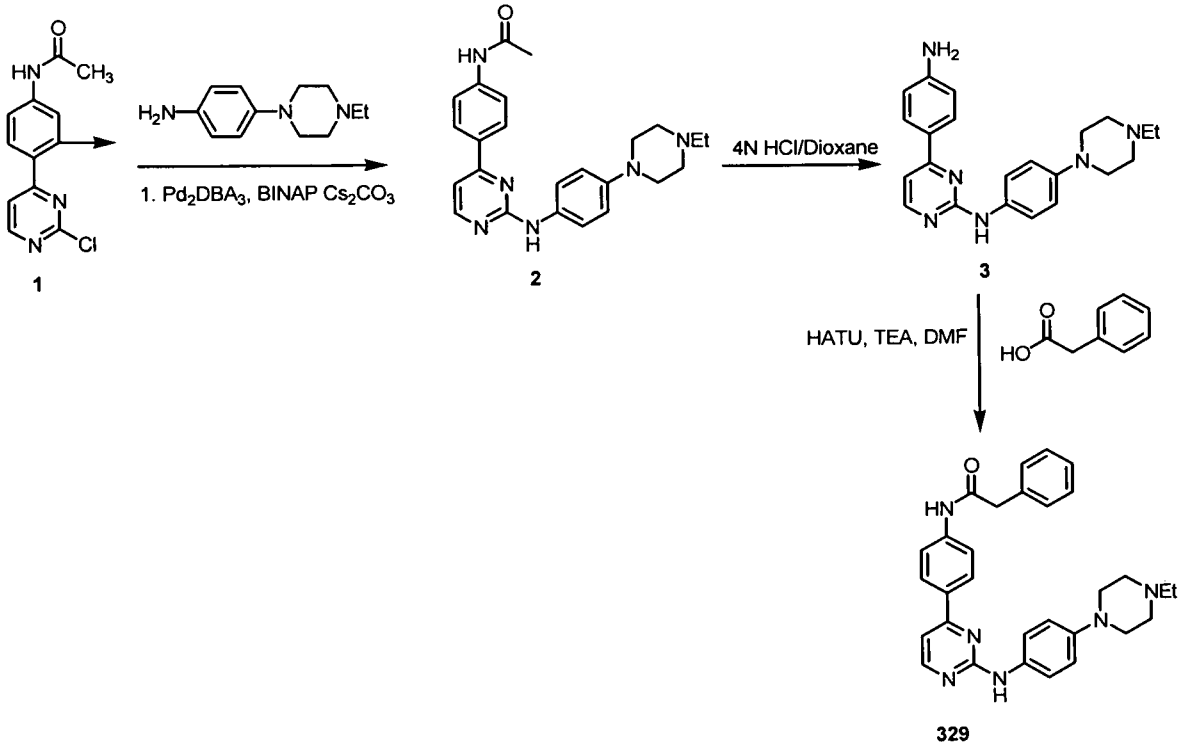
306

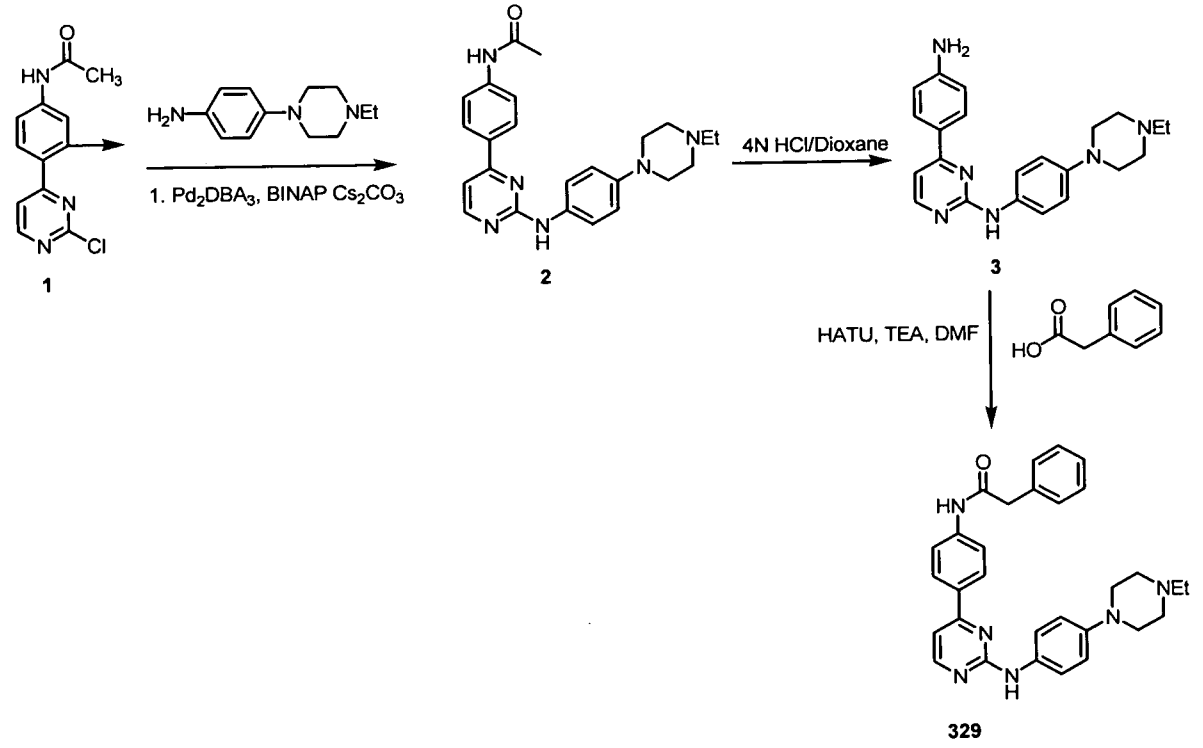
[0843] A round-bottomed flask was charged with 2,4-dichloro-5-fluoropyrimidine (0.84 g, 5 mmol), 2-methoxylaniline (0.61 g, 5 mmol) and dioxane (5 mL). The reaction mixture was heated at 85 °C overnight. The reaction was cooled down and diluted with acetonitrile/water, stirred for 30 min. and filtered. The collected solid was re-suspended in acetonitrile/water, stirred and filtered to give a 2-chloro-5-fluoro-N-(2-methoxyphenyl)pyrimidin-4-amine (0.9 g, 70% yield). To a seal tube was added 2-chloro-5-fluoro-N-(2-methoxyphenyl)pyrimidin-4-amine (254 mg), 3-methoxyaniline (500 mg, 4 eq.) and dioxane (5 mL). The mixture was heated to 130 °C overnight. The reaction mixture was cooled and partitioned between EtOAc and water. The organic layer was concentrated; the residue was triturated with a 1:1 mixture of dichloromethane and acetonitrile, then filtered to give the title product as a white solid (150 mg).

^{1}H NMR (400 MHz, d6-DMSO): 9.16 (s, 1H), 8.37 (s, 1H), 8.09 (s, 1H), 7.88 (d, 1H), 7.26 (t, 2H), 7.22-7.16 (m, 2H), 7.12-7.08 (m, 1H), 7.08-6.93 (m, 2H), 3.81 (s, 3H), 3.62 (s, 3H). MS (EI) for $C_{18}H_{17}FN_4O_2$: 341 (MH+).

Example 51

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}phenyl)-acetamide (Compound 329)

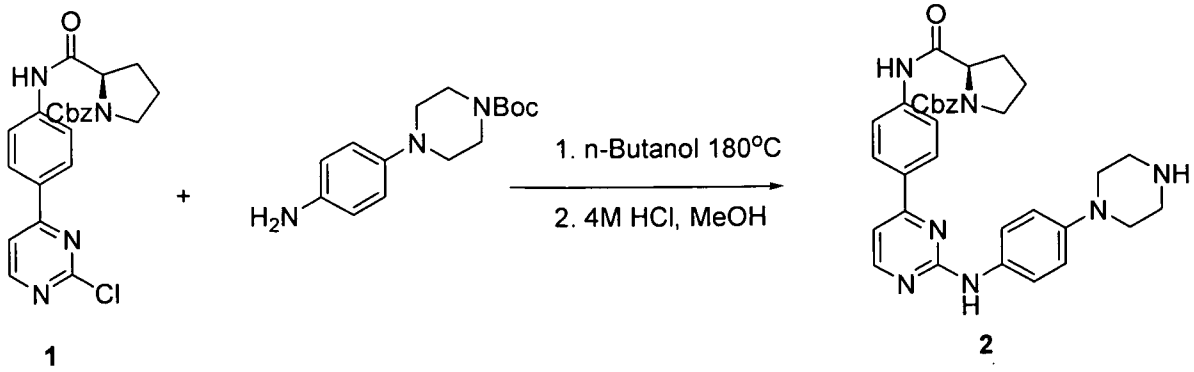




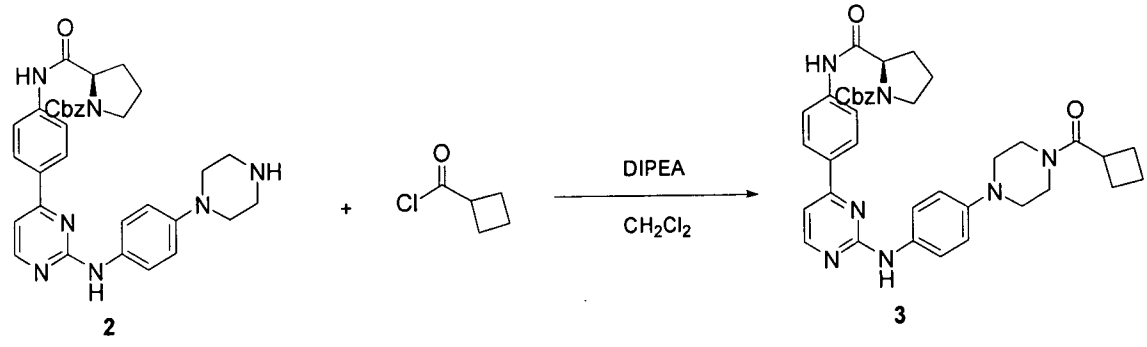
[0844] To a flask containing a solution of **1** (0.25g, 1 mmol), 4-(4-ethylpiperazin-1-yl)aniline (0.23g, 1.1 mmol), cesium carbonate (0.5g, 1.5 mmol), *racemic*-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (95mg, 0.15 mmol) in N,N-dimethylacetamide (5mL) purged with N_2 was added tris(dibenzylideneacetone)dipalladium(0) (0.14g, 0.15 mmol). This reaction was heated to 90 °C for 16 h under N_2. At this time the reaction was concentrated and the residue was purified via silica gel column chromatography. The column was eluted with ethyl acetate to remove the impurities and then with 85:10:5 (ethyl acetate/methanol/7M ammonia in methanol) to elute the desired product. The solid obtained was sonicated first in acetone (5mL) and then in ether (10mL) to yield intermediate **2** (0,23g, 48% yield) as a yellow solid. LCMS: m/z 417 (MH+). To a flask containing **2** (0.23g, 0.45 mmol) was added 4N HCl in dioxane (5mL) and the solution was heated at 50 °C for 4 h. To the cooled solution was added a 2N aqueous solution of sodium hydroxide (10mL) and the resulting precipitate was filtered and dried to yield **3** (0.2g, 99% yield) as a yellow solid. LCMS: m/z 375 $(M+H)^+$. To a flask with **3** (0.3g, 0.8 mmol), phenylacetic acid (0.125mL, 1 mmol), triethylamine (0.97mL, 7 mmol), and DMF (5mL) was added O-(7-azabenzotriazole-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HATU) (0.46g, 1.2 mmol). The reaction mixture was stirred at ambient temperature for 1 h then diluted with 5% aqueous solution of lithium chloride (100mL) and extracted with ethyl acetate (3 x 50mL). The combined organic layers were washed with an aqueous 5% sodium bicarbonate solution, a saturated aqueous solution of sodium chloride, dried over anhydrous sodium sulfate, filtered and concentrated. The residue obtained was purified by silica gel column chromatography (98:2 ethylacetate/methanol) to provide Compound **329** (0.25g, 63% yield) as an off-white solid.

Example 52

N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide (Compound 662)

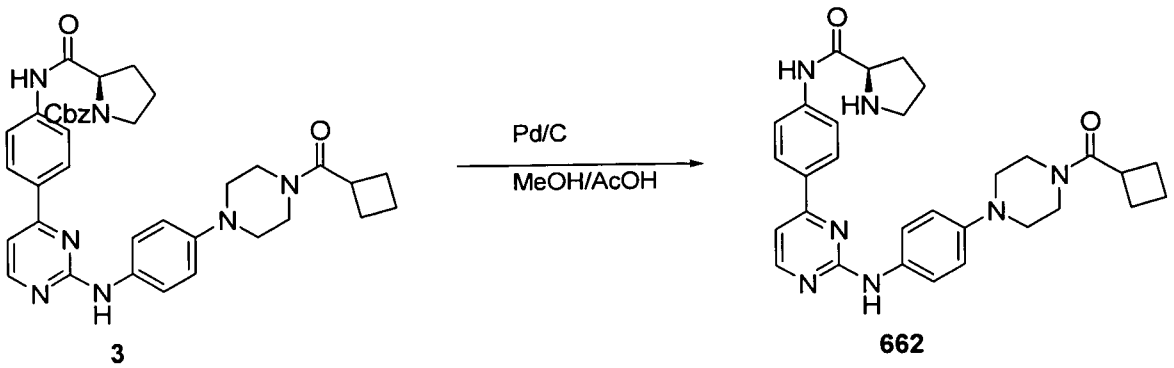


[0845] A solution of chloropyrimidine (**1**) (0.28g, 0.64 mmol) and tert-butyl 4-(4-aminophenyl)piperazine-1-carboxylate (0.18g, 0.6 mmol) in *n*-butanol (5ml) was heated at 180 °C in a sealed tube for 7 h. The reaction mixture was concentrated, the residue dissolved in methanol (5ml) and treated with HCl (3ml, 4M in dioxane) for 1 hour at room temperature. After concentration, the residue was dissolved in H_2O (200mL) and the pH adjusted to ca. 8-9 with 1N NaOH. The aqueous layer was extracted with CH_2Cl_2 (2 x 10ml) and the combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated. The residue was purified by silica gel column chromatography (85:15 ethyl acetate/methanol) to afford **2** (0.26g, 69%). $C_{33}H_{35}N_7O_3$: 578 (MH^+).



[0846] To a solution of **2** (0.41g, 0.7 mmol) and DIPEA (0.31ml, 1.75 mmol) in CH_2Cl_2 (7ml) was added cyclobutylcarbonyl chloride (0.80ml, 0.7 mmol) at room temperature. After 10 min, the reaction mixture was diluted with H_2O (10mL) and CH_2Cl_2 (10mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 5mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue obtained was purified by

silica gel column chromatography (98:2 ethyl acetate/methanol) to afford **3** (0.31g, 68%) as a white powder. $C_{38}H_{41}N_7O_4$: 660 (MH^+).

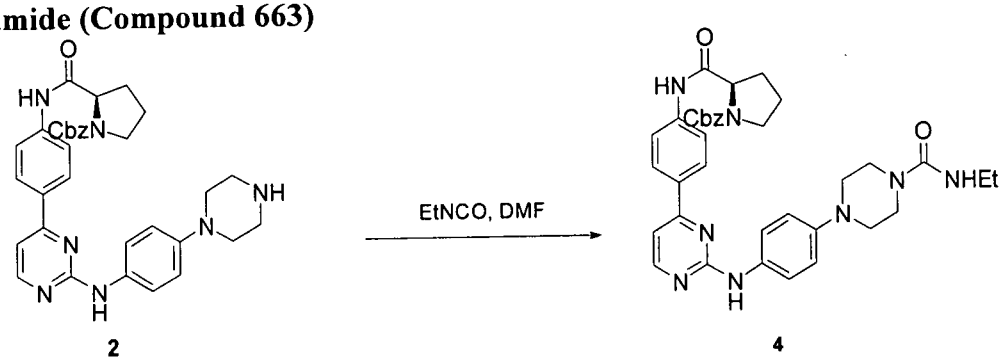


3 **662**

[0847] The mixture of **3** (0.31g, 0.47 mmol) and Pd/C (0.94g) AcOH (1mL) and MeOH (5mL) was stirred at room temperature for 24 h under a H_2 balloon. The palladium was filtered through celite and the filtrate was concentrated. The residue was purified by silica gel column chromatography (90:10 ethyl acetate/methanol) to afford product which was then washed with acetonitrile several times to afford Compound **662** (0.14g, 59% yield).

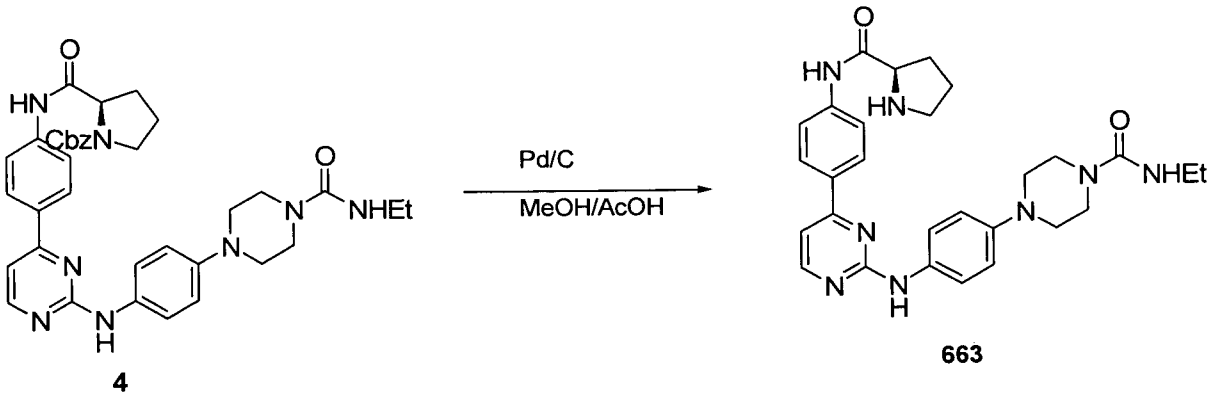
Example 53

N-ethyl-4-[4-({4-[4-(D-prolylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperazine-1-carboxamide (Compound 663)



2 **4**

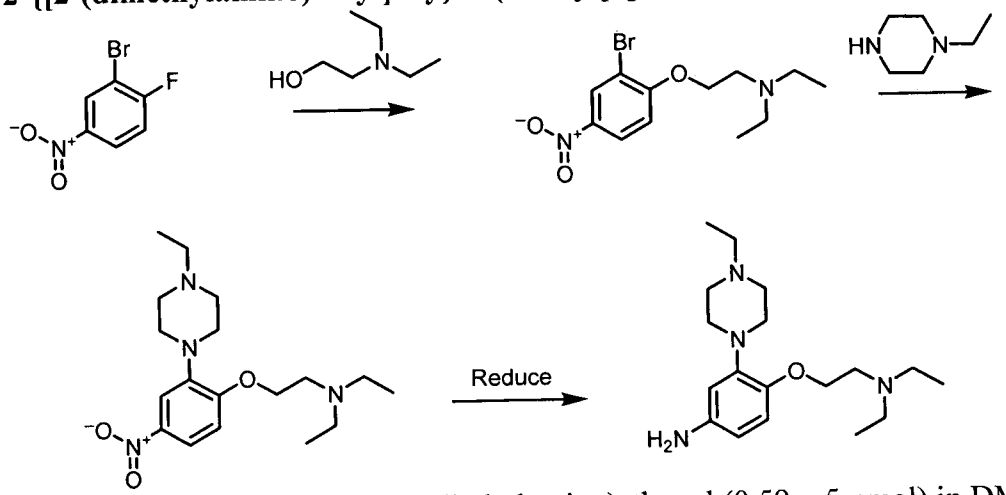
[0848] To a stirred solution of **2** (0.58g, 1 mmol) in DMF (4ml) was added ethyl isocyanate (3mL) at room temperature. After stirring for 30 min, the mixture was diluted with H_2O (5mL) and CH_2Cl_2 (5mL). The separated aqueous layer was extracted with CH_2Cl_2 (3 x 5mL). The combined extracts were dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by silica gel column chromatography (98:2 ethyl acetate/methanol) to afford **4** (0.46g, 71%). $C_{36}H_{40}N_8O_4$: 649 $(M+H)^+$.



4 663

[0849] A solution of **4** (0.46g, 0.71 mmol) and Pd/C (0.14g) in AcOH (1mL) and MeOH (5mL) was stirred for 24 h under a H_2 balloon. The palladium was filtered through celite and the filtrate was concentrated. The residue obtained was purified by silica gel column chromatography (90:10 ethyl acetate/methanol) to afford product which was then washed with acetonitrile several times to afford N-ethyl-4-[4-({4-[4-(D-prolylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperazine-1-carboxamide (663) (0.19g, 51%) as a white powder.

2-{[2-(dimethylamino)ethyl]oxy}-3-(4-ethylpiperazin-1-yl)aniline



[0850] To a solution of 2-(diethylamino)ethanol (0.59g, 5mmol) in DMA (5ml), sodium hydride (0.24g, 10mmol) was added in one portion. Fifteen minute later 2-bromo-4-nitroaniline (1.1g, 5mmol) was added and the content was stirred for 4 hr. Water (50ml) was added to the reaction mixture followed by chloroform. The organic layer was separated, washed with saturated sodium bicarbonate follow by brine. The organic layer was dried over sodium sulfate and concentrated to oil. The oil was dissolved in methanol and saturated with HCl gas. The resulting solution was concentrated and diethyl ester was added. The resulting precipitate was washed with ether and dried to yield 0.8g of 2-[(2-bromo-4-nitrophenyl)0xy]-N,N-diethylethanamine hydrochloride as a solid. LCMS: m/z 318 $(M+H)^+$.

[0851] A mixture of 2-[(2-bromo-4-nitrophenyl)0xy]-N,N-diethylethanamine hydrochloride (0.5g, 1.4mmol), $Pd(dba)_2$ (0.192g, 021mmol), BINAP (0.139g, 0.21mmol), 1-ethylpiperazine (0.182g, 1.68mmol), and cesium carbonate (0.91g, 2.8mmol) in DMA was heated at 80 ^{0}C with stirring for 72 hr. Saturated aqueous sodium bicarbonate and ethyl acetate was added, the phases separated, the solvent was removed under vacuum and the residue chromatographed on silica with ethyl acetate/methanol to give 0.32g of N,N-diethyl-2-{[2-(4-ethylpiperazin-1-yl)-4-nitrophenyl]oxy}ethanamine. LCMS: m/z 351 $(M+H)^+$.

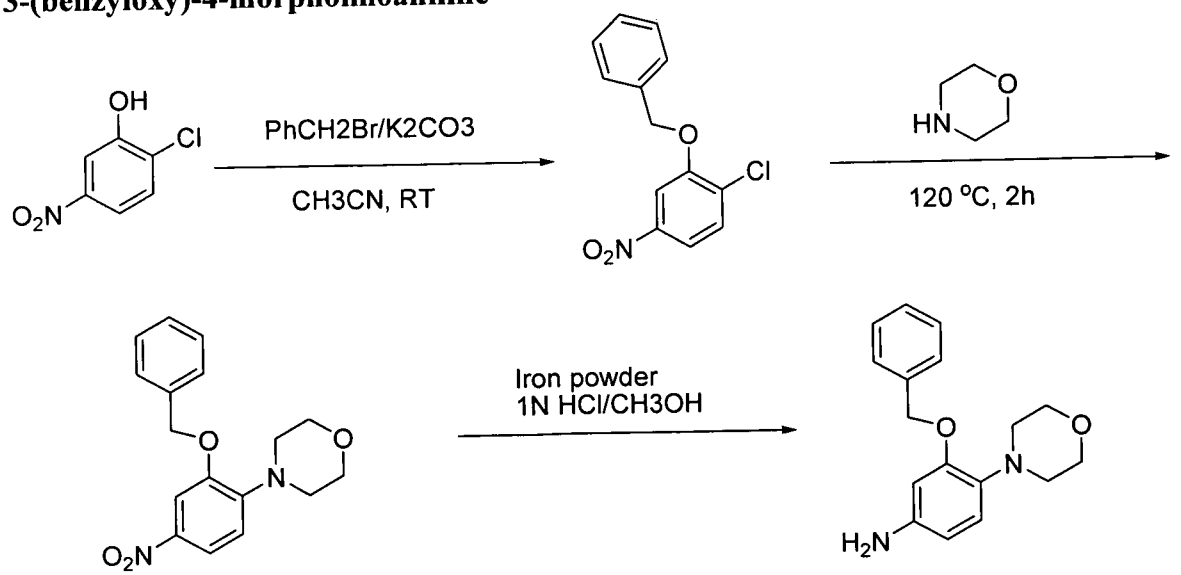
[0852] A solution of N,N-diethyl-2-{[2-(4-ethylpiperazin-1-yl)-4-nitrophenyl]oxy}ethanamine (0.280mg, 0.8mmol) in methanol (10ml) was added 10% Pd/C and stirred in hydrogen atmosphere at ambient temperature for 2hours. The reaction mixture was filtered through a pad of Celite and concentrated in vacuum. The residue was taken up in methanol, ether/HCl was added and the hydrochloride (0.270 mg) was precipitated. LCMS: m/z 321 $(M+H)^+$.

Example 54

(*R*)-*N*-(4-(2-(3-(benzyloxy)-4-morpholino-phenylamino)-pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide (Compound 376)

[0853] *R*)-*N*-(4-(2-(3-(benzyloxy)-4-morpholino-phenylamino)-pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide was synthesized in an analogous fashion to Example 3, wherein 4-morpholinoaniline was substituted with 3-(benzyloxy)-4-morpholinoaniline to afford the title compound.

3-(benzyloxy)-4-morpholinoaniline

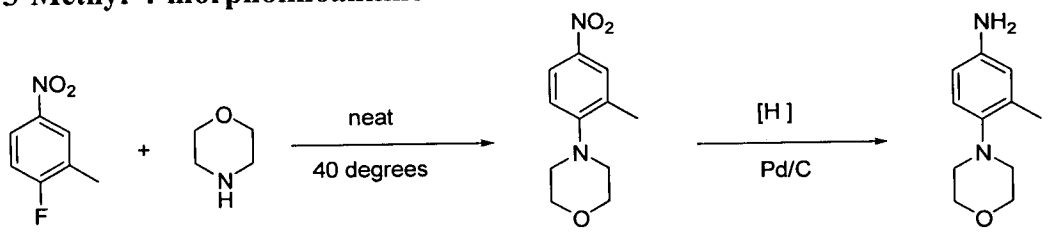


[0854] 4-(2-(Benzyloxy)-4-nitrophenyl)morpholine: A flask was charged with 2-chloro-5-nitrophenol (3.5 g, 20.2 mmol), potassium carbonate (4.0g, 30.3 mmol), benzyl bromide (2.9 mL, 24.24 mmol,) and acetonitrile (25 mL). The reaction mixture was stirred under an N_2 atmosphere at room temperature for 12 hours, after which time, the reaction mixture was filtered through Celite pat and washed with ethyl acetate (50 mL). The product was isolated by removal of the solvent with a rotary evaporator and used without further purification. NMR (400 MHz, $CDCl_3$): 7.80 (m, 2H), 7.27 – 7.58 (m, 6H), 5.24 (s, 2H). MS (EI) for $C_{13}H_{10}ClNO_3$: 264 (MH+).

Example 55

[0855] **(*S*)-2-amino-*N*-(4-(2-(3-methyl-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide** (Compound 384) was synthesized in an analogous fashion to Example 3, wherein 4-morpholinoaniline was substituted with 3-Methyl-4-morpholinoaniline to afford the title compound.

3-Methyl-4-morpholinoaniline



Intermediate 1

[0856] A flask was charged with 2-fluoro-5-nitrotuloene (3.0 mL, 20.2388 mmol). Exess amount of morpholine (10 mL) were added to the flask and heated to 40 °C for 6 hours. The reaction mixture was checked with LC/MS. Water was added to the reaction mixture and the precipitate, intermediate 1, was filtered and used without further purification. LC/MS: m/z 223 $(M+H)^+$.

[0857] A hydrogenation flask was charged with intermediate 1 (1.0 g, 4.4209 mmol) and palladium/carbon (200 mg). Ethyl alcohol (50 mL) was added to the flask and hydrogenation technique was used. The reaction mixture was checked with LC/MS. The reaction mixture was filtered through a celite plug and washed with methanol. The product, 3-methyl-4-morpholinoaniline, was isolated by removal of the solvent with a rotary evaporator and used without further purification. LC/MS: m/z 197 $(M+H)^+$.

Example 56

[0858] N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-chloro-6-fluoro-3-(methyloxy)benzamide (Compound 49) was synthesized in an analogous fashion to Example 2, wherein benzoylchloride was substituted with 2-chloro-3-methoxy-6-fluorobenzoylchloride (JRD Fluroochemicals) to afford the title compound.

Example 57

[0859] *N*-(4-{2-[(3-chloro-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide (Compound 296) was synthesized in an analogous fashion to Example 3, wherein aniline was substituted with 3-chloro-4-morpholinoaniline (Pfaltz and Bauer, Inc.) to afford the title compound.

Example 58

[0860] *N*-(4-{2-[(3-bromo-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide (Compound 315) was synthesized in an analogous fashion to Example 3, wherein aniline was substituted with 3-bromo-4-morpholinoaniline (Ryan Scientific, Inc.) to afford the title compound.

Example 59

[0861] (*R*)-*N*-(4-(2-(4-morpholino-3-(trifluoromethyl)-phenylamino)pyrimidin-4-yl)-phenyl)-pyrrolidine-2-carboxamide was synthesized in an analogous fashion to Example 3, wherein aniline was substituted with 3-trifluoromethyl-4-morpholinoaniline (Zerenex Limited) to afford the title compound.

Example 60

[0862] (*R*)-*N*-(4-(2-(3-fluoro-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide was synthesized in an analogous fashion to Example 3, wherein aniline was substituted with 3-fluoro-4-morpholinoaniline (Astatech, Inc.) to afford the title compound.

Example 61

[0863] *N*-[4-(2-{[3-(1,3-dioxan-2-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide was synthesized in an analogous fashion to Example 3, wherein aniline was substituted 3-(1,3-dioxan-2-yl)aniline (Oakwood Products, Inc.) to afford the title compound.

Example 62

[0864] ***N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]-5-(trifluoromethyl)pyrimidin-4-yl}phenyl)acetamide** was synthesized in an analogous fashion to Example 5, wherein pyrimidine was substituted with 5-trifluoromethyl-2,4-dichloropyrimidine (Astatech, Inc.) to afford the title compound.

[0865] Using the same or analogous techniques as illustrated in the preceding examples, the following compounds herein below were made. The skilled artisan would be able to make the necessary modifications and/or substitutions in the above synthetic procedures to arrive at the following compounds:

[0866] ***N*-(4-{2-[(3-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide** (Compound 21): ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 ppm (s, 1H), 9.511 ppm (s, 1H), 8.504 ppm (d, 1H), 8.154 ppm (d, 2H), 7.76 ppm (d, 3H), 7.343 ppm (d, 1H), 7.215-7.153 ppm (m, 2H), 6.584 ppm (d, 1H), 3.775 ppm (t, 4H), 3.14 ppm (t, 4H), 2.094 ppm (s, 3H); MS (EI) $C_{22}H_{23}N_5O_2$: 390.1 (MH^+).

[0867] ***N*-(4-{2-[(3-piperidin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide** (Compound 22): ^{1}H-NMR (400MHz, d_6-DMSO): 10.231 ppm (s, 1H), 9.466 ppm (s, 1H), 8.497 ppm (d, 1H), 8.16 ppm (d, 2H), 7.765 ppm (d, 3H), 7.337 ppm (d, 1H), 7.119 ppm (d, 2H), 6.553 ppm (m, 1H), 3.176 ppm (t, 4H), 2.092 ppm (s, 3H), 1.658 ppm (m, 4H), 1.571 ppm (m, 2H); MS (EI) $C_{23}H_{25}N_5O$: 388.1 (MH^+).

[0868] ***N*-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide** (Compound 33): ^{1}H-NMR (400MHz, d_6-DMSO): 10.269 ppm (s, 1H), 9.317 ppm (s, 1H), 8.411 ppm (d, 1H), 8.089 ppm (d, 2H), 7.743 ppm (d, 2H), 7.638 ppm (d, 2H), 7.243 ppm (d, 1H), 6.908 ppm (d, 2H), 3.048 ppm (br s, 4H), 2.350 ppm (q, 2H), 2.07 ppm (s, 3H), 1.027 ppm (t, 3H); MS (EI) $C_{24}H_{28}N_6O$: 417.4 (MH^+).

[0869] ***N*-(4-{2-[(4-piperidin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide** (Compound 34): ^{1}H-NMR (400MHz, d_6-DMSO): 10.229 ppm (s, 1H), 9.53 ppm (s, 1H), 8.481 ppm (d, 1H), 8.135 ppm (d, 2H), 7.76 ppm (t, 4H),l 7.325 ppm (d, 1H), 7.178 ppm (d, 2H), 3.025 ppm (br d, 2H), 2.59 ppm (m, 2H), 2.094 ppm (s, 3H), 2.08 ppm (br d, 2H), 1.54-1.439 ppm (m, 2H); MS (EI) $C_{23}H_{25}N_5O$: 388.3 (MH^+).

[0870] ***N*-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide** (Compound 17): ^{1}H-NMR (400MHz, d_6-DMSO): 10.718 ppm (s, 1H), 10.269 ppm (s, 1H), 9.678 ppm (s, 1H), 8.507 ppm (d, 1H), 8.419 ppm (s, 1H), 8.215 ppm (d, 2H), 7.758 ppm (d, 2H), 7.608 ppm (d, 2H), 7.532 ppm (t, 1H), 7.472 ppm (d, 1H), 7.380 ppm (d,

1H), 7.301 ppm (t, 1H), 7.216 ppm (d, 1H), 2.085 ppm (s, 3H); MS (EI) $C_{25}H_{19}Cl_2N_5O_2$: 492.2 (MH^+).

[0871] ***N*-{4-[2-({3-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide** (Compound 8): ^{1}H-NMR (400MHz, d_6-MEOD): 8.455 ppm (d, 1H), 8.15 ppm (m, 3H), 7.76-7.7 ppm (m, 3H), 7.435 ppm (t, 1H), 7.311 ppm (d, 1H), 7.1 ppm (d, 1H), 3.832 ppm (br s, 4H), 3.13 ppm (br s, 4H), 3.016 ppm (q, 2H), 2.162 ppm (s, 3H), 1.975 ppm (s, 3H, ACE), 1.299 ppm (t, 3H); MS (EI) $C_{25}H_{28}N_6O_2$: 445.4 (MH^+).

[0872] ***N*-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-fluorobenzamide** (Compound 10): ^{1}H NMR (DMSO-d_6) 10.40 (s, 1H), 10.21 (s, 1H), 9.66 (s, 1H), 8.49 (d, 1H), 8.41 (s, 1H), 8.20 (d, 2H), 7.74 (d, 2H), 7.69 (m, 1H), 7.58 (m, 1H), 7.48 (m, 1H), 7.37 (m, 3H), 7.28 (m, 2H), 2.09 (s, 3H). LCMS: m/z 442 $(M+H)^+$.

[0873] ***N*-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-fluoro-6-iodobenzamide** (Compound 11): ^{1}H NMR (DMSO-d_6) 10.65 (s, 1H), 10.19 (s, 1H), 9.67 (s, 1H), 8.50 (d, 1H), 8.41 (s, 1H), 8.21 (d, 2H), 7.76 (m, 3H), 7.41 (m, 3H), 7.28 (m, 3H), 2.08 (s, 3H). LCMS: m/z 567 $(M+H)^+$.

[0874] ***N*-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-bromobenzamide** (Compound 23): ^{1}H NMR (DMSO-d_6) 10.48 (s, 1H), 10.20 (s, 1H), 9.66 (s, 1H), 8.49 (d, 1H), 8.42 (s, 1H), 8.20 (d, 2H), 7.73 (d, 3H), 7.55 (m, 2H), 7.45 (m, 2H), 7.36 (m, 1H), 7.37 (d, 1H), 7.25 (m, 2H), 2.08 (s, 3H). LCMS: m/z 502, 503, 504, 505 $(M+H)^+$.

[0875] ***N*-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-3-fluorobenzamide** (Compound 24): ^{1}H NMR (DMSO-d_6) 10.33 (s, 1H), 10.23 (s, 1H), 9.69 (s, 1H), 8.50 (d, 1H), 8.44 (s, 1H), 8.21 (d, 2H), 7.85 (m, 1H), 7.79 (m, 1H), 7.73 (d, 2H), 7.61 (m, 1H), 7.50 (m, 1H), 7.36 (m, 1H), 7.29 (m, 2H), 2.09 (s, 3H). LCMS: m/z 442 $(M+H)^+$.

[0876] ***N*-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dimethylbenzamide** (Compound 12): ^{1}H NMR (DMSO-d_6) 10.37 (s, 1H), 10.20 (s, 1H), 8.55 (s, 1H), 8.49 (d, 1H), 8.22 (d, 2H), 7.72 (d, 2H), 7.36 (d, 2H), 7.22 (m, 3H), 7.12 (d, 2H), 2.33 (s, 6H), 2.08 (s, 3H). LCMS: m/z 452 $(M+H)^+$.

[0877] ***N*-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]pyridine-4-carboxamide** (Compound 14): ^{1}H NMR (DMSO-d_6) 10.59 (s, 1H), 10.34(s, 1H), 9.71 (s, 1H), 8.80 (dd, 2H), 8.50 (m, 2H), 8.21 (d, 2H), 7.90 (dd, 2H), 7.75 (d, 2H), 7.51 (m, 1H), 7.37 (d, 1H), 7.31 (m, 2H), 2.09 (s, 3H). LCMS: m/z 425 $(M+H)^+$.

[0878] ***N*-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,3,4,5,6-pentafluorobenzamide** (Compound 15): ^{1}H NMR (DMSO-d_6) 10.97 (s, 1H), 10.20 (s, 1H), 9.75 (s, 1H), 8.50 (d, 1H), 8.33 (s, 1H), 8.17 (d, 2H), 7.72 (d, 2H), 7.55 (m, 1H), 7.38 (d, 1H), 7.32 (t, 1H), 7.24 (d, 1H), 2.08 (s, 3H). LCMS: m/z 514 $(M+H)^+$.

[0879] **N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2,6-dichlorobenzamide** (Compound 1): ^{1}H NMR (DMSO-d_6) 10.15 (s, 1H), 8.68 (t, 1H), 8.27 (d, 1H), 8.04 (d, 2H), 7.67 (d, 2H), 7.49 (d, 2H), 7.41 (m, 1H), 7.13 (t, 1H), 7.06 (d, 1H), 3.41 (m, 2H), 3.30 (m, 2H), 2.06 (s, 3H), 1.80 (m, 2H). LCMS: m/z 458 $(M+H)^+$.

[0880] **2,6-dichloro-N-(3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}propyl)benzamide** (Compound 2): ^{1}H NMR (DMSO-d_6) 8.63 (s, 1H), 8.36 (d, 1H), 7.73 (s, 1H), 7.58 (d, 1H), 7.52 (d, 1H), 7.47 (m, 2H), 7.40 (m, 2H), 6.79 (d, 2H), 3.37 (m, 2H), 3.27 (m, 2H), 1.75 (t, 2H). LCMS: m/z 471 $(M+H)^+$.

[0881] **4-(2,4-dichlorophenyl)-*N*-{3-[(2-piperidin-1-ylethyl)oxy]phenyl}pyrimidin-2-amine** (Compound 19): ^{1}H NMR (DMSO-d_6) 9.79 (s, 1H), 8.58 (d, 1H), 7.77 (d, 1H), 7.68 (d, 1H), 7.58 (m, 2H), 7.24 (d, 1H), 7.10 (m, 2H), 6.50 (dd, 1H), 3.98 (t, 2H), 2.60 (t, 2H), 2.47 (m, 4H), 1.46 (m, 4H), 1.36 (m, 2H). LCMS: m/z 443 $(M+H)^+$

[0882] **N-(3-{[4-(4-aminophenyl)pyrimidin-2-yl]amino}propyl)-2,6-dichlorobenzamide** (Compound 6): ^{1}H NMR (400 MHz, DMSO): δ 8.76-8.79 (m, 1H), 8.45 (d, 6.0 Hz, 1H), 7.94-8.06 (m, 3H), 7.56 (m. 1H), 7.52-7.51 (m, 1H), 7.50 (s, 2H), 7.43-7.52 (m, 2H), 7.36-7.42 (m, 1H), 7.22-7.34 (bs, 1H), 3.44-3.64 (bs, 2H), 3.32-3.40 (m, 2H), 1.02-1.52 (bs, 2H). LC/MS MH=416.

[0883] **2,6-dichloro-N-(3-{[4-(2,3-dihydro-1-benzofuran-6-yl)pyrimidin-2-yl]amino}-propyl)benzamide** (Compound 4): ^{1}H NMR (400 MHz, DMSO): δ 8.724 (t, 5.6Hz, 1H), 8.29 (d, 5.6 Hz, 1H), 8.41-8.18 (bs, 1H), 7.92-8.15 (bs, 1H), 7.49-7.52 (m, 2H), 7.41-7.45 (m, 2H), 7.14-7.23 (bs, 1H), 6.88 (d, 8.4Hz, 1H), 4.61-4.65 (m, 2H), 3.62-3.93 (bs, 1H), 3.39-3.51 (bs, 1H), 3.33-3.36 (m, 2H), 3.23-3.27 (m, 2H), 1.80-1.87 (bs, 2H). LC/MS MH=443.

[0884] **2,6-dichloro-N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]-benzamide** (Compound 3): ^{1}H NMR (400 MHz, DMSO): δ 8.66 (t, 5.6Hz, 1H), 8.17 (d, 5.2 Hz, 1H), 7.95 (d, 8.8 Hz, 2H), 7.47-7.49 (m, 2H), 7.38-7.42 (m, 1H), 6.95-6.97 (m, 2H), 6.72-6.75 (m, 2H), 3.37-3.43 (m, 2H), 3.26-3.32 (m, 2H), 2.96 (s, 6H), 1.79 (t, 6.8Hz, 2H). LC/MS M-H=442.

[0885] ***N*-[3-({4-[4-(acetylamino)phenyl]-5-methylpyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide** (Compound 25): ^{1}H NMR (400MHz, DMSO-d_6) δ 10.67 (s, 1H), 10.15

(s, 1H), 9.57 (s, 1H), 8.38 (s, 1H), 8.16 (s, 1H), 7.72 (s, 4H), 7.60-7.50 (m, 4H), 7.26-7.23 (m, 2H), 2.26 (s, 3H), 2.09 (s, 3H). LCMS (EI) $C_{26}H_{22}Cl_2N_5O_2$: 506 (M+H).

[0886] ***N*-[3-({4-[4-(acetylamino)phenyl]-5-fluoropyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide** (Compound 28): ^{1}H NMR (400MHz, DMSO-d_6) δ 10.72 (s, 1H), 10.25 (s, 1H), 9.78 (s, 1H), 8.59 (d, J = 4.0Hz, 1H), 8.32 (s, 1H), 8.12 (d, J = 8.4Hz, 2H), 7.77 (d, J = 8.8Hz, 2H), 7.61-7.58 (m, 2H), 7.51 (dd, J = 8.8, 6.8Hz, 1H), 7.44 (d, J = 8.4Hz, 1H), 7.28 (t, J = 8.0Hz, 1H), 7.23 (t, J = 8.0Hz, 1H), 2.09 (s, 3H). LCMS (EI) $C_{25}H_{18}Cl_2FN_5O_2$: 510 (M+H).

[0887] ***N*-(4-{2-[(4-{[2-(4-ethylpiperazin-1-yl)-2-oxoethyl]oxy}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide** (Compound 64): ^{1}H-NMR (400MHz, d_6-DMSO): 10.222 ppm (s, 1H), 9.445 ppm (s, 1H), 8.457 ppm (d, 1H), 8.119 ppm (d, 2H), 7.75 ppm (d, 2H), 7.686 ppm (d, 2H), 7.299 ppm (d, 1H), 6.922 ppm (d, 2H), 4.76 ppm (s, 2H), 3.465 ppm (bs, 4H), 2.4 ppm (m, 4H), 2.31 ppm (m, 2H), 2.091 ppm (s, 3H), 1.02 ppm (t, 3H); MS (EI) $C_{26}H_{30}N_6O_3$: 475.4 (MH^+).

[0888] **1-ethyl-3-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)urea (Compound 250·HCl)** (Compound 250): ^{1}H-NMR (400MHz, d_6-DMSO): 10.064 ppm (s, 1H), 9.305 ppm (s, 1H), 8.483 ppm (d, 1H), 8.105 ppm (d, 2H), 7.832 ppm (bd, 2H), 7.603 ppm (d, 2H), 7.54 ppm (bs, 2H), 7.431 ppm (d, 1H), 6.55 ppm (bs, 1H), 3.89 ppm (bs, 4H), 3.426 ppm (bs, 4H), 3.15 ppm (m, 2H), 1.08 ppm (t, 3H)); MS (EI) $C_{23}H_{26}N_6O_2HCl$: 419.3 (MH^+).

[0889] ***N*-[6-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)pyrimidin-4-yl]-2,6-dichlorobenzamide** (Compound 301): ^{1}H NMR (400MHz, d_6-DMSO): 11.55 (s, 1H), 10.5 (s, 1H), 10.2 (s, 1H), 9.32 (s, 1H), 8.68 (d, 1H), 8.6 (s, 1H), 8.4 (d, 2H), 7.74 (d, 2H), 7.64 (d, 1H), 7.62-7.5 (m, 3H), 2.03 (s, 3H); MS (EI) for $C_{23}H_{17}Cl_2N_7O_2$: 494 (MH^+).

[0890] ***N*-[4-(2-{[4-(morpholin-4-ylmethyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide** (Compound 232): ^{1}H NMR (400MHz, d_6-DMSO): 10.3 (s, 1H), 9.6 (s, 1H), 8.46 (d, 1H), 8.13 (d, 2H), 7.78 (t, 4H), 7.35 (d, 1H), 7.47 (d, 1H), 7.23 (d, 2H), 3.58 (t, 4H), 3.4 (s, 2H), 2.33 (t, 4H), 2.1 (s, 3H); MS (EI) for $C_{23}H_{25}N_5O_2$: 404 (MH^+).

[0891] **4-(1*H*-indol-5-yl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine** (Compound 254): ^{1}H-NMR (400MHz, d_6-DMSO): 11.35 ppm (s, 1H), 9.33 ppm (s, 1H), 8.41 ppm (m, 2H), 7.94 ppm (dd, 1H), 7.71 ppm (d, 2H), 7.50 ppm (d, 1H), 7.44 ppm (t, 1H), 7.33 ppm (d, 1H), 6.94 ppm (d, 2H), 6.57 ppm (s,1H), 3.75 ppm (m, 4H), 3.05 ppm (m, 4H), 2.09 ppm (s, 3H); MS (EI) $C_{24}H_{25}N_5O_2$: 372.3 (MH^+).

[0892] ***N*-(3-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide** (Compound 79): ^{1}H-NMR (400MHz, d_6-DMSO): 10.14 ppm (s, 1H), 9.45 ppm (s, 1H), 8.49 ppm (d, 1H), 8.40 ppm (s, 1H), 7.77 ppm (d, 1H), 7.70 ppm (d, 3H), 7.45 ppm (t, 1H), 7.20 ppm (d, 1H), 6.93 ppm (d, 2H), 3.74 ppm (m, 4H), 3.04 ppm (m, 4H), 2.09 ppm (s, 3H); MS (EI) $C_{24}H_{25}N_5O_2$: 390.1 (MH^+).

[0893] **4-[4-(methyloxy)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine** (Compound 252): ^{1}H-NMR (400MHz, d_6-DMSO): 9.37 ppm (s, 1H), 8.42 ppm (d, 1H), 8.13 ppm (d, 2H), 7.67 ppm (d, 2H), 7.27 ppm (d, 1H), 7.08 ppm (d, 2H), 6.92 ppm (d, 2H), 3.84 ppm (s, 3H), 3.74 ppm (m, 4H), 3.04 ppm (m, 4H); MS (EI) $C_{24}H_{25}N_5O_2$: 363.1 (MH^+).

[0894] ***N*-(4-{2-[(3-piperazin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide** (Compound 312): ^{1}H-NMR (400MHz, d_6-DMSO): 10.32 ppm (s, 1H), 9.55 ppm (s, 1H), 8.50 ppm (d, 1H), 8.13 ppm (d, 2H), 7.78 ppm (d, 2H), 7.68 ppm (s, 1H), 7.35 ppm (dd, 2H), 7.20 ppm (t, 1H), 6.63 (dd, 1H), 3.38 (m, 4H), 3.25 (m, 4H), 2.13 ppm (s, 3H); MS (EI) $C_{22}H_{24}N_6O$: 389.1 (MH^+)

[0895] **2-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-phenyl-acetamide** (Compound 573): ^{1}H-NMR (400MHz, d_6-DMSO): 11.93 ppm (s, 1H), 10.18 (s, 1H), 9.08 ppm (s, 2H), 8.58 ppm (d, 1H), 8.18 ppm (d, 2H), 7.98-7.88 ppm (m, 2H), 7.82-7.75 ppm (m, 2H), 7.60-7.40 ppm (m, 6H), 7.30 ppm (s, 2H), 5.52-5.46 (m, 1H), 4.10 (t, 4H), 3.57 (t, 4H); MS (EI) $C_{28}H_{28}N_6O_2$: 481.3 (MH^+).

[0896] ***N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-alaninamide** (Compound 577): ^{1}H-NMR (400MHz, d_6-DMSO): 9.387 ppm (s, 1H), 8.443 ppm (d, 1H), 8.127 ppm (d, 2H), 7.825 ppm (d, 2H), 7.676 ppm (d, 2H), 7.287 ppm (d, 1H), 6.939 ppm (d, 2H), 3.747 ppm (m, 4H), 3.457 ppm (q, 1H), 3.050 ppm (m, 4H), 1.896 ppm (s, 3H (AcOH)), 1.243 ppm (d, 3H); MS (EI) $C_{23}H_{26}N_6O_2$: 419.1 (MH^+).

[0897] ***N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)valinamide** (Compound 575): ^{1}H-NMR (400MHz, d_6-DMSO): 9.390 ppm (s, 1H), 8.449 ppm (d, 1H), 8.124 ppm (d, 2H), 7.815 ppm (d, 2H), 7.686 ppm (d, 2H), 7.284 ppm (d, 1H), 6.939 ppm (d, 2H), 3.747 ppm (m, 4H), 3.147 ppm (d, 1H), 3.051 ppm (m, 4H), 1.953 ppm (m, 1H), 1.864 ppm (s, 3H (AcOH)), 0.943 ppm (d, 3H), 0.871 ppm (d, 3H); MS (EI) $C_{25}H_{30}N_6O_2$: 446.2 (MH^+).

[0898] **2-(dimethylamino)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-acetamide** (Compound 197): ^{1}H-NMR (400MHz, d_6-DMSO): 10.001 ppm (s, 1H), 9.384 ppm (s, 1H), 8.440 ppm (d, 1H), 8.118 ppm (d, 2H), 7.836 ppm (d, 2H), 7.673

ppm (d, 2H), 7.287 ppm (d, 1H), 6.939 ppm (d, 2H), 3.745 ppm (m, 4H), 3.114 ppm (s, 2H), 3.049 ppm (m, 4H), 2.290 ppm (s, 6H); MS (EI) $C_{24}H_{28}N_6O_2$: 432.5 (MH^+).

[0899] ***N*-(4-{2-[(4-{4-[3-(dimethylamino)-2,2-dimethylpropyl]piperazin-1-yl}phenyl)-amino]pyrimidin-4-yl}phenyl)acetamide** (Compound 578): ^{1}H-NMR (400MHz, d_6-DMSO):): 10.208 ppm (s, 1H), 9.358 ppm (s, 1H), 8.433 ppm (d, 1H), 8.106 ppm (d, 2H), 7.741 ppm (d, 2H), 7.648 ppm (d, 2H), 7.262 ppm (d, 1H), 6.909 ppm (d, 2H), 3.050 ppm (m, 4H), 2.595 ppm (m, 4H), 2.212 ppm (s, 6H), 2.172 ppm (s, 2H), 2.091 ppm (m, 5H), 0.843 ppm (s, 6H); MS (EI) $C_{29}H_{39}N_70$: 502.2 (MH^+).

[0900] ***N*-(4-{2-[(4-{4-[(1-methyl-1*H*-imidazol-2-yl)methyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide** (Compound 576): ^{1}H-NMR (400MHz, d_6-DMSO): 10.23 ppm (s, 1H), 9.37 ppm (s, 1H), 8.43 ppm (d, 1H), 8.106 ppm (d, 2H), 7.74 ppm (d, 2H), 7.65 ppm (d, 2H), 7.26 ppm (d, 1H), 7.10 ppm (s, 1H), 6.92 ppm (d, 2H), 6.78 ppm (s, 1H), 3.67 ppm (s, 3H), 3.58 ppm (s, 2H), 3.39-3.34 ppm (m, 4H), 3.02-3.08 ppm (M, 4H), 2.10 ppm (s, 3H); MS (EI) $C_{27}H_{30}N_8O$ 482.6 (MH^+).

[0901] ***N*-(4-(2-(4-(4-(cyclopropanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide** (Compound 349): ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 ppm (s, 1H), 9.41 ppm, (s, 1H), 8.44 ppm (d, 1H), 8.11 ppm (d, 2H), 7.74 ppm (d, 2H), 7.69 ppm (d, 2H), 7.28 ppm (d, 1H), 6.97 ppm (d, 2H), 3.83 ppm (s, 2H), 3.62 ppm (s, 2H), 3.15 ppm (s, 2H), 3.03 ppm (s, 2H), 2.09 ppm (s, 3H), 2.02-2.05 ppm (m, 1H), 0.74-0.76 ppm (m, 4H); MS (EI) $C_{26}H_{28}N_6O_2$: 456.5 (MH^+).

[0902] ***N*-{4-[2-({3-[(4-phenylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide** (Compound 78): ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 ppm (s,1H), 9.83 ppm (s,1H), 8.53 ppm (d, 1H), 8.13 ppm (d, 2H), 8.05 ppm (s, 1H), 7.95 ppm (s, 1H), 7.87 ppm (d, 1H), 7.75 ppm (d, 2H), 7.38-7.43 (m, 2H), 7.20-7.242 (m, 2H), 7.02 ppm (d, 2H) 6.95 ppm (d, 2H), 6.81 ppm (t, 1H), 3.68-3.88 ppm (m, 2H), 3.44-3.65 ppm (m, 2H), 3.02-3.11 ppm (m, 4H), 2.09 ppm (s, 3H); MS (EI) $C_{29}H_{28}N_6O_2$: 492.6 (MH^+).

[0903] ***N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-alaninamide** (Compound 578): ^{1}H-NMR (400MHz, d_6-DMSO): 11.13 ppm (s, 1H), 9.89 ppm (s, 1H), 8.53 ppm (d, 1H), 8.35 ppm (d, 3H), 8.20 ppm (d, 2H), 7.85 ppm (d, 4H), 7.49 ppm (br s, 2H), 7.43 ppm (d, 1H), 4.14 ppm (m, 1H), 3.96 ppm (br s, 4H), 3.40 ppm (br s, 4H), 1.50 ppm (s, 3H); MS (EI) $C_{23}H_{26}N_6O_2$: 419 (MH^+).

[0904] **(N-(4-{5-methyl-2-[(3-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl-acetamide):** ^{1}H-NMR (400MHz, d_6-DMSO): 10.17 (s, 1H), 9.41 (s, 1H), 8.38 (s, 1H), 7.84

(s, 1H), 7.72 (s, 4H), 7.09 (d, 2H), 6.51 (dd, 1H), 3.74 (t, 4H), 3.07 (t, 4H), 2.26 (s, 3H), 2.09 (s, 3H); MS (EI) $C_{23}H_{25}N_5O_2$: 404.3 $(M+H)^+$.

[0905] (N-(4-{6-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-acetamide): ^{1}H-NMR (400MHz, d_6-DMSO): 10.18 (s, 1H), 9.31 (s, 1H), 8.09 (d, 2H), 7.74-7,70 (m, 4H), 7.19 (s, 1H), 6.93 (d, 2H), 3.74 (t, 4H), 3.04 (t, 4H), 2.38 (s, 3H), 2.09 (s, 3H); MS (EI) $C_{23}H_{25}N_5O_2$: 404.3 $(M+H)^+$.

[0906] (N-(4-{2-[(4-morpholin-4-ylphenyl)amino]-5-(trifluoromethyl)pyrimidin-4-yl}-phenyl)acetamide): ^{1}H-NMR (400MHz, $CDCl_3$): 8.66 (s, 1H), 7.65-7.59 (m, 4H), 7.51 (d, 2H), 7.33 (d, 2H), 6.93 (d, 2H), 3.87 (t, 4H), 3.14 (t, 4H); MS (EI) $C_{26}H_{30}N_6O_3$: 458.1 $(M+H)^+$.

[0907] (N-(4-{2-[(3-aminophenyl)amino]-5-methylpyrimidin-4-yl}phenyl)acetamide): ^{1}H-NMR (400MHz, d_6-DMSO): 10.14 (s, 1H), 9.19 (s, 1H), 8.33 (d, 1H), 7.72 (d, 2H), 7.67 (dd, 2H), 7.03 (t, 1H), 6.94 (dd, 1H), 6.87 (t, 1H), 6.17-6.14 (m, 1H), 4.92 (s, 2H), 2.23 (s, 3H), 2.08 (s, 3H); MS (EI) $C_{19}H_{19}N_5O$: 334.0 $(M+H)^+$.

[0908] (N-(4-{2-[(3-aminophenyl)amino]-5-fluoropyrimidin-4-yl}phenyl)acetamide): ^{1}H-NMR (400MHz, d_6-DMSO): 10.26 (s, 1H), 9.41 (s, 1H), 8.54 (d, 1H), 8.04 (d, 2H), 7.78 (d, 2H), 7.03 (s, 1H), 6.95-6.91 (m, 2H), 6.20 (d, 1H), 5.00 (s, 2H), 2.10 (s, 3H); MS (EI) $C_{18}H_{16}FN_5O$: 338.3 $(M+H)^+$.

[0909] (N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-fluoropyrimidin-4-yl)phenyl]acetamide): ^{1}H-NMR (400MHz, d_6-DMSO): 10.26 (s, 1H), 9.45 (s, 1H), 8.52(d, 1H), 8.02 (d, 2H), 7.78 (d, 2H), 7.59 (d, 2H), 6.91 (d, 2H), 3.35 (bs, 4H), 3.07 (bs, 4H), 2.50 (q, 2H), 2.10 (s, 3H), 1.04 (t, 3H); MS (EI) $C_{24}H_{27}FN_6O$: 435.3 $(M+H)^+$.

[0910] (N-[3-({4-[4-(acetylamino)phenyl]-5-methylpyrimidin-2-yl}amino)phenyl]-2,6-dimethylbenzamide): ^{1}H-NMR (400MHz, d_6-DMSO): 10.32 (s, 1H), 10.15 (s, 1H), 9.51 (s, 1H), 8.37(s, 1H), 8.29 (s, 1H), 7.76-7.70 (m, 4H), 7.42-7.41 (m, 1H), 7.25-7.17 (m, 3H), 7.11 (d, 2H), 2.29 (s, 6H), 2.26 (s, 3H), 2.09(s, 3H); MS (EI) $C_{28}H_{27}N_5O_2$: 466.3 $(M+H)^+$.

[0911] (N-(4-{2-[(3,5-dimorpholin-4-ylphenyl)amino]-5-fluoropyrimidin-4-yl}phenyl)-acetamide): ^{1}H-NMR (400MHz, d_6-DMSO): 10.27 (s, 1H), 9.45 (s, 1H), 8.58(d, 1H), 8.07 (d, 2H), 7.77 (d, 2H), 7.06 (s, 2H), 6.17 (s, 1H), 3.75 (t, 8H), 3.10 (t, 8H), 2.10 (s, 3H); MS (EI) $C_{26}H_{29}FN_6O_3$: 493.4 $(M+H)^+$.

[0912] (N-{4-[2-(1H-indazol-6-ylamino)-5-methylpyrimidin-4-yl]phenyl}acetamide): ^{1}H-NMR (400MHz, d_6-DMSO): 12.80 (s, 1H), 10.18 (s, 1H), 9.72 (s, 1H), 8.44(d, 1H), 8.37

(d, 1H), 7.90 (s, 1H), 7.77-7.70 (m, 4H), 7.59 (d, 1H), 7.28 (dd, 1H), 2.27 (s, 3H), 2.10 (s, 3H); MS (EI) $C_{20}H_{18}N_60$: 359.3 $(M+H)^+$.

[0913] (N-{4-[2-(1H-indol-5-ylamino)-5-methylpyrimidin-4-yl]phenyl}acetamide): ^{1}H-NMR (400MHz, d_6-DMSO): 10.90 (s, 1H), 10.15 (s, 1H), 9.21 (s, 1H), 8.32(d, 1H), 8.00 (d, 1H), 7.72 (dd, 2H), 7.66 (dd, 2H), 7.36 (dd, 1H), 7.28-7.25 (m, 2H), 6.33 (t, 1H), 2.22 (s, 3H), 2.09 (s, 3H); MS (EI) $C_{21}H_{19}N_50$: 358.3 $(M+H)^+$.

[0914] (N-(4-{5-fluoro-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-acetamide): ^{1}H-NMR (400MHz, d_6-DMSO): 10.26 (s, 1H), 9.48 (s, 1H), 8.52 (d, 1H), 8.02 (d, 2H), 7.77 (d, 2H), 7.61 (d, 2H), 6.93 (d, 2H), 3.74 (t, 4H), 3.03 (t, 4H); MS (EI) $C_{22}H_{22}FN_50_2$: 408.3 $(M+H)^+$.

[0915] N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-cyclopropanecarboxamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.41 (s, 1H), 9.28 (s, 1H), 8.31(d, 1H), 7.73 (d, 2H), 7.66-7.62 (m, 4H), 6.89 (d, 2H), 3.73 (bs, 4H), 3.02 (bs, 4H), 2.22 (s, 3H), 1.85-1.79 (m, 1H), 0.84-0.81 (m, 4H); MS (EI) $C_{25}H_{27}N_50_2$: 430 (MH+).

[0916] N-{4-[2-(1H-indazol-5-ylamino)-5-methylpyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 12.88 (s, 1H), 10.16 (s, 1H), 9.49 (s, 1H), 8.37(s, 1H), 8.29 (d, 1H), 7.97 (s, 1H), 7.73 (d, 2H), 7.67 (d, 2H), 7.59 (dd, 1H), 7.44 (d, 1H), 2.24 (s, 3H), 2.10 (s, 3H); MS (EI) $C_{20}H_{18}N_60$: 359 (MH+).

[0917] N-(4-{2-[(3,5-dimorpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.36 (s, 1H), 8.48 (d, 1H), 8.15 (d, 2H), 7.74 (d, 2H), 7.32 (d, 1H), 7.12 (d, 2H), 6.17 (s, 1H), 3.75 (t, 4H), 3.11 (t, 4H), 2.09 (s, 3H); MS (EI) $C_{26}H_{30}N_60_3$: 475 (MH+).

[0918] 4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzonitrile: ^{1}H-NMR (400MHz, d_6-DMSO): 9.60 (s, 1H), 8.57 (d, 1H), 8.32 (d, 2H), 8.03 (d, 2H), 7.65 (d, 2H), 7.44 (d, 1H), 6.94 (d, 2H), 3.75 (t, 4H), 3.05 (t, 4H), ; MS (EI) $C_{21}H_{19}N_50$: 358 (MH+).

[0919] 4-(4-fluorophenyl)-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine: ^{1}H-NMR (400MHz, d_6-DMSO): 9.46 (s, 1H), 8.49 (d, 1H), 8.22 (dd, 2H), 7.66 (d, 2H), 7.38 (t, 2H), 7.33 (d, 1H), 6.93 (dd, 2H), 3.74 (t, 4H), 3.05 (t, 4H), ; MS (EI) $C_{20}H_{19}FN_40$: 358.3 $(M+H)^+$.

[0920] N-(4-morpholin-4-ylphenyl)-4-(4-pyrimidin-5-ylphenyl)pyrimidin-2-amine: ^{1}H-NMR (400MHz, d_6-DMSO): 9.50 (s, 1H), 9.26 (s, 2H), 9.24 (s, 1H), 8.53 (d, 1H), 8.32 (d, 2H), 8.02 (d, 2H), 7.69 (d, 2H), 7.44 (s, 1H), 6.94 (d, 2H), 3.75 (t, 4H), 3.06 (t, 4H); MS (EI) $C_{24}H_{22}N_60$: 411 (MH+).

[0921] N-(4-morpholin-4-ylphenyl)-4-[4-(pyridin-2-ylamino)phenyl]pyrimidin-2-amine: ^{1}H-NMR (400MHz, d_6-DMSO): 9.42 (s, 1H), 9.33 (s, 1H), 8.40 (d, 1H), 8.23 (dd,

1H), 8.09 (dd, 2H), 7.86 (d, 2H), 7.70 (d, 2H), 7.65-7.61 (m, 1H), 7.25 (d, 1H), 6.96-6.90 (m, 3H), 6.84-6.81 (m, 1H). 3.75 (t, 4H), 3.05 (t, 4H) ; MS (EI) $C_{25}H_{24}N_60$: 425 (MH+).

[0922] N-(4-morpholin-4-ylphenyl)-4-[4-(pyridin-3-ylamino)phenyl]pyrimidin-2-amine: ^{1}H-NMR (400MHz, d_6-DMSO): 9.33 (s, 1H), 8.81 (s, 1H), 8.45 (d, 1H), 8.40 (d, 1H), 8.14 (dd, 1H), 8.08 (d, 2H), 7.68 (d, 2H), 7.63-7.60 (m, 1H), 7.32 (dd, 1H), 7.23 (d, 1H), 7.19 (dd, 2H), 6.93 (d, 2H), 3.74 (t, 4H), 3.05 (t, 4H); MS (EI) $C_{25}H_{24}N_60$: 425 (MH+).

[0923] N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.23 (s, 1H), 9.42 (s, 1H), 8.45 (d, 1H), 8.31 (s, 1H), 8.13 (d, 2H), 7.84 (d, 2H), 7.69 (d, 2H), 7.30 (d, 1H), 6.97 (d, 2H), 4.09-4.04 (m, 1H), 3.77-3.73 (m, 1H), 3.67-3.61 (m, 4H), 3.09-3.03 (m, 4H), 2.92 (t, 2H), 2.10-2.03 (m, 1H), 1.85-1.77 (m, 1H), 1.71-1.64 (m, 2H), 1.19 (d, 3H); MS (EI) $C_{28}H_{34}N_8O_2$: 515 (MH+).

[0924] N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.23 (s, 1H), 9.42 (s, 1H), 8.45 (d, 1H), 8.34 (s, 1H), 8.13 (d, 2H), 7.84 (d, 2H), 7.69 (d, 2H), 7.30 (d, 1H), 6.97 (d, 2H), 4.06-4.01 (m, 1H), 3.77-3.73 (m, 1H), 3.67-3.61 (m, 4H), 3.09-3.02 (m, 4H), 2.92 (t, 2H), 2.10-2.03 (m, 1H), 1.85-1.77 (m, 1H), 1.71-1.64 (m, 2H), 1.18 (d, 3H); MS (EI) $C_{28}H_{34}N_8O_2$: 515 (MH+).

[0925] N-{4-[2-({4-[4-(piperazin-1-ylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.28 (s, 1H), 8.13 (d, 2H), 7.84 (d, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 6.96 (d, 2H), 3.76-3.73 (m, 1H), 3.69-3.59 (m, 4H), 3.19 (s, 2H), 3.10-3.02 (m, 4H), 2.91 (t, 2H), 2.81 (bs, 4H), 2.44 (bs, 4H), 2.10-2.04 (m, 1H), 1.85-1.77 (m, 1H), 1.71-1.64 (m, 2H); MS (EI) $C_{31}H_{39}N_9O_2$: 570 (MH+).

[0926] N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-alaninamide: ^{1}H-NMR (400MHz, d_6-DMSO): 9.43 (s, 1H), 8.47 (d, 1H), 8.17 (d, 2H), 7.80 (d, 2H), 7.69 (d, 2H), 7.31 (d, 1H), 6.98 (d, 2H), 3.82-3.78 (m, 4H), 3.66-3.62 (m, 4H), 3.09-3.03 (m, 4H), 2.97-2.90 (m, 1H), 1.39 (d, 3H), 1.03 (d, 6H); MS (EI) $C_{27}H_{33}N_7O_2$: 488 (MH+).

[0927] N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-alaninamide: ^{1}H-NMR (400MHz, d_6-DMSO): 9.42 (s, 1H), 8.45 (d, 1H), 8.33 (s, 1H), 8.13 (d, 2H), 7.82 (d, 2H), 7.69 (d, 2H), 7.30 (d, 1H), 6.98 (d, 2H), 4.13-4.07 (m, 1H), 3.70-3.59 (m, 5H), 3.11-3.01 (m, 4H), 1.27 (d, 3H), 1.21 (d, 3H); MS (EI) $C_{26}H_{32}N_8O_2$: 489 (MH+).

[0928] N-{4-[2-({4-[4-(tetrahydrofuran-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)-pyrimidin-4-yl]phenyl}-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.19 (s, 1H), 9.42 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.84 (d, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 6.96 (d, 2H), 3.89 (t, 1H), 3.74-3.69 (m, 4H), 3.67-3.63 (m, 4H), 3.45-3.37 (m, 1H), 3.09-3.02 (m, 4H), 2.90 (t, 2H), 2.08-1.99 (m, 3H), 1.84-1.76 (m, 1H), 1.70-1.64 (m, 2H); MS (EI) $C_{30}H_{35}N_7O_3$: 542 (MH+).

[0929] N-{4-[2-({4-[4-(tetrahydrofuran-2-ylcarbonyl)piperazin-1-yl]phenyl}amino)-pyrimidin-4-yl]phenyl}-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.83 (d, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 6.96 (d, 2H), 4.72 (dd, 1H), 3.82-3.72 (m, 3H), 3.69-3.58 (m, 4H), 3.08-3.02 (m, 4H), 2.91 (t, 2H), 2.11-1.99 (m, 3H), 1.88-1.79 (m, 3H), 1.71-1.66 (m, 2H); MS (EI) $C_{30}H_{35}N_7O_3$: 542 (MH+).

[0930] N-(4-{5-chloro-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.30 (s, 1H), 9.67 (s, 1H), 8.52 (s, 1H), 7.82 (s, 4H), 7.59 (d, 2H), 6.90 (dd, 2H), 3.84 (dd, 1H), 3.74-3.72 (m, 4H), 3.04-3.02 (m, 4H), 2.97 (t, 2H), 2.15-2.09 (m, 1H), 1.86-1.79 (m, 1H), 1.75-1.69 (m, 2H); MS (EI) $C_{25}H_{27}ClN_6O_2$: 479 (MH+).

[0931] (R)-N-(4-(2-(4-(4-(2-(pyrrolidin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.84 (d, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 6.95 (d, 2H), 3.75-3.71 (m, 1H), 3.69-3.59 (m, 4H), 3.07-3.01 (m, 4H), 2.91 (t, 2H), 2.50 (t, 4H), 2.48 (s, 2H), 2.11-2.02 (m, 1H), 1.86-1.78 (m, 1H), 1.72-1.63 (m, 6H); MS (EI) $C_{31}H_{38}N_8O_2$: 555 (MH+).

[0932] (R)-N-(4-(2-(4-(4-(2-morpholinoacetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.19 (s, 1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.84 (dd, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 6.96 (d, 2H), 3.74-3.69 (m, 3H), 3.61-3.57 (m, 6H), 3.19 (s, 2H), 3.11-3.09 (m, 2H), 33.04-3.01 (m, 2H), 2.90 (t, 2H), 2.41 (bs, 4H), 2.11-2.02 (m, 1H), 1.84-1.76 (m, 1H), 1.70-1.63 (m, 2H); MS (EI) $C_{31}H_{38}N_8O_3$: 571 (MH+).

[0933] N-{4-[2-({4-[2-(methyloxy)ethyl]-3,4-dihydro-2H-1,4-benzoxazin-7-yl}amino)-pyrimidin-4-yl]phenyl}-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.19 (s, 1H), 9.25 (s, 1H), 8.42 (d, 1H), 8.11 (d, 2H), 7.83 (d, 2H), 7.28-7.25 (m, 2H), 7.17 (dd, 1H), 6.68 (d, 1H), 4.15 (t, 2H), 3.72 (dd, 1H), 3.52 (t, 2H)), 3.41-3.36 (m, 4H), 3.27 (s, 3H), 2.90 (t, 2H), 2.10-2.01 (m, 1H), 1.84-1.75 (m, 1H), 1.70-1.63 (m, 2H); MS (EI) $C_{26}H_{30}N_6O_3$: 475 (MH+).

[0934] N-(4-{2-[(4-{4-[(2R)-tetrahydrofuran-2-ylcarbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 (s, 1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.84 (d, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 6.96 (d, 2H), 4.72 (dd, 1H), 3.82-3.72 (m, 3H), 3.69-3.58 (m, 4H), 3.08-3.03 (m, 4H), 2.90 (t, 2H), 2.11-1.98 (m, 3H), 1.88-1.75 (m, 3H), 1.70-1.65 (m, 2H); MS (EI) $C_{30}H_{35}N_7O_3$: 542 (MH+).

[0935] N-(4-{2-[(4-{4-[(2S)-tetrahydrofuran-2-ylcarbonyl]piperazin-1-yl}phenyl)-amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 (s, 1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.84 (d, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 6.96 (d, 2H), 4.72 (dd, 1H), 3.82-3.72 (m, 3H), 3.69-3.58 (m, 4H), 3.08-3.03 (m, 4H), 2.91 (t, 2H), 2.09-1.98 (m, 3H), 1.88-1.75 (m, 3H), 1.70-1.63 (m, 2H); MS (EI) $C_{30}H_{35}N_7O_3$: 542 (MH+).

[0936] N-{4-[2-(1,2,3,4-tetrahydroquinolin-6-ylamino)pyrimidin-4-yl]phenyl}-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.17 (s, 1H), 9.05 (s, 1H), 8.38 (d, 1H), 8.10 (dd, 2H), 7.84-7.81 (m, 2H), 7.29 (s, 1H), 7.21-7.18 (m, 2H), 6.40 (d, 1H), 5.36 (s, 1H), 3.72 (dd, 1H), 3.15 (t, 2H), 2.90 (t, 2H), 2.67 (t, 2H), 2.10-2.01 (m, 1H), 1.84-1.76 (m, 3H), 1.69-1.63 (m, 2H) ; MS (EI) $C_{24}H_{26}N_6O$: 415 (MH+).

[0937] N-{4-[2-({4-[(phenylmethyl)oxy]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.42 (s, 1H), 8.42 (d, 1H), 8.06 (d, 2H), 7.75-7.65 (m, 4H), 7.42-7.24 (m, 6H), 6.95 (d, 2H), 5.04 (s, 2H), 2.04 (s, 3H). MS (EI) for $C_{25}H_{22}N_4O_2$: 411 (MH+).

[0938] 4-(4-aminophenyl)-N-[4-(phenyloxy)phenyl]pyrimidin-2-amine: ^{1}H-NMR (400 MHz, d6-DMSO): 10.42 (s, 1H), 8.43 (d, 1H), 8.08 (d, 2H), 7.72 (d, 2H), 7.43-7.37 (m, 3H), 7.26-7.15 (m, 3H), 7.07-6.95 (m, 3H). MS (EI) for C22H18N4O: 355 (MH+).

[0939] N-[4-(2-{[4-(phenyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.64 (s, 1H), 8.49 (d, 1H), 8.11 (d, 2H), 7.85 (d, 2H), 7.75 (d, 2H), 7.38-7.32 (m, 3H), 7.10-7.03 (m, 3H), 6.97 (d, 1H). MS (EI) for $C_{24}H_{20}N_4O_2$: 397 (MH+).

[0940] N-(4-{2-[(4-{[2-(methyloxy)ethyl]amino}phenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.18 (s, 1H), 9.08 (s, 1H), 8.38 (d, 1H), 8.05 (d, 2H), 7.73 (d, 2H), 7.43 (d, 2H), 7.19 (d, 1H), 6.58 (d, 2H), 5.20 (t, 1H), 3.43 (t, 2H), 3.25 (s, 3H), 3.16 (t, 2H), 2.04 (s, 3H). MS (EI) for $C_{21}H_{23}N_5O_2$: 378 (MH+).

[0941] N-{4-[2-({4-[(pyridin-4-ylmethyl)oxy]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.43 (s, 1H), 8.60 (s,

2H), 8.43 (d, 1H), 8.10 (d, 2H), 7.79-7.72 (m, 4H), 7.43 (d, 1H), 7.30 (d, 1H), 7.01 (d, 2H), 5.08 (s,1H), 2.03 (s, 3H). MS (EI) for $C_{24}H_{21}N_5O_2$: 412 (MH+).

[0942] N-(4-{2-[(4-cyclohexylphenyl)amino]pyrimidin-4-yl}phenyl) acetamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.53 (s, 1H), 8.45 (d, 1H), 8.15 (d, 2H), 7.78-7.70 (m, 4H), 7.35 (d, 1H), 7.18 (d, 1H), 2.43-2.40 (m, 1H), 2.08 (s, 3H), 1.82-1.68 (m, 4H), 1.42-1.20 (m, 6H). MS (EI) for $C_{24}H_{26}N_4O$: 387 (MH+).

[0943] N-{4-[2-({4-[(tetrahydrofuran-2-ylmethyl)amino]phenyl}amino) pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.18 (s, 1H), 8.39 (d, 1H), 8.08 (d, 2H), 7.76 (d, 2H), 7.45 (d, 2H), 7.20 (d, 1H), 6.60 (d, 2H), 5.23 (t, 1H), 4.02-3.97 (m, 1H), 3.80-3.77 (m, 1H), 3.65-3.60 (m, 1H), 3.08-3.00 (m, 2H), 2.07 (s, 3H), 2.00-1.80 (m, 3H), 1.62-1.57 (m, 1H). MS (EI) for $C_{23}H_{25}N_5O_2$: 404 (MH+).

[0944] N-{4-[2-({4-[(phenylmethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.17 (s, 1H), 8.05 (d, 2H), 7.72 (d, 2H), 7.44-7.27 (m, 5H), 7.22-7.17 (m, 2H), 6.57 (d, 2H), 6.00 (t, 1H), 4.25 (d, 2H), 2.08 (s, 3H). MS (EI) for $C_{25}H_{23}N_5O$: 410 (MH+).

[0945] ethyl [4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl] acetate: ^{1}H-NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.53 (s, 1H), 8.45 (d, 1H), 8.15 (d, 2H), 7.78-7.70 (m, 4H), 7.32 (d, 1H), 7.17 (d, 2H), 4.05 (q, 2H), 3.45 (s, 2H), 1.35 (t, 3H). MS (EI) for $C_{22}H_{22}N_4O_3$: 391 (MH+).

[0946] N-(4-{2-[(3-chloro-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-acetamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.25 (s, 1H), 9.73 (s, 1H), 8.55 (d, 1H), 8.12 (d, 2H), 8.05 (s, 1H), 7.80-7.70 (m, 3H), 7.37 (d, 2H), 7.20 (d, 2H), 3.75 (t, 4H), 2.95 (t, 4H), 2.05 (s, 3H). MS (EI) for $C_{22}H_{22}ClN_5O_2$: 425 (MH+).

[0947] N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]-L-serinamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.50 (s, 1H), 8.45 (d, 1H), 8.18 (d, 2H), 7.83 (d, 2H), 7.70 (s, 1H), 7.37-7.30 (m, 2H), 6.90 (d, 1H), 3.82 (s, 3H), 3.72 (t, 4H), 3.60-3.57 (m, 2H), 3.43 (t, 1H), 2.92 (t, 4H). MS (EI) : 465 (MH+).

[0948] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-(1H-tetrazol-1-yl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.90 (s, 1H), 9.47 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.18 (d, 2H), 7.77 (d, 2H), 7.67 (d, 2H), 7.30 (d, 1H), 6.95 (d, 2H), 5.58 (s, 2H), 3.77 (t, 4H), 3.03 (t, 4H). MS (EI): 458 (MH+).

[0949] (3S)-3-hydroxy-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]butanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.19 (s, 1H), 9.48 (s, 1H), 8.48 (s, 1H), 8.17 (d, 2H), 7.78 (d, 2H), 7.65 (s, 1H), 7.31 (d,

2H), 6.88 (d, 1H), 4.80 (s, 1H), 4.15- 4.07 (m, 1H), 3.81 (s, 3H), 3.75 (t, 4H), 2.96 (t, 4H), 2.44-2.37 (m, 2H), 1.14 (d, 3H). MS (EI): 464 (MH+).

[0950] (3R)-3-hydroxy-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]butanamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.19 (s, 1H), 9.48 (s, 1H), 8.48 (s, 1H), 8.17 (d, 2H), 7.78 (d, 2H), 7.65 (s, 1H), 7.31 (d, 2H), 6.88 (d, 1H), 4.80 (s, 1H), 4.15-4.07 (m, 1H), 3.83 (s, 3H), 3.75 (t, 4H), 2.96 (t, 4H), 2.44-2.37 (m, 2H), 1.14 (d, 3H). MS (EI): 464 (MH+).

[0951] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2,5-dihydro-1H-pyrrole-2-carboxamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.19 (s, 1H), 9.40 (s, 1H), 8.43 (s, 1H), 8.17 (d, 2H), 7.83 (d, 2H), 7.68 (d, 2H), 7.30 (s, 1H), 6.96 (d, 2H), 6.02-5.98 (m, 1H), 5.93-5.89 (m, 1H), 4.60 (s, 1H), 3.82 (s, 2H), 3.75 (t, 4H), 3.05 (t, 4H). MS (EI): 443 (MH+).

[0952] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-[(2S)-pyrrolidin-2-yl]acetamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.86 (s, 1H), 10.10 (s, 1H), 9.37 (s, br, 1H), 9.28 (s, br, 1H), 8.55 (d, 1H), 8.20 (d, 2H), 7.95-7.85 (m, 4H), 7.70 (s, 2H), 7.45 (d, 1H), 4.10 (t, 4H), 3.83-3.78 (m, 2H), 3.73 (t, 4H), 3.25-3.18 (m, 1H), 3.03-2.95 (m, 2H), 2.20-2.10 (m, 1H), 2.00-1.80 (m, 2H), 1.68-1.56 (m, 1H). MS (EI): 459 (MH+).

[0953] 2,3-dihydroxy-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide: ^{1}H-NMR (400 MHz, d6-DMSO): 9.95 (s, 1H), 9.40 (s, 1H), 8.43 (d, 1H), 8.12 (d, 2H), 7.90 (d, 2H), 7.68 (d, 2H), 7.25 (s, 1H), 6.96 (d, 2H), 5.95 (s, br, 1H), 4.95 (s, br, 1H), 4.08 (t, 1H), 3.78-3.60 (m, 6H), 3.03 (t, 4H). MS (EI) : 436 (MH+).

[0954] 1-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenyl}amino) pyrimidin-4-yl]phenyl}-3-ethylurea: ^{1}H-NMR (400 MHz, d6-DMSO): 9.37 (s, 1H), 9.19 (s, 1H), 9.40 (d, 1H), 8.03 (d, 2H), 7.70 (d, 2H), 7.58 (d, 2H), 7.23 (d, 2H), 6.95 (d, 2H), 6.75 (t, 1H), 3.58 (t, 4H), 3.60 (t, 3H), 3.15-3.00 (m, 8H), 2.18 (s, 6H), 1.05 (t, 3H). MS (EI) : 503 (MH+).

[0955] N-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenyl}amino) pyrimidin-4-yl]phenyl}-3-(methyloxy)propanamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.40 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.78 (d, 2H), 7.67 (d, 2H), 7.27 (d, 1H), 6.95 (d, 2H), 3.73-3.58 (m, 6H), 3.24 (s, 3H), 3.14-3.00 (m, 6H), 2.60 (t, 3H), 2.20 (s, 6H). MS (EI): 518 (MH+).

[0956] N-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenyl}amino) pyrimidin-4-yl]phenyl}cyclopropanecarboxamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.26 (s, 1H), 9.40 (s, 1H), 8.43 (d, 1H), 8.14 (d, 2H), 7.78 (d, 2H), 7.67 (d, 2H), 7.27 (d, 1H), 6.95 (d, 2H),

3.70-3.58 (m, 4H), 3.10-3.00 (m, 6H), 2.20 (s, 6H), 1.84-1.80 (m, 1H), 0.83-0.80 (m, 4H). MS (EI): 500 (MH+).

[0957] N-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenylamino) pyimidin-4-yl]-phenyl}butanamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.18 (s, 1H), 9.40 (s, 1H), 8.43 (d, 1H), 8.12-8.05 (m, 3H), 7.80-7.68 (m, 3H), 7.28 (d, 1H), 6.99 (d, 2H), 2H), 3.70-3.60 (m, 4H), 3.28 (s, 2H), 3.14-3.00 (m, 4H), 2.35-2.20 (m, 8H), 1.64-1.58 (m, 2H), 0.95-0.88 (m, 3H). MS (EI): 502 (MH+).

[0958] N-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenyl}amino) pyrimidin-4-yl]phenyl}-N^2,N^2-dimethylglycinamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.00 (s, 1H), 9.40 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.82 (d, 2H), 7.65 (d, 2H), 7.25 (d, 1H), 6.95 (d, 2H), 3.65-3.57 (m, 4H), 3.23 (s, 2H), 3.12-3.00 (m, 6H), 2.28 (s, 6H), 2.20 (s, 6H). MS (EI): 517 (MH+).

[0959] N-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenyl}amino) pyrimidin-4-yl]phenyl}-D-alaninamide: ^{1}H-NMR (400 MHz, d6-DMSO): 9.40 (s, 1H), 8.43 (d, 1H), 8.15 (d, 2H), 7.85 (d, 2H), 7.70 (d, 2H), 7.30 (d, 1H), 6.95 (d, 2H), 3.70-3.57 (m, 4H), 3.50 (q, 1H), 3.18-3.00 (m, 6H), 1.83 (s, 6H), 1.21 (d, 3H). MS (EI): 503 (MH+).

[0960] N-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenyl}amino) pyrimidin-4-yl]phenyl}tetrahydrofuran-3-carboxamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.30 (s, 1H), 9.40 (s, 1H), 8.43 (d, 1H), 8.15 (d, 2H), 7.78 (d, 2H), 7.68 (d, 2H), 7.25 (d, 1H), 6.95 (d, 2H), 3.97 (t, 1H), 3.82-3.70 (m, 3H), 3.67-3.60 (m, 4H), 3.22-3.17 (m, 1 H), 3.12-3.00 (m, 4H), 2.35 (s, 6H), 2.12-2.05 (m, 2H). MS (EI): 530 (MH+).

[0961] (2R)-N-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-2-carboxamide: ^{1}H-NMR (400 MHz, d6-DMSO): 9.95 (s, 1H), 9.40 (s, 1H), 8.43 (d, 1H), 8.16 (d, 2H), 7.88 (d, 2H), 7.70 (d, 2H), 7.30 (d, 1H), 6.97 (d, 2H), 4.44-4.41 (m, 1H), 4.02-3.98 (m, 1H), 3.85-3.80 (m, 1H), 3.68-3.57 (m, 4H), 3.18-3.00 (m, 6H), 2.20 (s, 6H), 2.05-1.85 (m, 4H). MS (EI): 530 (MH+).

[0962] (2S)-N-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-2-carboxamide: ^{1}H-NMR (400 MHz, d6-DMSO): 9.95 (s, 1H), 9.40 (s, 1H), 8.43 (d, 1H), 8.16 (d, 2H), 7.88 (d, 2H), 7.70 (d, 2H), 7.30 (d, 1H), 6.98 (d, 2H), 4.45-4.42 (m, 1H), 4.02-3.98 (m, 1H), 3.85-3.80 (m, 1H), 3.70-3.57 (m, 4H), 3.20 (s, 2H), 3.10-3.00 (m, 6H), 2.22 (s, 6H), 2.05-1.85 (m, 4H). MS (EI): 530 (MH+).

[0963] N-(4-{2-[(6-morpholin-4-ylpyridin-3-yl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.38 (s, 1H), 10.10 (s, 2H), 9.03 (s, br,

1H), 8.75 (s, br, 1H), 8.60 (d, 2H), 8.30-8.20 (m, 3H), 7.85 (d, 2H), 7.55 (d, 2H), 4.48-4.42 (m, 1H), 3.82-3.70 (m, 8H), 3.37-3.20 (m, 2H), 2.43-2.40 (m, 1H), 2.10-1.95 (m, 3H). MS (EI): 446 (MH+).

[0964] 1-hydroxy-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-cyclopentanecarboxamide: ^{1}H-NMR (400 MHz, d6-DMSO): 9.95 (s, 1H), 9.45 (s, 1H), 8.42 (d, 1H), 8.10 (d, 2H), 7.95 (d, 2H), 7.70 (d, 2H), 7.30 (d, 1H), 7.05-6.95 (m, 2H), 5.68 (s, br, 1H), 3.80-3.70 (m, 4H), 3.15-3.05 (m, 4H), 2.10-1.97 (m, 3H), 1.87-1.68 (m, 5H). MS (EI) : 460 (MH+).

[0965] 2-hydroxy-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.95 (s, 1H), 9.39 (s, 1H), 8.43 (d, 1H), 8.12 (d, 2H), 7.90 (d, 2H), 7.70 (d, 2H), 7.28 (d, 1H), 6.95 (d, 2H), 5.75 (t, 1H), 4.03 (d, 2H), 3.78-3.70 (m, 4H), 3.10-3.00 (m, 4H). MS (EI): 406 (MH+).

[0966] 3-chloro-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-4-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.68 (s, 1H), 11.00 (s, 1H), 9.43 (s, 2H), 8.83 (s, 1H), 8.70 (d, 1H), 8.50 (d, 1H), 8.20 (d, 2H), 7.87 (d, 2H), 7.75-7.65 (m, 3H), 7.32 (d, 1H), 6.95 (d, 2H), 3.75 (t, 4H), 3.05 (t, 4H). MS (EI): 487 (MH+).

[0967] N-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.24 (s, br, 1H), 9.41 (s, 1H), 8.44 (d, 2H), 8.13 (d, 2H), 7.82 (d, 2H), 7.68 (d, 2H), 7.27 (d, 1H), 6.95 (d, 2H), 3.78-3.57 (m, 5H), 3.15-3.00 (m, 6H), 2.93 (t, 2H), 2.18 (s, 6H), 2.08-2.00 (m, 1H), 1.93-1.88 (m, 1H), 1.90-1.80 (m, 2H). MS (EI) : 529 (MH+).

[0968] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.18 (s, br, 1H), 9.18 (s, 1H), 8.40 (d, 1H), 8.13 (d, 2H), 7.78 (d, 2H), 7.63 (d, 2H), 7.25 (d, 1H), 6.93 (d, 2H), 3.77 (t, 4H), 3.07 (t, 4H), 2.16 (q, 2H), 1.10 (t, 3H). MS (EI): 404 (MH+).

[0969] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-pyridin-3-ylacetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.90 (s, 1H), 9.40 (s, 1H), 8.43 (s, 1H), 8.18 (d, 2H), 7.88 (d, 2H), 7.73-7.45 (m, 5H), 7.32 (d, 1H), 6.95 (d, 2H), 3.77 (t, 4H), 3.03 (t, 4H). MS (EI): 467 (MH+).

[0970] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyrimidine-5-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.82 (s, 1H), 9.42 (s, 1H), 9.38 (s, 1H), 9.31 (s, 2H), 8.45 (d, 1H), 8.20 (d, 2H), 7.97 (d, 2H), 7.70 (d, 2H), 7.33 (d, 1H), 6.95 (d, 2H), 3.77 (t, 4H), 3.03 (t, 4H). MS (EI): 454 (MH+).

[0971] N-[4-(2-{[3-(morpholin-4-ylmethyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400MHz, d_6-DMSO): 10.25 (s, 1H), 9.62 (s, 1H), 8.5 (d, 1H), 8.16 (d, 2H), 7.94 (s, 1H), 7.76 (d, 2H), 7.62 (d, 1H), 7.36 (d,1H), 7.26 (t, 1H), 6.9 (d, 1H), 3.6 (t, 4H), 3.45 (s, 2H), 2.39 (t, 4H), 2.1 (s, 3H), 1.86 (s, 3H). MS (EI) for $C_{23}H_{25}N_5O_2$: 404 (MH^+).

[0972] N-[4-(2-{[3-(1,3-dioxan-2-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.68 (s, 1H), 8.5 (d, 1H), 8.32 (s, 1H), 8.21 (d, 2H), 7.77 (d, 2H), 7.58 (d, 1H), 7.39 (d, 1H), 7.28 (t, 1H), 6.98 (d, 1H), 5,52 (s, 1H), 4.2 (dd, 2H), 4.0 (t, 2H), 2.1 (s, 3H), 2.05 (m, 1H), 1.5 (dd, 1H). MS (EI) for $C_{22}H_{22}N_4O_3$: 391 (MH^+).

[0973] N-(4-{2-[(6-aminopyridin-2-yl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 8.93 (s, 1H), 8.55 (d, 1H), 8.14 (d, 2H), 7.75 (d, 2H), 7.57 (d, 1H), 7.45-7.4 (m, 2H), 6.12 (d, 1H), 5.78 (s, 2H), 2.08 (s, 3H). MS (EI) for $C_{17}H_{16}N_6O$: 321 (MH^+).

[0974] N-(4-{2-[(6-aminopyrimidin-4-yl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.25 (s, 1H), 9.72 (s, 1H), 8.6 (d, 1H), 8.2-8.15 (m, 3H), 7.8 (d, 2H), 7.52 (d, 1H), 7.42 (s, 1H), 6.8 (br,2H), 2.08 (s, 3H). MS (EI) for $C_{16}H_{15}N_7O$: 322 (MH^+).

[0975] N-(4-morpholin-4-ylphenyl)-4-quinolin-6-ylpyrimidin-2-amine: ^{1}H NMR (400MHz, d_6-DMSO): 9.57 (s, 1H), 9.0 (d,1H), 8.8 (s, 1H), 8.58 (d, 1H), 8.52 (d, 2H), 8.18 (d, 1H), 7.72 (d, 2H), 7.63 (q, 1H), 7.51 (d, 1H), 6.96 (d, 2H), 3.75 (t, 4H), 3.07 (4H). MS(EI) for $C_{23}H_{21}N_5O$: 384 (MH^+).

[0976] N-(4-morpholin-4-ylphenyl)-4-quinoxalin-6-ylpyrimidin-2-amine: ^{1}H NMR (400MHz, d_6-DMSO): 9.6 (s, 1H), 9.04 (d, 2H), 8.88 (s, 1H), 8.63 (d, 1H), 8.6 (d, 1H), 8.27 (d, 1H), 7.7 (d, 2H), 7.63 (d, 1H), 6.95 (d, 2H), 3.75 (t, 4H), 3.06 (t, 4H). MS (EI) for $C_{22}H_{20}N_6O$: 385 (MH^+).

[0977] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-methylpyrimidin-4-yl)phenyl]-D-alaninamide: ^{1}H NMR (400MHz, d_6-DMSO): 9.25 (s, 1H), 8.3 (s, 1H), 7.7 (d, 2H), 7.66 (d, 2H), 7.6 (d, 2H), 6.85 (d, 2H), 3.5 (q, 1H), 3.03 (t, 4H), 2.5 (t, 4H), 2.35 (q, 2H), 2.21 (s, 3H), 1.23 (d, 3H), 1.02 (t, 3H). MS (EI) for $C_{26}H_{33}N_7O$: 460.5 (MH^+).

[0978] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-methylpyrimidin-4-yl)phenyl]-D-prolinamide: ^{1}H NMR (400MHz, d_6-DMSO): 10.27 (s, 1H), 9.25 (s, 1H), 8.3 (s, 1H), 7.8 (d, 2H), 7.65 (d, 2H), 7.61 (d, 2H), 6.86 (d, 2H), 3.73 (m, 1H), 3.03 (t, 4H), 2.9

(t, 2H), 2.5 (t, 4H), 2.36 (q, 2H), 2.2 (s, 3H), 2.1-2.0 (m, 1H), 1.85-1.75 (m, 1H), 1.67 (p,2H), 1.02 (t, 3H). MS (EI) for $C_{28}H_{35}N_7O$: 486 (MH^+).

[0979] N-ethyl-4-{4-[(4-{4-[(tetrahydrofuran-2-ylcarbonyl)amino]phenyl}pyrimidin-2-yl)amino]phenyl}piperazine-1-carboxamide: ^{1}H NMR (400MHz, d_6-DMSO): 9.93 (s, 1H), 9.4 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.88 (d, 2H), 7.67 (d, 2H), 7.3 (d, 1H), 6.96 (d, 2H), 6.6 (t, 1H), 4.43 (t, 1H), 4.0 (q, 1H), 3.86 (q, 1H), 3.42 (t, 4H), 3.05 (p, 2H), 3.01 (t, 4H), 2.27-2.17 (m, 1H), 2.06-1.97 (m, 1H), 1.88 (p, 2H), 1.02 (t, 3H). MS (EI) for $C_{28}H_{33}N_7O_3$: 516 (MH^+).

[0980] N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-1H-imidazole-4-carboxamide: ^{1}H NMR (400MHz, d_6-DMSO): 12.76 (br, 1H), 10.12(s, 1H), 9.39 (s, 1H), 8.43 (d, 1H), 8.13 (d, 2H), 8.01 (d, 2H), 7.87 (s, 2H), 7.7 (d, 2H), 7.3 (d, 1H), 6.93 (d, 2H), 3.74 (t, 4H), 3.05 (t, 4H). MS (EI) for $C_{24}H_{23}N_7O_2$: 442 (MH^+).

[0981] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1H-pyrrole-2-carboxamide: ^{1}H NMR (400MHz, d_6-DMSO): ^{1}H NMR (400MHz, d_6-DMSO): 11.75 (s, 1H), 10.0 (s, 1H), 9.39 (s, 1H), 8.44 (d, 1H), 8.15 (d, 2H), 7.92 (d, 2H), 7.7 (d, 2H), 7.3 (d, 1H), 7.12 (s, 1H), 7.0 (s, 1H), 6.93 (d, 2H), 6.2 (d, 1H), 3.74 (t, 4H), 3.05 (t, 4H). MS (EI) for $C_{25}H_{24}N_6O_2$: 441 (MH^+).

[0982] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1H-imidazole-2-carboxamide: ^{1}H NMR (400MHz, d_6-DMSO): 13.2 (br, 1H), 10.65 (s, 1H), 9.4 (s, 1H), 8.44 (d, 1H), 8.15 (d, 2H), 8.04 (d, 2H), 7.68 (d, 2H), 7.4-7.2 (m, 3H), 6.95 (d, 2H), 3.74 (t, 4H), 3.05 (t, 4H). MS (EI) for $C_{24}H_{23}N_7O_2$: 442 (MH^+).

[0983] N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(2-(pyridin-3-yl)-ethylamino)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.00 (s, 1H), 8.92 (d, 1H), 8.64 (d, 1H), 8.35 (d, 1H), 8.17-8.14 (m, 3H), 7.75 (d, 2H), 7.61 (d, 2H), 7.22 (d, 1H), 7.00 (d, 2H), 3.89-3.79 (m, 4H), 3.33-3.21 (m, 2H), 3.15-3.07 (m, 4H), 1.92 (s, 2H); MS (EI): 510.4 (MH+).

[0984] 2-(3-(4-methylpiperazin-1-yl)propylamino)-N-(4-(2-(4-morpholinophenyl-amino)pyrimidin-4-yl)phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.36 (d, 1H), 8.14 (d, 2H), 7.75 (d, 2H), 7.61 (d, 2H), 7.22 (d, 1H), 6.99 (d, 2H), 3.87-3.81 (m, 4H), 3.68 (s, 2H), 3.13-3.07 (m, 4H), 2.98-2.88 (m, 2H), 2.82-2.62 (m, 8H), 2.39 (s, 3H), 1.93 (s, 3H), 1.89-1.79 (m, 2H); MS (EI): 512.6 (MH+).

[0985] 2-(1-methylpiperidin-4-ylamino)-N-(4-(2-(4-morpholinophenylamino)-pyrimidin-4-yl)phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.35 (d, 1H), 8.14 (d, 2H), 7.75 (d, 2H), 7.61 (d, 2H), 7.22 (d, 1H), 6.99 (d, 2H), 3.87-3.81 (m, 4H), 3.47 (s, 2H),

3.15-3.09 (m, 4H), 3.06-2.95 (m, 2H), 2.69-2.55 (m, 1H), 2.39 (s, 3H), 2.38-2.22 (m, 2H), 2.03-1.93 (m, 2H), 1.90 (s, 2H), 1.63-1.43 (m, 2H); MS (EI): 545.2 (MH+).

[0986] 2-(2-amino-2-oxoethylamino)-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.27 (d, 1H), 8.04 (d, 2H), 7.68 (d, 2H), 7.53 (d, 2H), 7.13 (d, 1H), 6.91 (d, 2H), 4.54 (s, 2H), 3.79-3.73 (m, 4H), 3.39 (s, 2H), 3.06-3.00 (m, 4H), 1.86 (s, 2H); MS (EI): 462.1 (MH+).

[0987] 2-morpholino-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.0 (s, 1H), 9.40 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.82 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.94 (d, 2H), 3.78-3.70 (m, 4H), 3.69-3.61 (m, 4H), 3.08-3.02 (m, 4H), 2.56-2.46 (m, 4H); MS (EI): 475.3 (MH+).

[0988] 2-((2-aminoethyl)(methyl)amino)-N-(4-(2-(4-morpholinophenylamino)-pyrimidin-4-yl)phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.36 (d, 1H), 8.13 (d, 2H), 7.76 (d, 2H), 7.62 (d, 2H), 7.22 (d, 1H), 7.00 (d, 2H), 3.89-3.81 (m, 4H), 3.51 (s, 2H), 3.14-3.07 (m, 4H), 3.03-3.96 (m, 2H), 2.94-2.88 (m, 2H), 2.67 (s, 3H); MS (EI) $C_{25}H_{31}N_7O_2$: 462.4 (MH+).

[0989] 2-(1H-pyrazol-5-ylamino)-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)-phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.35 (d, 2H), 8.12 (d, 2H), 7.74 (d, 2H), 7.61 (d, 2H), 7.40 (s, 1H), 7.21 (d, 1H), 6.99 (d, 2H), 5.69 (s, 1H), 3.95 (s, 2H), 3.86-3.80 (m, 4H), 3.14-3.07 (m, 4H), 1.96 (s, 2H); MS (EI): 471.1 (MH+).

[0990] N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(piperazin-1-yl)-acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.39 (s, 1H), 9.53 (s, 1H), 8.87 (s, 2H), 8.48 (d, 1H), 8.17 (d, 1H), 7.80 (d, 2H), 7.10 (d, 2H), 7.33 (d, 1H), 7.04 (d, 2H), 3.82-3.74 (m, 4H), 3.32-3.24 (m, 2H), 3.19-3.09 (m, 4H), 3.08-3.02 (m, 2H), 2.95 (s, 2H), 2.79 (s, 2H), 1.96 (s, 2H); MS (EI): 474.2 (MH+).

[0991] (S)-benzyl 2-(2-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenylamino)-2-oxoethylamino)propanoate: ^{1}H-NMR (400MHz, CD3OD): 8.25 (d, 2H), 8.01 (d, 2H), 7.61 (d, 2H), 7.51 (d, 2H), 7.30-7.08 (m, 5H), 7.12 (d, 1H), 6.90 (d, 2H), 5.15-5.05 (m, 2H), 3.78-3.73 (m, 4H), 3.43 (q, 1H), 3.33 (d, 2H), 3.05-2.97 (m, 4H), 1.28 (d, 3H); MS (EI): 567.2 (MH+).

[0992] N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(pyrimidin-4-yl-amino)acetamide: ^{1}H-NMR (400MHz, CD3OD): 10.90 (s, 1H), 9.63 (s, 1H), 9.18 (d, 2H), 8.78 (s, 1H), 8.50 (s, 1H), 8.26 (d, 1H), 8.18 (d, 2H), 7.82-7.68 (m, 4H), 7.36 (d, 1H), 7.11 (d, 2H), 6.84 (s, 1H), 5.16 (s, 2H), 3.83-3.77 (m, 4H), 2.54-2.47 (m, 4H); MS (EI): 483.2 (MH+).

[0993] N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(piperidin-1-yl)-acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.98 (s, 1H), 9.84 (s, 1H), 9.65 (s, 1H), 8.50 (d, 1H), 8.20 (d, 2H), 7.90-7.70 (m, 4H), 7.36 (d, 1H), 7.11 (d, 2H), 4.12-4.07 (m, 2H), 3.87-3.77 (m, 4H), 3.62-3.42 (m, 2H), 3.23-3.13 (m, 4H), 2.51 (s, 2H), 1.94-1.64 (m, 6H), 1.45-1.38 (m, 2H); MS (EI): 473.4 (MH+).

[0994] 2-(ethylamino)-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.78 (s, 1H), 9.45 (s, 1H), 8.87 (s, 2H), 8.48 (d, 1H), 8.17 (d, 2H), 7.77 (d, 2H), 7.71 (d, 2H), 7.33 (d, 1H), 7.04 (d, 2H), 4.04-3.97 (m, 2H), 3.82-3.74 (m, 4H), 3.19-3.02 (m, 6H), 1.12 (t, 3H); MS (EI): 433.3 (MH+).

[0995] 2-(1H-imidazol-1-yl)-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.87 (s, 1H), 9.56 (s, 1H), 9.11 (s, 1H), 8.45 (d, 1H), 8.15 (d, 2H), 7.76 (d, 2H), 7.70 (d, 2H), 7.32 (d, 1H), 7.05 (d, 2H), 5.26 (s, 2H), 3.82-3.72 (m, 4H), 3.18-3.08 (m, 4H); MS (EI): 456.3 (MH+).

[0996] 4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)benzoic acid: ^{1}H-NMR (400MHz, d6-DMSO): 9.56 (s, 1H), 8.55 (d, 1H), 8.27 (d, 2H), 8.09 (d, 2H), 7.68 (d, 2H), 7.41 (d, 1H), 6.97 (d, 2H), 3.80-3.72 (m, 4H), 3.11-3.03 (m, 4H); MS (EI): 377.3 (MH+).

[0997] N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(phenylamino)-acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.29 (s, 1H), 9.59 (s, 1H), 8.46 (d, 1H), 8.14 (d, 2H), 7.79 (d, 2H), 7.73 (d, 2H), 7.33 (d ,1H), 7.19-7.00 (m, 4H), 6.70-6.50 (m, 3H), 3.96-3.88 (m, 4H), 3.22-3.12 (m, 4H); MS (EI): 481.1 (MH+).

[0998] 4-(4-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl)-N-(4-morpholinophenyl)-pyrimidin-2-amine: ^{1}H-NMR (400MHz, d6-DMSO): 9.53 (s, 1H), 8.54 (d, 1H), 8.35 (d, 2H), 8.12 (d, 2H), 7.65 (d, 2H), 7.40 (d, 1H), 6.92 (d, 1H), 3.76-3.70 (m, 4H), 3.06-3.00 (m, 4H), 2.59 (s, 3H); MS (EI): 415.3 (MH+).

[0999] (R)-4-(4-(4-(4-(2-aminopropanamido)phenyl)pyrimidin-2-ylamino)phenyl)-N-ethylpiperazine-1-carboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.41 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.82 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.96 (d, 2H), 6.59 (t, 1H), 3.54-3.46 (m, 1H), 3.44-3.36 (m, 4H), 3.12-2.97 (m, 6H), 1.24 (d, 3H), 1.02 (t, 2H), 0.95 (t, 2H); MS (EI): 487.1 (MH-).

[01000] (R)-2-amino-N-(4-(2-(4-(4-((R)-pyrrolidine-2-carbonyl)piperazin-1-yl)phenyl-amino)pyrimidin-4-yl)phenyl)propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.41 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.82 (d, 2H), 7.69 (d, 2H), 7.29 (d, 1H), 6.97 (d, 2H), 3.97-3.92 (m, 1H), 3.72-3.58 (m, 4H), 3.51-3.42 (m, 2H), 3.14-2.99 (m, 4H), 2.68-2.62 (m, 1H),

2.12-2.00 (m, 1H), 1.74-1.70 (m, 1H), 1.70-1.56 (m, 2H), 1.24 (d, 3H); MS (EI): 513.2 (MH-).

[01001] (R)-2-amino-N-(4-(2-(4-(4-((S)-pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.41 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.83 (d, 2H), 7.69 (d, 2H), 7.29 (d, 1H), 6.97 (d, 2H), 4.65 (t, 1H), 3.89-3.81 (m, 1H), 3.75-3.58 (m, 3H), 3.54-3.28 (m, 2H), 3.15-2.98 (m, 4H), 2.72-2.58 (m, 1H), 2.06-1.97 (m, 2H), 1.74-1.54 (m, 2H), 1.24 (d, 3H); MS (EI): 515.4 (MH+).

[01002] N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-alaninamide: 1H-NMR (400MHz, d6-DMSO): 9.40 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.83 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.97 (d, 2H), 3.57 (dd, 1H), 3.68-3.58 (m, 4H), 3.46 (dd, 1H), 3.12-2.98 (m, 4H), 1.23 (d, 3H), 1.12 (d, 3H); MS (EI): 489.4 (MH+).

[01003] (R)-2-amino-N-(4-(2-(4-(4-((S)-2-aminopropanoyl)piperazin-1-yl)phenylamino)-pyrimidin-4-yl)phenyl)propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.40 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.83 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.97 (d, 2H), 3.17 (s, 2H), 3.12-3.07 (m, 1H), 3.05-2.98 (m, 1H), 2.70-2.64 (m, 4H), 2.36-2.28 (m, 4H), 1.23 (d, 3H); MS (EI): 544.4 (MH+).

[01004] 3,3,3-trifluoro-2-hydroxy-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.42 (br s, 1H), 9.41 (s, 1H), 8.46 (d, 1H), 8.15 (d, 2H), 7.89 (d, 2H), 7.68 (d, 2H), 7.57 (br s, 1H), 7.31 (d, 1H), 6.94 (d, 2H), 4.83-4.74 (m, 1H), 3.78-3.70 (m, 4H), 3.09-3.01 (m, 4H); MS (EI): 474.3(MH+).

[01005] (R)-2-hydroxy-2-methyl-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.72 (s, 1H), 9.34 (s, 1H), 8.41 (d, 1H), 8.08 (d, 2H), 7.89 (d, 2H), 7.64 (d, 2H), 7.27 (d, 1H), 6.91 (d, 2H), 5.66 (s, 1H), 4.21-4.13 (m, 1H), 3.72 (q, 1H), 3.15 (d, 3H), 3.12-3.02 (m, 4H), 1.80-1.72 (m, 1H), 1.59-1.51 (m, 1H), 1.32 (s, 3H), 0.82 (t, 3H); MS (EI): 448.4 (MH+).

[01006] (S)-2-hydroxy-2-methyl-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)-phenyl)butanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.72 (s, 1H), 9.34 (s, 1H), 8.41 (d, 1H), 8.08 (d, 2H), 7.89 (d, 2H), 7.64 (d, 2H), 7.27 (d, 1H), 6.91 (d, 2H), 5.66 (s, 1H), 4.21-4.13 (m, 1H), 3.72 (q, 1H), 3.19-3.11 (d, 3H), 3.07-3.02 (m, 4H), 1.81-1.71 (m, 1H), 1.60-1.50 (m, 1H), 1.32 (s, 3H), 0.82 (t, 3H); MS (EI): 448.1 (MH+).

[01007] (R)-2-methoxy-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.07 (s, 1H), 9.35 (s, 1H), 8.41 (d, 1H), 8.11 (d, 2H), 7.84 (d, 2H), 7.64 (d, 2H), 7.26 (d, 1H), 6.90 (d, 2H), 3.89 (q, 1H), 3.75-3.67 (m, 4H), 3.30 (s, 3H), 3.04-2.96 (m, 4H), 1.31 (d, 3H); MS (EI): 434.3 (MH+).

[01008] (S)-2-methoxy-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.07 (s, 1H), 9.35 (s, 1H), 8.41 (d, 1H), 8.11 (d, 2H), 7.84 (d, 2H), 7.64 (d, 2H), 7.26 (d, 1H), 6.90 (d, 2H), 3.89 (q, 1H), 3.75-3.67 (m, 4H), 3.30 (s, 3H), 3.04-2.96 (m, 4H), 1.31 (d, 3H); MS (EI): 434.3 (MH+).

[01009] 1-amino-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-cyclopentanecarboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.39 (s, 1H), 8.44 (d, 1H), 8.14 (d, 2H), 7.87 (d, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 6.94 (d, 2H), 3.78-3.70 (m, 4H), 3.08-3.00 (m, 4H), 2.10-2.00 (m, 2H), 1.86-1.75 (m, 2H), 1.74-1.62 (m, 2H), 1.60-1.50 (m, 2H); MS (EI): 459.4 (MH+).

[01010] (S)-2-hydroxy-3,3-dimethyl-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.83 (s, 1H), 9.39 (s, 1H), 8.45 (d, 1H), 8.11 (d, 2H), 7.89 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.95 (d, 2H), 5.85 (d, 1H), 3.78-3.70 (m, 4H), 3.47 (q, 1H), 3.09-3.01 (m, 4H), 0.97 (d, 9H); MS (EI): 462.4 (MH+).

[01011] (R)-2-cyclohexyl-2-hydroxy-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.91 (s, 1H), 9.39 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.89 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.94 (d, 2H), 5.76 (br s, 1H), 3.85 (d, 1H), 3.77-3.69 (m, 4H), 3.10-3.02 (m, 4H), 1.80-1.51 (m, 6H), 1.30-1.02 (m, 5H); MS (EI): 488.1 (MH+).

[01012] (S)-2-cyclohexyl-2-hydroxy-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.91 (s, 1H), 9.39 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.89 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.94 (d, 2H), 5.76 (br s, 1H), 3.85 (d, 1H), 3.77-3.69 (m, 4H), 3.07-2.98 (m, 4H), 1.78-1.50 (m, 6H), 1.25-1.00 (m, 5H); MS (EI): 488.1 (MH+).

[01013] (S)-2-hydroxy-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.95 (s, 1H), 9.39 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.90 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.94 (d, 2H), 5.87 (br s, 1H), 4.23-4.15 (m, 1H), 3.79-3.71 (m, 4H), 3.08-3.00 (m, 4H), 2.51 (d, 3H); MS (EI): 420.4 (MH+).

[01014] 1-amino-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-cyclobutanecarboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.39 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.87 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.94 (d, 2H), 3.79-3.71 (m, 4H), 3.09-3.00 (m, 4H), 2.00-1.85 (m, 4H), 1.84-1.76 (m, 2H); MS (EI): 445.4 (MH+).

[01015] 4-(4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)-N-(4-morpholinophenyl)pyrimidin-2-amine: ^{1}H-NMR (400MHz, d6-DMSO): 9.57 (s, 1H), 8.57

(d, 1H), 8.39 (d, 2H), 8.26 (d, 2H), 7.67 (d, 2H), 7.44 (d, 1H), 6.95 (d, 2H), 3.78-3.72 (m, 4H), 3.09-3.03 (m, 4H), 2.46 (s, 3H); MS (EI): 415.0 (MH+).

[01016] N-(4-(2-(4-(4-ethylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-2-phenylacetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.45 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.12 (d, 2H), 7.76 (d, 2H), 7.64 (d, 2H), 7.38-7.33 (m, 3H), 7.27 (d, 1H), 6.92 (d, 2H), 3.69 (s, 2H), 3.10-3.04 (m, 4H), 2.35 (q, 3 H), 1.89 (s, 2H), 1.03 (t, 2H); MS (EI): 493.1 (MH+).

[01017] 1-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidin-2-one: ^{1}H-NMR (400MHz, d6-DMSO): 8.26 (d, 1H), 8.14 (d, 2H), 7.77 (d, 2H), 7.65 (d, 2H), 7.36 (d, 1H), 7.25 (d, 2H), 3.92-3.84 (m, 5H), 3.82-3.74 (m, 1H), 3.74-3.60 (m, 1H), 3.42-3.30 (m, 4H), 3.06-3.02 (m, 1H), 2.16-2.06 (m, 2H); MS (EI): 416.1 (MH+).

[01018] (S)-2-hydroxy-3-methyl-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.90 (s, 1H), 9.39 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.90 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.94 (d, 2H), 5.76 (d, 1H), 3.86 (dd, 1H), 3.78-3.73 (m, 4H), 3.08-3.02 (m, 4H), 0.96 (d, 3H), 0.87 (d, 3H); MS (EI): 448.3 (MH+).

[01019] (R)-2-hydroxy-3-methyl-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.90 (s, 1H), 9.39 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.90 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.94 (d, 2H), 5.76 (d, 1H), 3.86 (dd, 1H), 3.78-3.73 (m, 4H), 3.08-3.02 (m, 4H), 0.96 (d, 3H), 0.87 (d, 3H); MS (EI): 448.3 (MH+).

[01020] (R)-2-amino-N-(4-(2-(4-(4-(cyclobutanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.41 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.82 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.95 (d, 2H), 3.63-3.56 (m, 2H), 3.43-3.37 (m, 3H), 3.18 (d, 1H), 3.07-2.98 (m, 4H), 2.25-2.02 (m, 4H), 1.98-1.83 (m, 1H), 1.82-1.70 (m, 1H), 1.23 (d, 3H); MS (EI): 500.2 (MH+).

[01021] (R)-2-amino-N-(4-(2-(4-(4-pivaloylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.41 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.82 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.95 (d, 2H), 3.73-3.67 (m, 4H), 3.52-4.42 (m, 1H), 3.08-3.02 (m, 4H), 1.25 (s, 3H), 1.23 (d, 3H); MS (EI): 502.4 (MH+).

[01022] 4-[4-(ethylamino)phenyl]-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine: ^{1}H-NMR (400 MHz, DMSO): 9.202 (s, 1H), 8.3 (d, 2H), 7.948 (d, 2H), 7.689 (q, 2H), 7.134 (d, 1H), 6.93 (d, 2H), 6.657(d, 2H), 6.285 (t, 1H), 3.754 (t, 4H), 3.132-3.113 (m, 2H), 3.04 (t, 4H), 1.187 (t, 3H). MS (EI) for $C_{22}H_{25}N_5O$: 376.3 (MH^+).

[01023] N-{4-[2-(phenylamino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, DMSO): 10.233 (s, 1H), 9.63 (s, 1H), 8.513 (d, 1H), 8.147 (d, 2H), 7.854 (d, 2H), 7.774 (d, 2H), 7.362-7.305 (m, 3H), 6.961 (t, 1H), 2.098 (s, 3H). MS (EI) for $C_{18}H_{16}N_4O$: 305.3 (MH^+).

[01024] N-{4-[2-({4-[(4-ethylpiperazin-1 yl)carbonyl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H NMR (400 MHz, DMSO): 10.236 (s, 1H), 9.889 (s, 1H), 8.549 (d, 1H), 8.167-8.134 (m, 2H), 7.93-7.903 (m, 2H), 7.782 (d, 2H), 7.418-7.369 (m, 3H), 3.509 (br s, 4H), 2.378-2.324 (m, 6H), 2.097 (s, 3H), 1.025 (t, 3H). MS (EI) for $C_{25}H_{28}N_6O_2$: 445.4 (MH^+).

[01025] N-[4-(2-{[3-(morpholin-4-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H NMR (400 MHz, DMSO): 10.237 (s, 1H), 9.823 (s, 1H), 8.541 (d, 1H), 8.152 (d, 2H), 8.026 (t, 1H), 7.847 (d, 1H), 7.772 (d, 2H), 7.392 (m, 2H), 6.996 (d, 1H), 3.76-3.36 (br s, 8H), 2.094 (s, 3H). MS (EI) for $C_{23}H_{23}N_5O_3$: 418.3 (MH^+).

[01026] N-(4-(2-(3-(2-(dimethylamino)ethoxy)phenylamino)pyrimidin-4-yl)phenyl)-acetamide: ^{1}H NMR (400 MHz, DMSO): 10.471 (br s, 1H), 10.42 (s, 1H), 9.816 (s, 1H), 8.534 (d, 1H), 8.158 (d, 2H), 7.804 (d, 2H), 7.7 (t, 1H), 7.413-7.383 (m, 2H), 7.29 (t, 1H), 6.636 (m, 1H), 4.381 (t, 2H), 3.531 (q, 2H), 2.883 (d, 6H), 2.106 (s, 3H). MS (EI) for $C_{22}H_{25}N_5O_2$: 392.3 (MH^+).

[01027] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide: ^{1}H-NMR (400 MHz, DMSO): 10.532 (s, 1H), 9.407 (s, 1H), 8.47 (d, 1H) 8.189 (d, 2H), 7.982 (m, 4H), 7.7-7.54 (m, 5H), 7.325 (d, 1H), 6.959 (d, 2H), 3.747 (t, 4H), 3.054 (t, 4H). MS (EI) for $C_{27}H_{25}N_5O_2$: 452.1 (MH^+).

[01028] N-[4-(2-{[4-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400 MHz, DMSO): 10.222 (s, 1H), 9.433 (s, 1H), 8.455 (s, 1H), 8.121 (d, 2H), 7.725 (q, 4H), 7.293 (d, 1H), 6.91 (d, 2H), 3.739 (s, 3H), 2.093 (s, 3H). MS (EI) for $C_{19}H_{18}N_4O_2$: 335 (MH^+).

[01029] 4-(4-chlorophenyl)-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine: ^{1}H-NMR (400 MHz, DMSO): 9.488 (s, 1H), 8.514 (d, 1H), 8.185 (d, 2H), 7.665-7.606 (q, 4H), 7.354 (d, 1H), 6.918 (d, 2H), 3.757 (t, 4H), 3.048 (t, 4H). MS (EI) for $C_{20}H_{19}ClN_4O$: 367 (MH^+).

[01030] N-[4-(2-{[3-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400 MHz, DMSO): 10.235 (s, 1H), 9.633 (s, 1H), 8.52 (d, 1H), 8.15 (d, 2H), 7.65 (t, 1H), 7.369 (d, 2H), 7.209 (t, 1H), 6.535 (q, 1H), 3.77 (s, 3H), 2.092 (s, 3H). MS (EI) for $C_{19}H_{18}N_4O_2$: 335 (MH^+).

[01031] 1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-(phenylmethyl)urea: ^{1}H NMR (400 MHz, DMSO): 9.347 (s, 1H), 9 (s, 1H), 8.414 (d, 1H), 8.067 (d, 2H), 7.688 (d, 2H), 7.583 (d, 2H), 7.351-7.31 (m, 4H), 7.237 (d, 2H), 6.943 (d, 2H), 6.831 (t, 1H), 4.33 (d, 2H), 3.742 (t, 4H), 3.044 (t, 4H). MS (EI) for $C_{28}H_{28}N_6O_2$: 481.4 (MH^+).

[01032] N-(4-{2-[(4-{4-[(2S)-pyrrolidin-2-ylmethyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H NMR (400 MHz, DMSO): 10.231 (br s, 1H), 9.376 (s, 1H), 8.443 (d, 1H), 8.134 (d, 2H), 7.848 (d, 2H), 7.663 (d, 2H), 7.29 (d, 1H), 6.936 (d, 2H), 3.74 (m, 1H), 3.505 (m, 1H), 3.08-2.89 (m, 6H), 2.64 (m, 2H), 2.374 (m, 1H), 2.069 (m, 1H), 1.938-1.648 (m, 9H), 1.452 (m, 1H). MS (EI) for $C_{30}H_{38}N_8O$: 527.3 (MH^+).

[01033] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2,3-dihydro-1H-isoindole-1-carboxamide: ^{1}H NMR (400 MHz, DMSO): 11.345 (s, 1H), 10.326 (br s, 1H), 9.525 (s, 1H), 9.479 (br s, 1H), 8.474 (d, 1H), 8.19 (d, 2H), 7.799 (d, 2H), 7.7-7.627 (m, 3H), 7.469-7.415 (m, 3H), 7.323 (d, 1H), 7.025 (d, 2H), 5.688 (br s, 1H), 4.578 (m, 2H), 3.757 (s, 4H), 3.105 (s, 4H). MS (EI) for $C_{29}H_{28}N_6O_2$: 492.58 (MH^+).

[01034] N-{4-[2-({4-[4-(2-piperazin-1-ylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, DMSO): 9.938 (s, 1H), 9.412 (s, 1H), 8.456 (d, 1H), 7.135 (d, 2H), 7.886 (d, 2H), 7.691 (d, 2H), 7.304 (d, 1H), 6.975 (d, 2H), 4.45 (m, 1H), 4.01 (q, 1H), 3.878 (q, 1H), 3.705 (br s, 4H), 3.592 (br s, 4H), 3.148 (s, 2H), 3.1 (br s, 2H), 3.02 (br s, 2H), 2.719 (br s, 4H), 2.354 (br s, 4H), 2.21 (m, 1H), 2.021 (m, 1H), 1.862 (m, 2H). MS (EI) for $C_{31}H_{38}N_8O_3$: 571 (MH^+).

[01035] N-(4-{2-[(4-{4-[(4-chloro-1-methyl-1H-pyrazol-3-yl)methyl]piperazin-1-yl}-phenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H NMR (400 MHz, DMSO): 10.215 (s, 1H), 9.363 (s, 1H), 8.439 (d, 1H), 8.131 (d, 2H), 7.901 (s, 1H), 7.841 (d, 2H), 7.651 (d, 2H), 7.286 (d, 1H), 6.916 (d, 2H), 3.802 (s, 3H), 3.7 (m, 1H), 3.47 (s, 2H), 3.048 (br s, 4H), 2.92 (t, 2H), 2.568 (t, 4H), 2.08 (m, 1H), 1.816 (m, 1H), 1.691 (m, 2H). MS (EI) for $C_{30}H_{34}ClN_9O$: 572.4 (MH^+).

[01036] N-{4-[2-({4-[4-(2-hydroxyethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}-D-prolinamide: ^{1}H NMR (400 MHz, DMSO): 10.176 (s, 1H), 9.927 (s, 1H), 8.374 (d, 1H), 8.065 (d, 2H), 7.773 (d, 2H), 7.587 (d, 2H), 7.219 (d, 1H), 6.857 (d, 2H), 4.396 (br s, 1H), 3.715 (t, 1H), 3.468 (br s, 4H), 2.996-2.954 (m, 6H), 2.873 (t, 2H), 2.74 (s, 1H0, 2.368 (t, 2H) 2.369 (t, 2H) 2.368 (t, 2H), 2.038 (m, 1H), 1.749 (m, 1H), 1.61 (m, 2H). MS (EI) for $C_{27}H_{33}N_7O_2$: 488.3 (MH^+).

[01037] N-(4-{2-[(4-{4-[(1-methyl-1H-pyrrol-2-yl)methyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H NMR (400 MHz, DMSO):

10.194 (s, 1H), 9.349 (s, 1H), 8.42 (d, 1H), 8.11 (d, 2H), 7.822 (d, 2H), 7.636 (d, 2H), 7.267 (d, 1H), 7.076 (s, 1H), 6.902 (d, 2H), 6.75 (s, 1H), 3.738 (m, 1H), 3.701 (s, 3H), 3.553 (s, 2H), 3.306 (m, 4H), 3.031 (br s, 4H), 2.892 (t, 2H), 2.728 (s, 1H), 2.054 (m, 1H), 1.803 (m, 1H), 1.647 (m, 2H). MS (EI) for $C_{31}H_{36}N_8O$: 538.3 (MH^+).

[01038] N-(4-{2-[(4-{4-[(2R)-pyrrolidin-2-ylmethyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H NMR (400 MHz, DMSO): 8.319-8.251 (m, 3H), 7.86 (d, 2H), 7.636 (d, 2H), 7.56 (d, 1H), 7.282 (d, 2H), 4.479 (t, 1H), 4.106 (m, 1H), 3.514 (br s, 4H), 3.496-3.303 (m, 11H),. 2.252 (m, 1H), 2.342 (m, 1H), 2.19-2.094 (m, 6H), 1.835 (m, 1H). MS (EI) for $C_{30}H_{36}N_8O$: 528.5 (MH^+).

[01039] (2S,3aS,7aS)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-octahydro-1H-indole-2-carboxamide: ^{1}H NMR (400 MHz, DMSO): 10.857 (s, 1H), 9.84 (s, 1H), 9.714 (br s, 1H), 8.531 (d, 1H), 8.207 (m, 3H), 7.816 (d, 4H), 7.42 (d, 1H), 4.448 (m, 1H), 3.874 (t, 4H), 3.681 (br s, 1H), 3.322 (t, 4H), 2.504 (m, 2H), 2.09 (m, 1H), 1.913 (m, 1H), 1.615 (m, 4H), 1.371-1.259 (m, 3H). MS (EI) for $C_{29}H_{34}N_6O_2$: 499.5 (MH^+).

[01040] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-cyclopropane-carboxamide: ^{1}H NMR (400 MHz, DMSO): 10.476 (s, 1H), 9.383 (s, 1H), 8.443 (d, 1H), 8.123 (d, 2H), 7.768 (d, 2H), 7.686 (d, 2H), 7.279 (d, 1H), 6.946 (d, 2H), 3.74 (t, 4H), 3.046 (t, 4H), 1.824 (m, 1H), 0.829 (m, 4H). MS (EI) for $C_{24}H_{25}N_5O_2$: 416 (MH^+).

[01041] N-[4-(2-{[4-(dimethylamino)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.38 (s, br, 1H), 9.92 (s, br, 1H), 8.85 (d, 2H), 8.11 (d, 2H), 7.92 (d, 2H), 7.79 (d, 2H), 7.67 (s, 2H), 7.42 (d, 1H), 3.10 (s, 6H), 2.10 (s, 3H). MS (EI): 348 (MH+).

[01042] N-(4-{2-[(4-chlorophenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.30 (s, 1H), 9.88 (s, 1H), 8.53 (d, 1H), 8.14 (d, 2H), 7.87 (d, 2H), 7.75 (d, 2H), 7.41 (d, 2H), 7.37 (1H), 2.10 (s, 3). MS (EI): 339 (MH+).

[01043] N-[4-(2-{[4-(1H-pyrrol-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.26 (br s, 1H), 9.78 (br s, 1H), 8.52 (d, 1H), 8.15 (d, 2H), 7.92 (d, 2H), 7.77 (d, 2H), 7.54 (d, 2H), 7.38 (d, 1H), 7.31 (m, 2H), 6.24 (m, 2H). 2.09 (s, 3H). MS (EI): 370 (MH+).

[01044] ethyl 1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-piperidine-4-carboxylate: ^{1}H NMR (400 MHz, d6-DMSO): 10.25 (s, 1H), 9.49 (br s, 1H), 8.45 (d, 1H), 8.11 (d, 2H), 7.75 (d, 4H0, 7.30 (d, 1H), 4.10 (q, 2H), 3.56 (d, 2H), 2.86 (br s, 2H), 2.09 (s, 3H), 1.97 (br d, 2H), 1.35 (m, 2H), 1.30 (m, 2H), 0.88 (t, 3H). MS (EI): 460 (MH+).

[01045] N-[4-(2-{[4-(4-phenylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.28 (s, 1H), 9.68 (br s 1H), 9.49 (d, 1H), 8.14 (d, 2H), 7.82 (br s 1H), 7.70 (d, 2H), 7.35 (d, 1H), 7.28 (t, 2H), 7.08 (d, 2H), 6.88 (t, 1H), 3.45 (br s, 8H), 2.09 (s, 3H). MS (EI): 465 (MH+).

[01046] N-{4-[2-({4-[(2R,6S)-2,6-dimethylmorpholin-4-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.28 (s, 1H), 9.79 (br s, 1H), 8.47 (d, 1H), 8.12 (d, 1H), 8.10 (d, 1H), 7.80 (br d, 2H), 7.75 (d, 2H), 7.37 (d, 2H), 3.69 (br s, 4H), 3.54 (d, 2H), 2.07 (s, 3H), 1.16 (s, 3H), 1.14 (s, 3H) MS (EI): 418 (MH+).

[01047] 4-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-tetrahydro-2H-thiopyran-4-carboxamide 1,1-dioxide: 1H NMR (400 MHz, d6-DMSO):11.06 (br s, 1H), 9.97 (br s, 1H), 9,29 (s, 2H0), 8.56 (d, 1H), 8.21 (d, 2H), 7.94 (d, 2H), 7.89 (d, 1H), 7.58 (s, 1H), 7.47 (d, 1H), 5.32 (br s, 3H), 3.99 (s, 4H), 3.48 (m, 4H), 3.38 (m, 4H), 2.84 (m, 2H), 2.46 (m, 2H). MS (EI): 523 (MH+).

[01048] (2R)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-piperazine-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.33 (br s, 1H), 10.31 (br s, 1H), 8.58 (d, 1H), 8.22 (d, 2H), 7.94 (d, 2H), 7.89 (d, 2H), 7.77 (d, 2H), 7.53 (d, 1H), 4.55 (d, 1H), 4.08 (s, 5H), 3.54 (s, 5H), 3.43 (m, 2H), 3.28 (m, 2H). MS (EI): 460 (MH+).

[01049] 2-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1,2,3,4-tetrahydronaphthalene-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.10 (br s, 1H), 10.07 (br s, 1H), , 8.89 (d, 2H), 8.56 (d, 1H), 8.20 (d, 2H), 7.98 (d, 2H), 7.92 (d, 2H), 7.70 (d, 2H), 7.48 (d, 1H), 7.10 (m, 4H), 6.10 (br s, 3H), 4.40 (s, 4H), 3.70 (d, 1H), 3.50 (s, 4H), 3.39 (d, 4H), 2.89 (m, 1H), 2.71 (m, 1H), 2.1 (m, 1H), 1.26 (m, 1H), 1.17 (m, 1H). MS (EI): 521 (MH+).

[01050] 4-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-tetrahydro-2H-pyran-4-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO):10.85 (br s, 1H), 9.85 (br s , 1H), 8.97 (s, 2H), 8.53 (d, 1H), 8.20 (d, 2H), 7.94 (d, 2H), 7.83 (d, 2), 7.43 (d, 2H), 4.39 (br s, 3H), 3.94 (s, 4H), 3.87 (d, 4H), 3.72 (m, 4H), 2.45 (m, 2H), 1.97 (d, 2H). MS (EI): 475 (MH+).

[01051] (4S)-4-hydroxy-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.38 (s, 1H), 10.25 (m, 1H), 10.31 (s, 1H), 8.84 (m, 1H), 8.57 (d, 1H), 8.21 (d, 2H), 7.93 (d, 2H), 7.87 (d, 2H), 7.75 (d, 2H), 7.49 (d, 1H), 6.62 (m, 1H), 4.50 (s, 1H), 4.06 (s, 4H), 3.53 (s, 4H), 3.42 (m, 1H)< 3.17 (m, 1H), 2.45 (t, 1H), MS (EI): 461 (MH+).

[01052] 1-acetyl-4-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)piperidine-4-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.72 (s, 1H), 8.51 (d, 1H), 8.14 (dd, 2H), 8.12 (d, 1H), 8.08 (d, 1H), 7.00 (dd, 1H), 7.39 (d, 1H), 7.17 (d, 1H), 4.15 (d, 1H), 3.70 (m, 4H), 3.68 (d, 1H), 4.41(m, 4H),3.41 (m, 4H), 3.01 (m,1H), 2.93 (m, 4H), 2.02 (s, 3H), 1.98 (m, 1H), 1.84 (m, 1H). MS (EI): 516 (MH+).

[01053] O-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-serinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.51 (br s, 1H), 9.99 (br s, 1H), 8.55 (d, 1H), 8.50 (br s, 2H), 8.19 (d, 2H), 7.88 (m, 4H), 7.46 (d, 1H), 5.19 (br s, 3H), 4.36 M, 1H), 4.02 (br s, 4H), 3.88 (m, 1H), 3.46 br s, 4H), 3.33 (s, 3H). MS (EI): 449 (MH+).

[01054] N-[4-(2-{[4-(2,6-dimethylmorpholin-4-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.30 (br s, 1H), 9.83 (br s, 1H), 8.50 (d, 1H), 8.14 (d, 2H), 7.81 (br s, 1H), 7.77 (d, 2H), 7.39 (d, 1H),4.10 (br s, 4H), 3.56 (d, 2H), 2.10 (s, 3H), 1.18 (s, 3H), 1.71 (s, 3H). MS (EI): 418 (MH+).

[01055] N-(4-{2-[(4-piperidin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400 MHz, d6-DMSO): 10.32 (br s, 1H), 9.89 (br s, 1H), 8.52 (d, 1H), 8.11 (d, 2H), 7.94 (d, 2H), 7.76 (d, 4H), 7.40 (d, 1H), 3.45 (Br s, 4H), 3.36 (6H), 2.07 (s, 3H). MS (EI): 388 (MH+).

[01056] O-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-serinamide: ^{1}H NMR (400 MHz, d6-DMSO):11.51 (br s, 1H), 9.99 (br s, 1H), 8.55 (d, 1H), 8.50 (br s, 2H), 8.19 (d, 2H), 7.88 (m, 4H), 7.46 (d, 1H), 5.19 (br s, 3H), 4.36 M, 1H), 4.02 (br s, 4H), 3.88 (m, 1H), 3.46 br s, 4H), 3.33 (s, 3H). MS (EI): 449 (MH+).

[01057] 1,1-dimethylethyl (2R)-2-{[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]carbonyl}pyrrolidine-1-carboxylate: ^{1}H NMR (400 MHz, d6-DMSO): 10.26 (brs ,1H), 9.38 (br s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.78 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.94 (d, 2H), 4.22 (m, 1H), 3.74 (m, 4H), 3.43 (m, 1H), 3.34 (m, 1H), 3.04 (m, 4H), 2.20 (m, 1H), 1.90 (m, 1H), 1.81 (m, 1H), 1.40 (s, 3H), 1.27 (s, 6H). (MS (EI) 4: 545 (MH+).

[01058] 4-[4-(methylsulfonyl)phenyl]-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine: ^{1}H-NMR (400 MHz, d6-DMSO): 9.62 (s,1H), 8.59 (d, 1H), 8.39 (d, 2H), 8.09 (d, 2H), 7.68 (d, 2H), 7.45 (d, 1H), 7.0 (s, br, 1H), 3.81-3.71 (m, 4H), 3.29 (s, 3H), 3.04-3.14 (m, 4H). MS (EI): 411 (MH+).

[01059] 4-[3-(methylsulfonyl)phenyl]-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine: ^{1}H-NMR (400 MHz, d6-DMSO): 9.60 (s,1H), 8.72 (s, 1H), 8.57 (d, 1H), 8.47 (d, 1H), 8.10

(d, 1H), 7.85 (d, 1H), 7.66 (d, 1H), 7.46 (d, 1H), 6.92 (d, 1H), 3.81-3.71 (m, 4H), 3.31 (s, 3H), 3.0-3.11 (m, 4H). MS (EI): 411 (MH+).

[01060] 4-[4-(methylthio)phenyl]-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine: ^{1}H-NMR (400 MHz, d6-DMSO): 9.42 (s,1H), 8.46 (d, 1H), 8.09 (d, 2H), 7.66 (d, 2H), 7.40 (d, 2H), 7.31 (d, 1H), 6.92 (d, 2H), 3.79-3.69 (m, 4H), 3.1-3.0 (m, 4H), 2.55 (s, 3H). MS (EI): 379 (MH+).

[01061] N-(4-{2-[(3-bromo-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s,1H), 9.72 (s, 1H), 8.52 (d, 1H), 8.27 (d, 1H), 8.13 (d, 2H), 7.81-7.71 (m, 3H), 7.42-7.32 (m, 1H), 7.18 (d, 1H), 3.78-3.69 (m, 4H), 2.97-2.87 (m, 4H), 2.09 (s, 3H). MS (EI): 469 (MH+).

[01062] N-[4-(2-{[4-{[2-(diethylamino)ethyl]oxy}-3-(4-ethylpiperazin-1-yl)phenyl]-amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO):10.21 (s, 1H), 9.36 (s,1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.73 (d, 2H), 7.54 (s, 1H), 7,36-7.26 (m, 2H), 6,88 (d, 1H), 4.02-3.92 (m, 2H), 2.81-2.71 (m, 2H), 2.59-2.49 (m, 4H), 2.45-2.35 (m, 2H), 1.04 (t, 3H), 0.98 (t, 6H). MS (EI): 533 (MH+).

[01063] N^2,N^2-dimethyl-N-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)glycinamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.99 (s,1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.11 (d, 2H), 7.84 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.95 (d, 2H), 3.63-3.59 (m, 4H), 3.25 (s, 3H), 3.11 (s, 2H), 3.10-3.05 (m, 2H, 3.04-2.99 (m, 2H), 2.65 (t, 2h), 2.29 (s, 6H). MS (EI): 519 (MH+).

[01064] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-cyclobutane-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.99 (s, 1H), 9.37 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.77 (d, 2H), 7.67 (d, 2H), 7.27 (d, 1H), 6.93 (d, 2H), 3.75 (m, 4H), 3.32 (m, 1H), 3.05 (m, 4H), 2.24 (m, 2H), 2.12 (m, 2H), 1.93 (m, 1H), 1.82 (m, 1H). MS (EI): 430 (MH+).

[01065] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)azetidine-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.10 (s, 1H), 9.36 (s, 1H), 8.42 (d, 1H), 8.09 (d, 2H), 7.74 (d, 2H), 7.64 (d, 2H), 7.24 (d, 1H), 6.91 (d, 2H), 3.71 (m, 4H), 3.61 (m, 1H), 3.52 (m, 4H), 3.02 (m, 4H). MS (EI): 431 (MH+).

[01066] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.35 (s, 1H), 8.40 (d, 1H), 8.08 (d, 2H), 7.73 (d, 2H), 7.64 (d, 2H), 7.24 (d, 1H), 6.90 (d, 2H), 3.72 (m, 4H), 3.41 (m, 4H), 3.02 (m, 4H), 2.83 (m, 1H), 2.62 (m, 1H), 1.58 (m, 2H), 1.37 (m, 1H),. MS (EI): 459 (MH+).

[01067] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-4-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.12 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.76 (d, 2H), 7.67 (d, 2H), 7.27 (d, 1H), 6.93 (d, 2H), 3.74 (m, 4H), 3.37 (m, 1H), 3.03 (m, 4H), 3.00 (m, 1H), 2.50 (m, 2H), 2.47 (m, 1H), 1.73 (m, 2H), 1.54 (m, 2H). MS (EI): 459 (MH+).

[01068] 2-(methyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.05 (s, 1H), 9.36 (s, 1H), 8.42 (d, 1H), 8.09 (d, 2H), 7.82 (d, 2H), 7.65 (d, 2H), 7.26 (d, 1H), 6.91 (d, 2H), 4.02 (s, 2H), 3.72 (m, 4H), 3.38 (s, 3H), 3.02 (m, 4H). MS (EI): 420 (MH+).

[01069] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.85 (s, br, 1H), 9.31 (s, 1H), 8.36 (d, 1H), 8.04 (d, 2H), 7.75 (d, 2H), 7.60 (d, 2H), 7.21 (d, 1H), 6.87 (d, 2H), 3.67 (m, 4H), 3.21 (m, 1H), 2.98 (m, 4H), 2.93 (m, 1H), 2.47 (m, 1H), 1.70 (m, 2H), 1.37 (m, 4H). MS (EI) 2: 459 (MH+).

[01070] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.37 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.82 (d, 2H), 7.66 (d, 2H), 7.27 (d, 1H), 6.93 (d, 2H), 3.75 (m, 4H), 3.62 (br s, 2H), 3.32 (m, 2H), 3.05 (m, 4H). MS (EI): 405 (MH+).

[01071] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)furan-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.44 (s, 1H), 9.40 (s, 1H), 8.46 (d, 1H), 8.16 (d, 2H), 7.98 (m, 1H), 7.93 (m, 2H), 7.68 (d, 2H), 7.39 (d, 1H), 7.30 (d, 1H), 6.93 (d, 2H), 6.74 (d, 1H), 3.75 (m, 4H), 3.05 (m, 4H). MS (EI): 3: 442 (MH+).

[01072] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.91 (s, 1H), 9.36 (s, 1H), 8.41 (d, 1H), 8.09 (d, 2H), 7.84 (d, 2H), 7.67 (d, 2H), 7.22 (d, 1H), 6.91 (d, 2H), 4.41 (dd, 1H), 3.96 (q, 1H), 3.83 (q, 1H), 3.72 (m, 4H), 3.02 (m, 4H), 2.19 (m, 1H), 1.99 (m, 1H), 1.88 (m, 2H). MS (EI): 446 (MH+).

[01073] 5-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-pyrazine-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.90 (s, 1H), 9.38 (s, 1H), 9.17 (s, 1H), 8.71 (s, 1H), 8.43 (d, 1H), 8.16 (d, 2H), 8.08 (d, 2H), 7.66 (d, 2H), 7.31 (d, 1H), 6.92 (d, 2H), 3.71 (m, 4H), 3.03 (m, 4H), 2.62 (s, 3H),. MS (EI): 468 (MH+).

[01074] 2-(ethyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.94 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.10 (d,

2H), 7.80 (d, 2H), 7.65 (d, 2H), 7.26 (d, 1H), 6.91 (d, 2H), 4.05 (s, 2H), 3.72 (m, 4H), 3.55 (q, 2H), 3.02 (m, 4H), 1.17 (t, 3H). MS (EI): 434 (MH+).

[01075] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-(phenyloxy)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.37 (s, 1H), 9.39 (s, 1H), 8.44 (d, 1H), 8.14 (d, 2H), 7.82 (d, 2H), 7.67 (d, 2H), 7.31 (m, 3H), 6.98 (m, 4H), 4.75 (s, 2H), 3.73 (m, 4H), 3.04 (m, 4H). MS (EI): 482 (MH+).

[01076] methyl 4-[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]-4-oxobutanoate: ^{1}H NMR (400 MHz, d6-DMSO): 10.28 (s, 1H), 9.37 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.67 (d, 2H), 7.27 (d, 1H), 6.93 (d, 2H), 3.74 (m, 4H), 3.60 (s, 3H), 3.06 (m, 4H), 2.65 (m, 4H). MS (EI): 462 (MH+).

[01077] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)butanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.15 (s, 1H), 9.37 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.75 (d, 2H), 7.67 (d, 2H), 7.26 (d, 1H), 6.93 (d, 2H), 3.73 (m, 4H), 3.04 (m, 4H), 2.33 (t, 2H), 1.63 (q, 2H), 0.93 (t, 3H). MS (EI): 418 (MH+).

[01078] 2-(2-methylphenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.44 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.76 (d, 2H), 7.67 (d, 2H), 7.27 (m, 2H), 7.16 (m, 3H), 6.93 (d, 2H), 3.75 (m, 6H), 3.03 (m, 4H), 2.31 (m, 3H). MS (EI): 480 (MH+).

[01079] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-cyclopentane-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.14 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.77 (d, 2H), 7.67 (d, 2H), 7.27 (d, 1H), 6.93 (d, 2H), 3.75 (m, 4H), 3.04 (m, 4H), 2.80 (m, 1H), 1.87 (m, 2H), 1.72 (m, 4H), 1.55 (m, 2H). MS (EI): 444 (MH+).

[01080] (2S)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-azetidine-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.09 (br s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.86 (d, 2H), 7.67 (d, 2H), 7.29 (d, 1H), 6.94 (d, 2H), 4.32 (t, 1H), 3.73 (m, 4H), 3.62 (m, 1H), 3.06 (m, 4H), 2.58 (m, 1H), 2.29 (m, 1H), 0.99 (m, 1H). MS (EI): 431 (MH+).

[01081] N-{4-[2-({4-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.19 (s, 1H), 9.19 (s, 1H), 8.40 (d, 1H), 8.11 (d, 2H), 7.83 (d, 2H), 7.56 (d, 2H), 7.22 (d, 1H), 6.53 (d, 2H), 3.72 (m, 1H), 3.41 (m, 1H), 3.33 (m, 1H), 3.22 (m, 1H), 3.02 (m, 1H), 2.90 (m, 2H), 2.78 (m, 1H), 2.20 (s, 6H), 2.05 (m, 2H), 1.75 (m, 2H), 1.66 (m, 2H). MS (EI): 472 (MH+).

[01082] 4-(4-aminophenyl)-N-{4-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]phenyl}-pyrimidin-2-amine: ^{1}H NMR (400 MHz, d6-DMSO): 8.99 (s, 1H), 8.25 (s, 1H), 7.87 (d, 2H), 7.57 (d, 2H), 7.05 (d, 1H), 6.63 (d, 2H), 6.52 (d, 2H), 5.70 (s, 2H), 3.41 (m, 1H), 3.31 (m, 1H), 3.21 (m, 1H), 3.01 (m, 1H), 2.77 (m, 1H), 2.20 (s, 6H), 2.15 (m, 1H), 1.77 (m, 1H). MS (EI): 375 (MH+).

[01083] N-{4-[2-({4-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-3-(methyloxy)propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.19 (s, 1H), 8.40 (d, 1H), 8.10 (d, 2H), 7.75 (d, 2H), 7.58 (d, 2H), 7.23 (d, 1H), 6.54 (d, 2H), 3.63 (t, 2H), 3.41 (m, 1H), 3.25 (m, 3H), 3.21 (m, 1H), 3.01 (m, 1H), 2.77 (m, 1H), 2.59 (t, 2H), 2.52 (m, 1H) 2.20 (s, 6H), 2.13 (m, 1H), 1.79 (m, 1H). MS (EI): 461 (MH+).

[01084] 1-ethyl-3-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)-amino]pyrimidin-4-yl}phenyl)urea: ^{1}H NMR (400 MHz, d6-DMSO): 9.35 (s, 1H), 8.76 (s, 1H), 8.41 (d, 1H), 8.04 (d, 2H), 7.68 (d, 2H), 7.54 (d, 2H), 7.23 (d, 1H), 6.95 (d, 2H), 6.26 (t, 1H), 3.59 (m, 4H), 3.56 (q, 2H), 3.23 (s, 3H), 3.14 (m, 2H), 3.07 (m, 2H), 3.01 (m, 2H), 2.61 (t, 2H), 1.06 (t, 3H). MS (EI): 504 (MH+).

[01085] 3-(methyloxy)-N-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)-amino]pyrimidin-4-yl}phenyl)propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.76 (d, 2H), 7.68 (d, 2H), 7.27 (d, 1H), 6.95 (d, 2H), 3.60 (m, 8H), 3.25 (s, 3H), 3.23 (s, 3H), 3.08 (m, 2H), 3.01 (m, 2H), 2.61 (m, 4H). MS (EI): 519 (MH+).

[01086] N-{4-[2-({4-[4-(3-hydroxypropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.19 (s, 1H), 9.40 (s, 1H), 8.42 (d, 1H), 8.10 (d, 2H), 7.84 (d, 2H), 7.67 (d, 2H), 7.28 (d, 1H), 6.95 (d, 2H), 3.74 (dd, 1H), 3.66 (t, 2H), 3.62 (m, 4H), 3.09 (m, 2H), 3.03 (m, 2H), 2.91 (t, 2H), 2.52 (m, 2H), 2.05 (m, 1H), 1.79 (m, 1H), 1.66 (m, 2H). MS (EI): 516 (MH+).

[01087] N-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)-D-alaninamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.40 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.82 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.95 (d, 2H), 3.59 (m, 4H), 3.57 (t, 2H), 3.46 (m, 1H), 3.23 (s, 3H), 3.07 (m, 2H), 3.02 (m, 2H), 2.61 (t, 2H), 1.24 (d, 3H). MS (EI): 504 (MH+).

[01088] N-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.11 (d, 2H), 7.83 (d, 2H), 7.66 (d, 2H), 7.28 (d, 1H), 6.95 (d,

2H), 3.75 (dd, 1H), 3.60 (m, 4H), 3.56 (t, 2H), 3.23 (s, 3H), 3.08 (m, 2H), 3.03 (m, 2H), 2.91 (t, 2H), 2.61 (t, 2H), 2.17 (m, 1H), 1.80 (m, 1H), 1.67 (m, 2H). MS (EI): 530 (MH+).

[01089] N-2-,N-2-dimethyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.98 (s, 1H), 9.39 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.83 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.93 (d, 2H), 3.74 (m, 4H), 3.11 (s, 2H), 3.05 (m, 4H), 2.29 (s, 6H). MS (EI): 433 (MH+).

[01090] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.18 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.13 (d, 2H), 7.83 (d, 2H), 7.67 (d, 2H), 7.27 (d, 1H), 6.93 (d, 2H), 3.74 (m, 4H), 3.71 (m, 1H), 3.04 (m, 4H), 2.90 (t, 2H), 2.05 (m, 1H), 1.80 (m, 1H), 1.66 (m, 2H). MS (EI): 445 (MH+).

[01091] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-phenyl-propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.12 (s, 1H), 9.31 (s, 1H), 8.37 (d, 1H), 8.05 (d, 2H), 7.67 (d, 2H), 7.60 (d, 2H), 7.21 (m, 5H), 7.12 (m, 1H), 6.83 (d, 2H), 3.67 (m, 4H), 2.98 (m, 4H), 2.86 (t, 2H), 2.61 (t, 2H). MS (EI): 480 (MH+).

[01092] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenyl-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.44 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.77 (d, 2H), 7.67 (d, 2H), 7.34 (m, 4H), 7.26 (m, 2H), 6.93 (d, 2H), 3.75 (m, 4H), 3.69 (m, 2H), 3.04 (m, 4H). MS (EI): 466 (MH+).

[01093] N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-fluoro-6-iodobenzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.16 ppm (s, 1H), 8.64 ppm (t, 1H), 8.30 ppm (d, 1H), 8.06 ppm (d, 2H), 7.70 ppm (m, 3H), 7.30 ppm (m, 1H), 7.20 ppm (m, 1H), 7.13 ppm (m, 1H), 7.07 ppm (m, 1H), 3.34 ppm (m, 4H), 2.08 ppm (s, 3H), 1.83 ppm (m, 2H); MS (EI) $C_{22}H_{21}FIN_5O_2$: 533.9 (MH^+).

[01094] N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-difluoro-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.78 ppm (s, 1H), 10.12 ppm (s, 1H), 9.70 ppm (s, 1H), 8.50 ppm (d, 1H), 8.39 ppm (s, 1H), 8.12 ppm (d, 2H), 7.73 ppm (d, 2H), 7.61 ppm (m, 1H), 7.47 ppm (m, 1H), 7.40 ppm (m, 1H), 7.27 ppm (m, 4H), 2.09 ppm (s, 3H); MS (EI) $C_{25}H_{19}F_2N_5O_2$: 460 (MH^+).

[01095] N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,4,5-trifluoro-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.52 ppm (s, 1H), 10.29 ppm (s, 1H), 9.71 ppm (s, 1H), 8.50 ppm (d, 1H), 8.36 ppm (s, 1H), 8.20 ppm (d, 2H), 7.87 ppm (m, 1H), 7.75 ppm (d, 3H), 7.51 ppm (m, 1H), 7.37 ppm (d, 1H), 7.28 ppm (m, 2H), 2.09 ppm (s, 3H); MS (EI) $C_{25}H_{18}F_3N_5O_2$: 478 (MH^+).

[01096] N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.27 ppm (s, 1H), 10.21 ppm (s, 1H), 9.67 ppm (s, 1H), 8.51 ppm (d, 1H), 8.47 ppm (s, 1H), 8.13 ppm (d, 2H), 8.00 ppm (m, 2H), 7.75 ppm (m, 2H), 7.58 ppm (m, 3H), 7.48 ppm (m, 1H), 7.37 ppm (d, 1H), 7.29 ppm (m, 2H), 2.09 ppm (s, 3H); MS (EI) $C_{25}H_{21}N_5O_2$: 424(MH^+).

[01097] N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-3,5-difluoro-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.37 ppm (s, 1H), 10.20 ppm (s, 1H), 9.70 ppm (s, 1H), 8.51 ppm (d, 1H), 8.41 ppm (s,1H), 8.21 ppm (d, 2H), 7.73 ppm (m, 4H), 7.55 ppm (m, 2H), 7.37 ppm (d, 1H), 7.29 ppm (m, 2H), 2.08 ppm (s, 3H); MS (EI) $C_{25}H_{19}F_2N_5O_2$: 468.0 (MH^+).

[01098] N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-chloro-6-fluoro-4-methylbenzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.72 ppm (s, 1H), 10.20 ppm (s, 1H), 9.69 ppm (s, 1H), 8.50 ppm (d, 1H), 8.41 ppm (s,1H), 8.21 ppm (d, 2H), 7.74 ppm (d, 2H), 7.50 ppm (m, 2H), 7.37 ppm (d, 1H), 7.28 ppm (m, 8H), 2.38 ppm (s, 3H), 2.08 ppm (s, 3H); MS (EI) $C_{26}H_{21}ClFN_5O_2$: 490.0 (MH^+).

[01099] N-(4-{2-[(3-{[(2,6-dimethylphenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 ppm (s, 1H), 9.36 ppm (s, 1H), 8.47 ppm (d, 1H), 8.16 ppm (d, 2H), 7.72 ppm (d, 2H), 7.35 ppm (s, 1H), 7.31 ppm (d, 1H), 7.12 ppm (m, 1H), 7.07 ppm (m, 2H), 6.99 ppm (m, 3H), 6.38 ppm (d, 1H), 5.46 ppm (t, 1H), 4.14 ppm (d, 2H), 2.36 ppm (s, 6H), 2.08 ppm (s, 3H); MS (EI) $C_{27}H_{27}N_5O$: 438.1 (MH^+).

[01100] N-(3-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)thiophene-2-carboxamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.66 ppm (s, 1H), 10.28 ppm (s, br, 2H), 10.10 ppm (s, 1H), 8.74 ppm (s, 1H), 8.63 ppm (d, 1H), 8.25 ppm (m, 2H), 7.94 ppm (m, 3H), 7.75 ppm (t, 1H), 7.55 ppm (t, 1H), 7.45 ppm (m, 2H), 7.26 ppm (m, 1H), 6.97 ppm (m,1H); MS (EI) $C_{21}H_{17}N_5O_2S$: 388.0 (MH^+).

[01101] N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-1-methylpiperidine-4-carboxamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 ppm (s, 1H), 9.84 ppm (s, 1H), 9.60 ppm (s, 1H), 8.49 ppm (d, 1H), 8.29 ppm (s, 1H), 8.20 ppm (d, 2H), 7.74 ppm (d, 2H), 7.36 ppm (m, 2H), 7.18 ppm (m, 2H), 2.84 ppm (m, 2H), 2.31 ppm (m, 1H), 2.17 ppm (s, 3H), 2.09 ppm (s, 3H), 1.87 ppm (m, 2H), 1.72 ppm (m, 4H); MS (EI) $C_{25}H_{28}N_5O_2$: 445 (MH^+).

[01102] 4-(4-aminophenyl)-N-[3-(morpholin-4-ylsulfonyl)phenyl]pyrimidin-2-amine: ^{1}H-NMR (400MHz, d_6-DMSO): 9.94 ppm (s, 1H), 8.76 ppm (s, 1H), 8.42 ppm (d, 1H), 7.98

ppm (d, dH), 7.90 ppm (m, 1H), 7.57 ppm (t, 1H), 7.28 ppm (m, 2H), 6.65 ppm (d, 2H), 5.81 ppm (s, 2H), 3.64 ppm (m, 4H), 2.90 ppm (m, 4H); MS (EI) $C_{20}H_{21}N_5O_3S$: 412 (MH^+).

[01103] N-(4-{2-[(3-{[(2-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 ppm (s, 1H), 9.35 ppm (s, 1H), 8.45 ppm (d, 1H), 8.12 ppm (d, 2H), 7.74 ppm (d, 2H), 7.43 ppm (m, 2H), 7.29 ppm (m, 2H), 7.16 ppm (m, 3H), 6.99 ppm (m, 2H), 6.21 ppm (m, 2H), 4.33 ppm (d, 2H), 2.09 ppm (s, 3H); MS (EI) $C_{25}H_{22}FN_5O$: 428 (MH^+).

[01104] N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 ppm (s, 1H), 9.31 ppm (s, 1H), 8.46 ppm (d, 1H), 8.13 ppm (d, 2H), 7.75 ppm (d, 2H), 7.30 ppm (d, 1H), 7.13 ppm (s, 1H), 6.94 ppm (m, 2H), 6.20 ppm (d, 1H), 5.01 ppm (s, 2H), 2.10 ppm (s, 3H); MS (EI) $C_{18}H_{17}IN_5O$: 320 (MH^+).

[01105] N-(4-{2-[(3-{[(4-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.26 ppm (s, 1H), 9.33 ppm (s, 1H), 8.45 ppm (d, 1H), 8.13 ppm (d, 2H), 7.75 ppm (d, 2H), 7.37 ppm (m, 2H), 7.31 ppm (m, 3H), 7.21 ppm (m, 2H), 6.97 ppm (m, 2H), 6.23 ppm (m, 2H), 4.48 ppm (d, 2H), 2.09 ppm (s, 3H); MS (EI) $C_{25}H_{23}N_5O$: 410 (MH^+).

[01106] N-(4-{2-[(3-{[(3-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.36 ppm (s, 1H), 9.35 ppm (s, 1H), 8.45 ppm (d, 1H), 8.12 ppm (d, 2H), 7.76 ppm (d, 2H), 7.33 ppm (m, 2H), 7.19 ppm (m, 3H), 6.99 ppm (m, 3H), 6.32 ppm (t, 1H), 6.20 ppm (m, 2H), 4.30 ppm (d, 2H), 2.09 ppm (s, 3H); MS (EI) $C_{25}H_{22}FN_5O$: 428 (MH^+).

[01107] N-(4-{2-[(3-{[(4-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 ppm (s, 1H), 9.33 ppm (s, 1H), 8.45 ppm (d, 1H), 8.12 ppm (d, 2H), 7.74 ppm (d, 2H), 7.39 ppm (m, 2H), 7.30 ppm (d, 1H), 7.21 ppm (s, 1H), 7.13 ppm (t, 2H), 6.96 ppm (m, 2H), 6.22 ppm (m, 2H), 2.09 ppm (s, 3H); MS (EI) $C_{25}H_{22}FN_5O$: 428 (MH^+).

[01108] 4-[4-({4-[4-(butanoylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-N-ethyl-piperazine-1-carboxamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 ppm (s, 1H), 9.39 ppm (s, 1H), 8.44 ppm (d, 1H), 8.11 ppm (d, 2H), 7.77 ppm (d, 2H), 7.68 ppm (d, 2H), 7.28 ppm (d, 1H), 6.96 ppm (d, 2H), 6.59 ppm (t, 1H), 3.43 ppm (t, 4H), 3.07 ppm (m, 2H), 3.02 ppm (t, 4H), 2.34 ppm (t, 2H), 1.63 ppm (m, 2H), 1.02 ppm (t, 3H), 0.98 ppm (t, 3H); MS (EI) $C_{27}H_{33}N_7O_2$: 488 (MH^+).

[01109] N-{4-[2-({4-[4-(2-piperazin-1-ylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}butanamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.18 ppm (s, 1H), 9.40 ppm (s,

1H), 8.44 ppm (d, 1H), 8.11 ppm (d, 2H), 7.77 ppm (d, 2H), 7.68 ppm (d, 2H), 7.28 ppm (d, 1H), 6.97 ppm (d, 2H), 3.72 ppm (m, 2H), 3.59 ppm (m, 2H), 3.13 ppm (m, 4H), 3.01 ppm (m, 2H), 2.67 ppm (m, 4H), 2.33 ppm (m, 4H), 1.63 ppm (m, 2H), 0.93 ppm (t, 3H); MS (EI) $C_{30}H_{38}N_8O_2$: 543 (MH^+).

[01110] N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-butanamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.15 ppm (s, 1H), 9.40 ppm (s, 1H), 8.44 ppm (d, 1H), 8.11 ppm (d, 2H), 7.76 ppm (d, 2H), 7.69 ppm (d, 2H), 7.28 ppm (d, 1H), 6.97 ppm (d, 2H), 3.79 ppm (m, 1H), 3.62 ppm (m, 4H), 3.06 ppm (m, 4H), 2.33 ppm (t, 2H), 1.91 ppm (br. s, 2H), 1.63 ppm (m, 2H), 1.09 ppm (d, 3H), 0.93 ppm (t, 3H); MS (EI) $C_{27}H_{33}N_7O_2$: 488 (MH^+).

[01111] N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-butanamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 ppm (s, 1H), 9.41 ppm (s, 1H), 8.44 ppm (d, 1H), 8.11 ppm (d, 2H), 7.77 ppm (d, 2H), 7.69 ppm (d, 2H), 7.28 ppm (d, 1H), 6.97 ppm (d, 2H), 3.85 ppm (m, 1H), 3.62 ppm (m, 4H), 3.04 ppm (m, 5H), 2.62 ppm (m, 1H), 2.34 ppm (t, 2H), 2.00 ppm (m, 1H), 1.62 ppm (m, 6H), 0.93 ppm (t, 3H); MS (EI) $C_{29}H_{35}N_7O_2$: 514 (MH^+).

[01112] (3R)-1-(2-hydroxyethyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyrrolidine-3-carboxamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 ppm (s, 1H), 9.38 ppm (s, 1H), 8.44 ppm (d, 1H), 8.11 ppm (d, 2H), 7.76 ppm (d, 2H), 7.67 ppm (d, 2H), 7.28 ppm (d, 1H), 6.94 ppm (d, 2H), 4.50 ppm (m, 1H), 3.75 ppm (m, 4H), 3.49 ppm (m, 2H), 3.05 ppm (m, 6H), 2.91 ppm (t, 1H), 2.67 ppm (m, 1H), 2.56 ppm (m, 3H), 1.98 ppm (m, 2H); MS (EI) $C_{27}H_{32}N_6O_3$: 489 (MH^+).

[01113] N-(4-{2-[(3-fluoro-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 ppm (s, 1H), 9.69 ppm (s, 1H), 8.51 ppm (d, 1H), 8.13 ppm (d, 2H), 7.85 ppm (d, 2H), 7.79 ppm (m, 1H), 7.52 ppm (m, 1H), 7.37 ppm (d, 1H), 7.03 ppm (t, 1H), 3.74 ppm (m, 5H), 3.14 ppm (br.s, 1H), 2.95 ppm (m, 4H), 2.91 ppm (m, 2H), 2.06 ppm (m, 1H), 1.80 ppm (m, 1H), 1.66 ppm (m, 2H); MS (EI) $C_{25}H_{27}FN_6O_2$: 463 (MH^+).

[01114] N-(4-{2-[(3-fluoro-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-alaninamide: ^{1}H-NMR (400MHz, d_6-DMSO): 9.69 ppm (s, 1H), 8.51 ppm (d, 1H), 8.13 ppm (d, 2H), 7.84 ppm (d, 2H), 7.79 ppm (m, 1H), 7.54 ppm (m, 1H), 7.37 ppm (m, 1H), 7.37 ppm (m, 1H), 7.03 ppm (t, 1H), 3.74 ppm (m, 4H), 3.47 ppm (m, 1H), 2.95 ppm (m, 4H), 1.23 ppm (d, 3H); MS (EI) $C_{23}H_{25}FN_6O_2$: 437 (MH^+).

[01115] N-(4-{2-[(3-methyl-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 ppm (s, 1H), 9.45 ppm (s, 1H), 8.46 ppm (d, 1H), 8.14 ppm (d, 2H), 7.85 ppm (d, 2H), 7.63 ppm (d, 2H), 7.32 ppm (d, 1H), 7.32 ppm (d, 1H), 3.73 ppm (m, 5H), 3.08 ppm (br.s., 1H), 2.90 ppm (t, 2H), 2.80 ppm (m, 4H), 2.27 ppm (s, 3H), 2.06 ppm (m, 1H), 1.80 ppm (m, 1H), 1.66 ppm (m, 2H); MS (EI) $C_{26}H_{30}N_6O_2$: 459 (MH^+).

[01116] N-(4-{2-[(3-methyl-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-alaninamide: ^{1}H-NMR (400MHz, d_6-DMSO): 9.44 ppm (s, 1H), 8.47 ppm (d, 1H), 8.14 ppm (d, 2H), 7.83 ppm (d, 2H), 7.64 ppm (m, 2H), 7.32 ppm (d, 1H), 7.02 ppm (m, 1H), 3.73 ppm (m, 4H), 3.46 ppm (m, 1H), 2.80 ppm (m, 4H), 2.28 ppm (m, 4H), 1.23 ppm (d, 3H); MS (EI) $C_{24}H_{28}N_6O_2$: 433 (MH^+).

[01117] 1-hydroxy-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-cyclopropanecarboxamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.14 ppm (s, 1H), 9.39 ppm (s, 1H), 8.44 ppm (d, 1H), 8.11 ppm (d, 2H), 7.94 ppm (d, 2H), 7.68 ppm (d, 2H), 7.29 ppm (d, 1H), 6.94 ppm (d, 2H), 6.81 ppm (s, 1H), 3.74 ppm (m, 4H), 3.05 ppm (m., 4H), 1.18 ppm (m, 2H), 1.00 ppm (m, 2H); MS (EI) $C_{24}H_{25}N_5O_3$: 432 (MH^+).

[01118] N-(4-(2-(4-(4-(4-chloro-2,6-dimethylphenylsulfonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.42 (s, 1H), 8.41 (m, 1H), 8.08 (d, 2H), 7.77 (s, 1H), 7.71 (d, 2H), 7.64 (m, 2H), 7.57 (s, 1H), 7.27 (m, 1H), 6.93 (m, 2H), 3.41 (m, 4H), 3.15 (m, 4H), 2.53 (s, 3H), 2.37 (s, 3H), 2.06 (s, 3H). MS (EI): 591 (MH+).

[01119] N-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.31 (s, 1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.96 (d, 2H), 3.96 (t, 1H), 3.75 (m, 5H), 3.60 (m, 2H), 3.32 (m, 1H), 3.19 (m, 1H), 3.12 (s, 2H), 3.10 (m, 2H), 3.01 (m, 2H), 2.68 (m, 4H), 2.32 (m, 4H), 2.10 (m, 2H). MS (EI): 571 (MH+).

[01120] N-(4-(2-(4-(4-pivaloylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.30 (s, 1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.95 (d, 2H), 3.96 (t, 1H), 3.74 (m, 6H), 3.19 (m, 2H), 3.05 (m, 4H), 2.10 (q, 2H), 1.23 (s, 9H). MS (EI): 529 (MH+).

[01121] 1-ethyl-3-(4-(5-methyl-2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)urea: ^{1}H NMR (400 MHz, d6-DMSO): 9.24 (s, 1H), 8.87 (s, 1H), 8.29 (s, 1H),

7.64 (d, 2H), 7.59 (m, 2H), 7.53 (m, 2H), 6.88 (d, 2H), 6.41 (m, 1H), 3.73 (m, 4H), 3.12 (m, 2H), 3.02 (m, 4H), 2.23 (s, 3H), 1.06 (t, 3H). MS (EI): 433 (MH+).

[01122] 3-methoxy-N-(4-(5-methyl-2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.17 (s, 1H), 9.30 (s, 1H), 8.31 (s, 1H), 7.74 (m, 2H), 7.66 (m, 4H), 6.90 (m, 2H), 3.74 (m, 4H), 3.64 (t, 2H), 3.26 (s, 3H), 3.03 (m, 4H), 2.59 (m, 2H), 2.22 (s, 3H). MS (EI): 448 (MH+).

[01123] N-(4-(2-(4-(4-(ethylsulfonyl)piperazine-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.38 (s, 1H), 8.42 (d, 1H), 8.08 (d, 2H), 7.72 (d, 2H), 7.66 (d, 2H), 7.26 (d, 1H), 6.95 (d, 2H), 3.36 (m, 4H), 3.12 (m, 4H), 2.48 (m, 2H), 2.07 (s, 3H), 1.22 (t, 3H). MS (EI): 481 (MH+).

[01124] 4-(4-(4-(4-acetamidophenyl)pyrimidin-2-ylamino)phenyl)-N-ethylpiperazine-1-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.41 (d, 1H), 8.08 (d, 2H), 7.72 (d, 2H), 7.64 (d, 2H), 7.25 (d, 1H), 6.94 (d, 2H), 6.57 (d, 1H), 3.50 (m, 2H), 3.39 (m, 4H), 2.99 (m, 4H), 2.07 (s, 3H), 1.00 (t, 3H). MS (EI): 460 (MH+).

[01125] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)morpholine-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.87 (s, 1H), 9.37 (s, 1H), 8.43 (s, 1H), 8.04-8.16 (d, 2H), 7.81-7.93 (d, 2H), 7.60-7.72 (d, 2H), 7.27 (s,1H), 6.85-6.99 (d, 2H), 4.08-4.69 (s, br, 1H), 4.00-4.07 (d, 1H), 3.85-3.94 (d, 1H), 3.72 (s, 3H), 3.51-3.63 (d, 1H), 2.58-2.80 (m, 3H), 1.86 (s, 6H). MS (EI): 461 (MH+).

[01126] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-beta-alaninamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.38 (s, 1H), 10.65 (d, 1H), 8.07-8.16 (d, 2H), 7.72-7.81 (d, 2H), 7.62-7.72 (d,2H), 7.28 (s, 1H), 6.89-6.98 (d, 2H). MS (EI): 419 (MH+).

[01127] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)phenylalaninamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.39 (s, 1H), 8.42-8.46 (d, 1H), 8.09-8.14 (d, 2H), 7.75-7.81 (d, 2H), 7.64-7.70 (d, 2H), 7.23-7.32 (m, 6H), 7.16-7.22 (m, 2H), 6.90-6.97 (d, 2H), 3.71-3.78 (m, 4H), 3.57-3.63 (m, 1H), 3.02-3.08 (m, 4H), 2.98-3.02 (m, 1H), 2.71-2.79 (m, 1H). MS (EI): 495 (MH+).

[01128] N^2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-glycinamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.39 (s, 1H), 8.45 (s, 1H), 8.09-8.17 (d, 2H), 7.78-7.86 (d, 2H), 7.65-7.73 (d, 2H), 7.29 (s, 1H), 6.90-7.00 (d, 2H), 3.74 (s, 4H), 3.05 (s, 4H), 2.33 (s, 3H), 1.92 (s, 1H). MS (EI):419 (MH+).

[01129] 2-cyclopentyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.13 (s, 1H), 9.37 (s, 1H), 8.42-

8.45 (d, 1H), 8.07-8.14 (d, 2H), 7.73-7.79 (d, 2H), 7.65-7.71 (d, 2H), 7.25-7.28 (d, 1H), 6.90-6.97 (d, 2H), 3.71-3.77 (m, 4H), 3.02-3.07 (m, 4H), 2.33-2.37 (d, 2H), 2.20-2.30 (m, 1H), 1.71-1.82 (m, 2H), 1.48-1.66 (m, 4H), 1.14-1.25 (m, 2H). MS (EI): 458 (MH+).

[01130] 6-(methyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)pyridine-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.50 (s, 1H), 9.44 (s, 1H), 8.80-8.83 (d, 1H), 8.44-8.49 (d, 1H), 8.24-8.28 (m, 1H), 8.15-8.21 (d, 2H), 7.92-7.97 (d, 2H), 7.67-7.72 (d, 2H), 7.30-7.34 (d, 1H), 6.93-7.02 (m, 3H), 3.94-3.96 (s, 3H), 3.72-3.79 (m, 4H), 3.04-3.11 (m, 4H). MS (EI): 483 (MH+).

[01131] N,N-dimethyl-N'-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)butanediamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.36 (s, 1H), 8.43 (s, 1H), 8.05-8.17 (d, 2H), 7.71-7.79 (d, 2H), 7.61-7.71 (d, 2H), 7.26-7.31 (d, 1H), 6.89-7.00 (d, 2H), 3.68-3.79 (m, 4H), 3.02-3.08 (m, 4H), 3.00 (s, 3H), 2.82 (s, 3H), 2.56-2.66 (m, 4H). MS (EI): 475 (MH+).

[01132] N-[4-(2-{[4-morpholin-4-yl-3-(trifluoromethyl)phenyl]amino} pyrimidin-4-yl)-phenyl]-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.31 (s, 1H), 9.94 (s, 1H), 8.53-8.57 (d, 1H), 8.48 (s, 1H), 8.14-8.21 (d, 2H), 7.93-7.98 (m, 1H), 7.82-7.88 (d, 2H), 7.56-7.61 (d, 1H), 7.42-7.46 (d, 1H), 3.79-3.86 (m, 1H), 3.67-3.75 (m, 4H), 2.93-3.00 (m, 2H), 2.79-2.86 (m, 4H), 2.05-2.17 (m, 1H), 1.79-1.89 (m, 1H), 1.65-1.75 (m, 2H). MS (EI): 513 (MH+).

[01133] 3-(methyloxy)-N-[4-(2-{[4-morpholin-4-yl-3-(trifluoromethyl)phenyl]amino}-pyrimidin-4-yl)phenyl]propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.24 (s, 1H), 9.94 (s, 1H), 8.53-8.56 (d, 1H), 8.47 (s, 1H), 8.13-8.19 (d, 2H), 7.94-8.00 (d, 1H), 7.76-7.81 (d, 1H), 7.56-7.62 (d, 1H), 7.41-7.45 (d, 1H), 3.67-3.74 (m, 4H), 3.60-3.67 (m, 2H), 3.35 (s, 3H), 2.80-2.86 (d, 4H), 2.57-2.63 (m, 2H). MS (EI): 502 (MH+).

[01134] N-(4-{2-[(4-{4-[3-(dimethylamino)-2,2-dimethylpropyl]piperazin-1-yl}phenyl)-amino]pyrimidin-4-yl}phenyl)-5-oxo-L-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.34 (s, 1H), 9.37 (s, 1H), 8.43-8.46 (d, 1H), 8.12-8.16 (d, 2H), 7.94 (s, 1H), 7.77-7.81 (d, 2H), 7.62-7.67 (d, 2H), 7.26-7.30 (d, 1H), 6.88-6.94 (d, 2H), 4.20-4.26 (m, 1H), 3.02-3.08 (m, 4H), 2.57-2.64 (m, 4H), 2.21 (s, 6H), 2.17 (s, 2H), 2.10 (s, 2H), 1.89 (s, 4H), 0.84 (s, 6H). MS (EI): 571 (MH+).

[01135] (2R)-N-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.94 (s, 1H), 9.41 (s, 1H), 8.43-8.46 (d, 1H), 8.09-8.15 (d, 2H), 7.85-7.90 (d, 2H), 7.65-7.71 (d, 1H), 6.92-6.98 (d, 2H), 4.39-4.48 (m, 1H), 3.95-4.05 (m, 1H), 3.79-3.89 (m,

1H), 3.52-3.64 (m, 6H), 3.32 (s, 1H), 3.23 (s, 2H), 2.98-3.11 (m, 4H), 2.58-2.65 (m, 2H), 2.15-2.25 (m, 1H), 1.96-2.07 (m, 1H), 1.83-1.93 (m, 2H). MS (EI): 531 (MH+).

[01136] (2S)-N-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.94 (s, 1H0, 9.41 (s, 1H), 8.42-8.47 (d, 2H), 8.09-8.16 (d, 2H), 7.84-7.91 (d, 2H), 7.64-7.72 (d, 2H), 7.27-7.37 (d, 1H), 6.93-6.99 (d, 2H), 4.40-4.47 (m, 1H), 3.95-4.05 (m, 1H), 3.80-3.89 (m, 1H), 3.53-3.65 (m, 6H), 3.32 (s, 1H), 3.23 (s, 2H), 2.98-3.10 (m, 4H), 2.59-2.65 (m, 2H), 2.15-2.27 (m, 1H), 1.95-2.07 (m, 1H), 1.83-1.93 (m, 2H). MS (EI): 531 (MH+).

[01137] (2R,4S)-4-hydroxy-N-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenyl-amino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.42-8.46 (d, 1H), 8.09-8.15 (d, 2H), 7.80-7.86 (d, 2H), 7.65-7.71 (d, 2H), 7.27-7.31 (d, 1H), 6.93-6.98 (d, 1H), 4.20-4.26 (m, 1H), 3.88-3.94 (m, 1H), 3.53-3.64 (m, 6H), 3.17 (s, 1H), 2.99-3.10 (m, 4H), 2.89-2.93 (m, 1H), 2.77-2.84 (m, 1H), 2.58-2.64 (m, 3H), 1.99-2.07 (m, 2H), 1.73-1.83 (m, 2H). MS (EI): 546 (MH+).

[01138] N-(4-{2-[(3-fluoro-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.07 (s, 1H), 9.89 (s, 1H), 8.46-8.56 (d, 1H), 8.08-8.21 (d, 2H), 7.74-7.91 (m, 3H), 7.47-7.57 (d, 1H), 7.35-7.41 (d, 1H), 6.98-7.08 (m, 1H), 3.70-3.82 (m, 5H), 2.87-3.03 (m, 5H), 2.01-2.16 (m, 1H), 1.92 (s, 2H), 1.75-1.87 (m, 1H), 1.61-1.74 (m, 2H). MS (EI): 463 (MH+).

[01139] N-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.30 (s, 1H), 9.40 (s, 1H), 8.42-8.47 (d, 1H), 8.09-8.15 (d, 2H), 7.74-7.80 (d, 2H), 7.64-7.71 (d, 2H), 7.27-7.30 (d, 1H), 6.92-7.00 (d, 2H), 3.92-3.99 (m, 1H), 3.68-3.84 (m, 4H), 3.53-3.64 (m, 5H), 3.32 (s, 1H), 3.23 (s, 2H), 3.16-3.22 (m, 1H), 2.98-3.10 (m, 4H), 2.59-2.65 (m, 1H), 2.06-2.15 (m, 2H). MS (EI): 531 (MH+).

[01140] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-pyridin-3-ylpropanamide: ^{1}H NMR (400 MHz, d6-DMSO):10.21 (s, 1H), 9.37 (s, 1H), 8.39-8.51 (m, 3H), 8.08-8.13 (d, 2H), 7.64-7.76 (m, 5H), 7.25-7.35 (m, 2H), 6.91-6.98 (d, 2H), 3.72-3.77 (m, 4H), 3.01-3.08 (m, 4H), 2.91-2.98 (m, 2H), 2.65-2.75 (m, 2H). MS (EI): 481 (MH+).

[01141] N-(3-(4-(4-acetamidophenyl)pyrimidin-2-ylamino)phenyl)-2-chlorobenzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.497(s, 1H), 10.201 (s, 1H), 9.668 (s, 1H), 8.505 (d, 1H), 8.505 (d, 1H), 8.427 (s, 1H), 8.223 (d, 2H), 7.748 (d, 2H), 7.59 (m, 2H), 7.477 (m, 3H), 7.374 (d, 1H), 7.253 (m, 2H), 2.083 (s, 3H). MS (EI): 458 (MH+).

[01142] N-(3-(4-(4-acetamidophenyl)pyrimidin-2-ylamino)phenyl)-2-methylbenzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.284(d, 2H), 9.622 (s, 1H), 8.487(m, 2H), 8.235(d, 2H), 7.749 (d, 2H), 7.352(m, 8H), 2.084(s, 3H). MS (EI): 438 (MH+).

[01143] N-(3-(4-(4-acetamidophenyl)pyrimidin-2-ylamino)phenyl)-2,4-dichlorobenzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.533 (s, 1H), 10.198(s, 1H), 9.687(s, 1H), 8.506(d, 1H), 8.406(s, br, 1H), 8.220(d, 2H), 7.787(d, 1H), 7.747(d, 2H), 7.659(d, 1H), 7.591(d, 1H), 7.464 (d, 1H), 7.377(d, 1H), 7.247(m, 2H), 2.085(s, 3H). MS (EI): 492 (MH+).

[01144] N-(3-(4-(4-acetamidophenyl)pyrimidin-2-ylamino)phenyl)-2,5-dichlorobenzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.510(s, 1H), 10.198(s, 1H), 9.696(s, 1H), 8.507(s, 1H), 8.389(s, 1H), 8.220(d, 2H), 7.744(m, 3H), 7.617(m, 2H), 7.487(d, 1H), 7.379(d, 1H), 7.282(m, 2H), 2.081(s, 3H). MS (EI): 492 (MH+).

[01145] N-(3-(4-(4-acetamidophenyl)pyrimidin-2-ylamino)phenyl)-2-chloro-6-fluoro-3-methoxybenzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.726(s, 1H), 10.204(s, 1H), 9.709(s, 1H), 8.509(d, 1H), 8.402(s, 1H), 8.217(d, 2H), 7.743(d, 2H), 7.488(d, 1H), 7.386(m, 2H), 7.282(m, 2H), 7.221(d, 1H), 3.904(s, 3H), 2.082(s, 3H). MS (EI): 506 (MH+).

[01146] N-(3-(4-(4-acetamidophenyl)pyrimidin-2-ylamino)phenyl)-2,3-dichlorobenzamide: ^{1}H-NMR(400MHz, d6-DMSO): 10.6 (s,1H), 10.2(s, 1H), 9.7(s, 1H), 8.5(d, 1H), 8.4(s, 1H), 8.2(d, 2H), 7.8(m, 3H), 7.6(d, 1H), 7.5(m, 2H), 7.4(d, 1H), 7.2(m, 2H), 2.081(s,3H). MS (EI): 492 (MH+).

[01147] (R)-N-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)-pyrimidin-4-yl) phenyl)cyclopropanecarboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.476(s, 1H), 9.406(s, 1H), 8.448(d, 1H), 8.124(d, 2H), 7.767(m, 4H), 7.287(d, 1H), 6.977(d, 2H), 3.85(m, 1H), 3.65(m, 4H), 3.0(m, 4H), 2.95(m, 1H), 2.6(m, 1H), 2.0(m, 1H), 1.8(m, 1H), 1.613(m, 3H), 0.84(m, 4H). MS (EI): 512 (MH+).

[01148] N-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.480(s, 1H), 9.399(s,1H), 8.447(d, 1H), 8.124(d, 2H), 7.769(d, 2H), 7.692(d, 2H), 7.285(d, 1H), 6.975(d, 2H), 3.170(m, 2H), 3.592(m, 2H), 3.134(s, 2H), 3.099(m, 2H), 3.028(m, 2H), 2.694(m, 4H), 2.331(m, 4H), 0.842(m, 4H). MS (EI): 541 (MH+).

[01149] 4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.5(s, 1H), 8.5(d, 1H), 8.2(d, 2H), 8.15(s, 1H), 8(d, 2H), 7.7(d, 1h), 7.5(s, 1H), 7.4(d, 1H), 6.9(d, 1H), 4.8(m, 4h), 3.0(m, 4H). MS (EI): 376 (MH+).

[01150] (R)-N-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide: ^{1}H-NMR (400MHz, d6-MeOD): 8.355(d, 1H), 8.114(d, 2H), 7.177(d, 2H), 7.639(d, 2H), 7.217(d, 1H), 7.028(d, 2H), 4.394(m, 1H), 3.797 (m, 2H), 3.692(m, 2H), 3.137(m, 4H), 3.1(m, 1H), 2.410(m, 1H), 1.992(m, 2H), 1.827(m, 2H), 0.981(m, 2H), 0.85(m, 2H). MS (EI): 512 (MH+).

[01151] (S)-N-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide: ^{1}H-NMR (400MHz, MeOD): 8.357(d, 1H), 8.116(d, 2H), 7.718(d, 2H), 7.642(d, 2H), 7.221(d, 1H), 7.033(d, 2H), 4.1(m, 1H), 3.85(m, 1H), 3.7(m, 4H), 3.2(m, 4H), 1.8(m, 1H), 1.4(d, 3H), 0.9(m, 2H), 0.85(m, 2H). MS (EI): 486 (MH+).

[01152] (R)-N-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide: ^{1}H-NMR (400MHz, MeOD): 8.4(d, 1H), 8.15(d, 2H), 7.8(d, 2H0, 7.6(d, 2H), 7.2(d,1H), 7.0(d, 2H), 4.0(m, 1H), 3.7(m, 4H), 3.2(m, 4H), 1.8(m, 1H), 1.3(d, 3H), 0.9(m, 2H), 0.85(m, 2H). MS (EI): 486 (MH+).

[01153] (R)-N-(4-(2-(4-(4-acetylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.193(s, 1H), 9.411(s, 1H), 8.452-8.439(d, 1H), 8.136-8.144(d, 2H), 7.849-7.828 ((d, 2H), 7.690-7.688(d, 2H), 7.302-7.289(d, 1H), 6.971-6.948(d, 2H), 3.743(m, 1H), 3.588(m, 4H), 3.085-3.016(m, 4H), 2.905(t, 2H), 2.046(s, 3H), 1.808(m, 1H), 1.663(m, 2H). MS (EI): 486 (MH+).

[01154] (R)-N-(4-(2-(4-(4-(2-methoxyacetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.198(s, 1H), 9.414(s, 1H), 8.452(d, 1H), 8.136(d, 2H), 7.850(d, 2H), 7.691(d, 2H), 7.302(d, 1H), 6.970(d, 2H), 4.136(s, 2H), 3.744(m, 1H), 3.599-3.535(m, 4H), 3.302(s, 3H), 3.078(m, 4H), 2.905(t, 2H), 2.079(m, 1H), 1.791(m, 1H), 1.646((m, 2H). MS (EI): 516 (MH+).

[01155] N-{1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]pyrrolidin-3-yl}acetamide: NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.20 (s, 1H), 8.60 (s, 1H), 8.15-8.20 (m, 3H), 7.79-7.86 (m, 4H), 7.20 (s, 1H), 6.58 (d, 2H), 4.39 (m, 1H), 3.43 (m, 1H), 3.23 (m, 1H), 3.10 (m, 1H), 2.18 (m, 1H), 2.07 (s, 3H), 1.85 (m, 1H), 1.80 (s, 3H). MS (EI): 431 (MH+).

[01156] N-[4-(2-{[4-(3-oxopiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.40 (s, 1H), 8.41 (s, 1H), 8.06 (d, 2H), 8.02 (s, 1H), 7.65 – 7.80 (m, 4H), 7.25 (s, 1H), 6.97 (d, 2H), 3.64 (s, 2H), 3.35 – 3.40 (m, 4H), 2.05 (s, 3H). MS (EI): 403 (MH+).

[01157] ethyl N-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-N-methylglycinate: MS (EI): 420 (MH+).

[01158] ethyl 1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperidine-3-carboxylate: NMR (400 MHz, d6-DMSO): 10.40 (s, 1H), 10.00 (s, 2H), 8.65 (d, 1H), 8.14 (d, 2H), 7.78 (d, 2H), 7.50 – 7.62 (m, 4H), 7.40 (d, 1H), 2.09 (s, 3H), 2.00 (s, 3H). MS (EI): 362 (MH+).

[01159] ethyl 1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperidine-3-carboxylate: MS (EI): 460 (MH+).

[01160] N-(4-{2-[(4-{bis[2-(methyloxy)ethyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: MS (EI) for $C_{24}H_{29}N_5O_3$: 436 (MH+).

[01161] N-[4-(2-{[4-(morpholin-4-ylsulfonyl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: MS (EI) for $C_{22}H_{23}N_5O_4S$: 454 (MH+).

[01162] 3-hydroxy-3-methyl-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}-pyrimidin-4-yl)phenyl]butanamide: NMR (400 MHz, d6-DMSO): 10.04 (s, 1H), 9.46 (s, 1H), 8.45 (d, 1H), 8.11 (d, 2H), 7.75 (d, 2H), 7.65 (s, 1H), 7.29 (d, 1H), 6.91 (d, 1H), 3.79 (s, 3H), 3.68 (m, 4H), 2.89 (m, 4H), 2.44 (s, 2H), 1.23 (s, 6H). MS (EI) for $C_{26}H_{31}N_5O_4$: 478 (MH+).

[01163] 1-methyl-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide: NMR (400 MHz, d6-DMSO): 10.0 (s, 1H), 9.44 (s, 1H), 8.42 (d, 1H), 8.18 (d, 2H), 7.82 (d, 2H), 7.62 (s, 1H), 7.30 (m, 2H), 6.81 (d, 1H), 3.80 (s, 3H), 3.68 (m, 4H), 2.85 – 3.10 (m, 6H), 2.37 – 2.48 (m, 5H), 2.20 (m, 1H), 1.80 (m, 2H). MS (EI) for $C_{27}H_{32}N_6O_3$: 489 (MH+).

[01164] N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]-D-alaninamide: NMR (400 MHz, d6-DMSO): 11.40 (s, 1H), 10.10 (s, 1H), 8.57 (d, 1H), 8.45(d, 2H), 8.02 (d, 2H), 7.87 (m, 3H), 7.47 (m, 2H), 4.15 (m, 1H), 3.95 – 4.10 (m, 7H), 3.58 (m, 4H), 1.48 (d, 3H). MS (EI) for $C_{24}H_{28}N_6O_3$: 449 (MH+).

[01165] N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]-cyclopropanecarboxamide: NMR (400 MHz, d6-DMSO): 10.45 (s, 1H), 9.43 (s, 1H), 8.42 (d, 1H), 8.17 (d, 2H), 7.75 (d, 2H), 7.64 (s, 1H), 7.15 (m, 2H), 6.84 (d, 1H), 3.80 (s, 3H), 3.75 (m, 4H), 2.96 (m, 4H), 2.52 (m, 2H), 0.80 (m, 2H). MS (EI) for $C_{25}H27N_5O_3$: 446 (MH+).

[01166] N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]-butanamide: NMR (400 MHz, d6-DMSO): 10.18 (s, 1H), 9.43 (s, 1H), 8.44 (d, 1H), 8.17 (m, 2H), 7.75 (d, 2H), 7.64 (s, 1H), 7.25 (m, 2H), 6.84 (d, 1H), 3.80 (s, 3H), 3.75

(m, 4H), 2.96 (m, 4H), 2.35 (q, 2H), 1,62 (m, 2H), 0.92 (q, 3H). MS (EI) for $C_{25}H_{29}N_5O_3$: 448 (MH+).

[01167] N-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)butanamide: NMR (400 MHz, d6-DMSO): 10.18 (s, 1H), 9.40 (s, 1H), 8.41 (d, 1H), 8.17 (d, 2H), 7.78 (d, 2H), 7.68 (d, 2H), 7.24 (s, 1H), 6.94 (d, 2H), 3.60 (m, 6H), 3.21 (s, 3H), 3.0 – 3.09 (m, 4H), 2.60 (q, 2H), 2.35 (m, 2H), 1,60 (m, 2H), 0.95 (q, 3H). MS (EI) for $C_{28}H_{34}N_6O_3$: 503 (MH+).

[01168] O-methyl-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]-L-serinamide: NMR (400 MHz, d6-DMSO): 11.60 (s, 1H), 10.1 (s, 1H), 8.60 (s, 1H), 8.55 (m, 2H), 8.20 (m, 2H), 7.98 (s, 1H), 7.90 (d, 2H), 7.80 (s, 1H), 7.48 (m, 2H), 4.35 (m, 1H), 4.04 (m, 5H), 3.98 (s, 3H), 3.85 (m, 4H), 3.60 (m, 4H). MS (EI) for $C_{25}H_{30}N_6O_4$: 479 (MH+).

[01169] N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide: NMR (400 MHz, d6-DMSO): 11.57 (s, 1H), 10.25 (br, 1H), 10.06 (s, 1H), 8.76 (br, 1H), 8.60 (d, 1H), 8.22 (d, 2H), 8.05 (s, 1H), 7.87 (m, 3H), 7.50 (m, 2H), 4.18 – 4.52 (m, 5H), 4.08 (m, 2H), 3.99 (s, 3H), 3.62 (m, 4H), 3.30 (m, 2H), 1.95 (m, 2H). MS (EI) for $C_{26}H_{30}N_6O_3$: 475 (MH+).

[01170] N-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)cyclopropanecarboxamide: NMR (400 MHz, d6-DMSO): 10.45 (s, 1H), 9.40 (s, 1H), 8.41 (s, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.98 (d, 2H), 3.60 (m, 6H), 3.22 (s, 3H), 3.0 – 3.11 (m, 4H), 6.62 (q, 2H), 0.82 (m, (4H). MS (EI) for $C_{28}H_{32}N_6O_3$: 501 (MH+).

[01171] N-{4-[2-({4-[4-(Piperidin-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)-pyrimidin-4-yl]phenyl}-D-prolinamide: ^{1}H NMR (400 MHz, d_6-DMSO): 11.40 (s, 1H), 10.0 (m, 1H), 9.96 (s, 1H), 9.11 (br d, 1H), 8.7-8.8 (m, 2H), 8.55 (d, 1H), 8.20 (d, 2H), 7.87 (m, 4H), 7.59 (br s, 2H), 7.45 (d, 1H), 4.48 (m, 1H), 3.4-3.5 (m, 4H), 3.25-3.30 (m, 4H) 3.0-3.1 (m, 1H), 2.9-3.0 (m, 2H), 2.4-2.5 (m, 1H), 1.9-2.0 (m, 3H), 1.7-1.9 (m, 4H); MS (EI) for $C_{31}H_{38}N_8O_2$: 555 (MH^+).

[01172] 3-(Methyloxy)-N-{4-[2-({4-[4-(piperidin-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}propanamide: ^{1}H NMR (400 MHz, d_6-DMSO): 10.49 (s, 1H), 9.93 (s, 1H), 9.07 (m, 1H), 8.72 (m, 1H), 8.50 (d, 1H), 8.13 (d, 2H), 7.85 (d, 2H), 7.79 (d, 2H), 7.56 (br s, 2H), 7.42 (d, 1H), 3.61 (t, 2H), 3.3-3.5 (m, 4H), 3.2-3.30 (m, 5H) 3.0-3.1 (m, 1H), 2.85-3.0 (m, 2H), 2.59 (t, 2H), 1.7-1.9 (m, 4H); MS (EI) for $C_{30}H_{37}N_7O_3$: 544 (MH^+).

[01173] 1-Ethyl-3-{4-[2-({4-[4-(piperidin-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)-pyrimidin-4-yl]phenyl}urea: ^{1}H NMR (400 MHz, d_6-DMSO): 9.96 (s, 1H), 9.20 (s, 1H), 8.93 (m, 1H), 8.65 (m, 1H), 8.46 (d, 1H), 8.09 (d, 2H), 7.79 (m, 2H), 7.58 (d, 2H), 7.41 (m, 3H), 6.51 (br s, 1H), 3.2-3.4 (m, 6H), 3.13 (q, 2H) 3.0-3.1 (m, 1H), 2.9-3.0 (m, 2H), 1.7-1.9 (m, 4H), 1.06 (t, 3H); MS (EI) for $C_{29}H_{36}N_8O_2$: 529 (MH^+).

[01174] N-(4-{2-[(4-{4-[3-(Dimethylamino)-2,2-dimethylpropanoyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d_6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.28 (d, 1H), 6.96 (d, 2H), 6.57 (br s, 1H), 3.70 (m, 4H), 3.07 (m, 4H) 2.60 (br s, 2H), 2.28 (br s, 6H), 2.09 (s, 3H), 1.23 (s, 6H); MS (EI) for $C_{29}H_{37}N_7O_2$: 516 (MH^+).

[01175] 2-(Methyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-ethanesulfonamide: ^{1}H NMR (400 MHz, d_6-DMSO): 9.39 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.67 (d, 2H), 7.31 (d, 2H), 7.26 (d, 1H), 6.94 (d, 2H), 3.74 (m, 4H), 3.67 (t, 2H) 3.43 (t, 2H), 3.18 (s, 3H), 3.05 (m, 4H); MS (EI) for $C_{23}H_{27}N_5O_4S$: 470 (MH^+).

[01176] 3-(Methyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propane-1-sulfonamide: MS (EI) for $C_{24}H_{29}N_5O_4S$: 484 (MH^+).

[01177] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(tetrahydrofuran-2-ylmethyl)benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s, 1H), 9.77 (s, 1H), 8.52 (d, 1H), 8.45 (d, 1H), 8.43 (d, 1H), 8.19 (d, 1H), 8.17 (d,1H), 7.88-7.86 (m,1H), 7.76 (s, 1H), 7.74 (s, 1H), 7.43-7.38 (m, 3H), 4.01-3.98 (m, 1H), 3.81-3.76 (m, 2H), 3.65-3.62 (m, 2H), 2.09 (s, 3H), 1.85-1.80 (m, 3H), 1.64-1.61 (m, 1H). MS (EI): 432.5 (MH+).

[01178] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[3-(2-oxopyrrolidin-1-yl)propyl]benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s, 1H), 9.78 (s, 1H), 8.52 (d, 1H), 8.49 (s, 1H), 8.41 (t, 1H), 8.19 (dd, 2H), 7.87-7.84 (m,1H), 7.76 (s, 1H), 7.74 (s, 1H), 7.40-7.38 (m, 3H), 3.27-3.23 (m, 6H), 2.22 (t, 2H), 2.09 (s, 3H), 1.96-1.88 (m, 2H), 1.73-1.70 (m, 2H). MS (EI): 473.5 (MH+).

[01179] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(3s,5s,7s)-tricyclo-[3.3.1.1~3,7~]dec-1-yl]benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.73 (s, 1H), 8.52 (d, 1H), 8.35 (s, 1H), 8.16 (d, 2H), 7.84-7.81 (m, 1H), 7.76 (d, 2H), 7.55 (s, 1H), 7.39-7.31 (m, 3H), 2.09 (s, 3H), 1.67 (m, 15H). MS (EI): 482.6 (MH+).

[01180] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[2-(methyloxy)ethyl]-benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s, 1H), 9.77 (s, 1H), 8.52 (d, 1H), 8.46

(d, 2H), 8.19 (d, 1H), 8.18 (d, 1H), 7.88-7.85 (m,1H), 7.77 (s, 1H), 7.75 (s, 1H), 7.43-7.39 (m, 3H), 3.48-3.41 (m, 4H), 3.29-3.27 (m, 3H), 2.09 (s, 3H). MS (EI): 406.3 (MH+).

[01181] N-[4-(2-{[3-(1,3-thiazolidin-3-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s, 1H), 9.84 (s, 1H), 8.52 (d, 1H), 8.19-8.12 (m, 3H), 7.90-7.87 (m, 1H), 7.77-7.75 (m, 2H), 7.43-7.38 (m, 2H), 7.11 (d, 1H), 4.64 (m, 2H), 3.77 (m, 2H), 3.06 (m, 2H), 2.09 (s, 3H). MS (EI): 420.6 (MH+).

[01182] N-{4-[2-({3-[(4-pyridin-2-ylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.83 (s, 1H), 8.53 (d, 1H), 8.14-8.11 (m, 3H), 8.04 (t, 1H), 7.89-7.86 (m, 1H), 7.73 (d, 2H), 7.57-7.53 (m, 1H), 7.43-7.39 (m, 2H), 7.03-7.01 (m, 1H), 6.83 (d, 1H), 6.69-6.66 (m, 1H), 3.74 (m, 4H), 3.49 (m, 4H), 2.08 (s, 3H). MS (EI): 494.5 (MH+).

[01183] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-{[2-(methyloxy)phenyl]-methyl}benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.79 (s, 1H), 8.80 (d, 1H), 8.53-8.49 (m, 2H), 8.19 (dd, 2H), 7.94-7.91 (m, 1H), 7.74 (d, 2H), 7.52-7.49 (m, 1H), 7.44-7.39 (m, 1H), 7.26-7.19 (m, 2H), 6.99 (dd, 1H), 6.93-6.89 (m, 1H), 4.46 (d, 2H), 3.84 (s, 3H), 2.09 (s, 3H). MS (EI): 468.5 (MH+).

[01184] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-{[3-(methyloxy)phenyl]-methyl}benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.79 (s, 1H), 8.97 (t, 1H), 8.53-8.49 (m, 2H), 8.20-8.18 (m, 2H), 7.93-7.90 (m, 1H), 7.75 (d, 2H), 7.48-7.46 (m, 1H), 7.43-7.39 (m, 1H), 7.27-7.23 (m, 1H), 6.92-6.90 (m, 2H), 6.83-6.80 (m, 1H), 4.47 (d, 2H), 3.71 (s, 3H), 2.09 (s, 3H). MS (EI): 468.4 (MH+).

[01185] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(2-fluorophenyl)methyl]-benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.79 (s, 1H), 8.97 (t, 1H), 8.53-8.49 (m, 2H), 8.19-8.17 (m, 2H), 7.93-7.90 (m, 1H), 7.75 (d, 2H), 7.50-7.47 (m, 1H), 7.43-7.37 (m, 2H), 7.32-7.29 (m, 1H), 7.22-7.16 (m, 2H), 4.40 (d, 2H), 2.09 (s, 3H). MS (EI): 456.4 (MH+).

[01186] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(4-fluorophenyl)methyl]-benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.79 (s, 1H), 9.00 (t, 1H), 8.53-8.50 (m, 2H), 8.19-8.17 (m, 2H), 7.90-7.88 (m, 1H), 7.75 (d, 2H), 7.47-7.36 (m, 4H), 7.19-7.13 (m, 2H), 4.47 (d, 2H), 2.09 (s, 3H). MS (EI): 456.5 (MH+).

[01187] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(3,3-dimethylbutyl)-benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.76 (s, 1H), 8.53-8.51 (d, 1H), 8.41 (s, 1H), 8.33 (t, 1H), 8.18-8.17 (m, 2H), 7.88-7.85 (m, 1H), 7.75 (d, 2H), 7.39-7.37 (m,

2H), 3.30-3.26 (m, 2H), 2.08 (s, 3H), 1.48-1.44 (m, 2H), 0.94 (s, 9H). MS (EI): 432.4 (MH+).

[01188] N-[4-(2-{[3-(thiomorpholin-4-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s, 1H), 9.82 (s, 1H), 8.53 (d, 1H), 8.15-8.20 (m, 2H), 7.99 (t, 1H), 7.85-7.82 (m, 1H), 7.76 (d, 2H), 7.41-7.37 (m, 2H), 6.98-6.96 (m, 1H), 3.88 (m, 4H), 3.60 9m, 4H), 2.09 (s, 3H). MS (EI): 434.5 (MH+).

[01189] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(2-thienylmethyl)benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.79 (s, 1H), 9.09 (t, 1H), 8.53-8.50 (m, 2H), 8.18 (d, 2H), 7.89-7.86 (m, 1H), 7.75 (d, 2H), 7.44-7.38 (m, 3H), 7.03 (m, 1H), 6.98-6.96 (m, 1H), 4.64 (d, 2H), 2.09 (s, 3H). MS (EI): 444.4 (MH+).

[01190] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[3-(dimethylamino)-propyl]benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.79 (s, 1H), 8.74 (m, 1H), 8.55-8.50 (m, 2H), 8.21-8.18 (m, 2H), 7.95-7.87 (m, 1H), 7.75 (d, 2H), 7.45-7.40 (m, 2H), 3.05 (s, 2H), 2.75 (s, 6H), 2.55-2.54 (m, 2H), 2.09 (s, 3H), 1.25-1.21 (m, 2H). MS (EI): 433.4 (MH+).

[01191] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[2-(2-chlorophenyl)-ethyl]benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.77 (s, 1H), 8.54-8.51 (m, 2H), 8.44 (m, 1H), 8.18 (d, 2H), 7.88-7.86 (m, 1H), 7.75 (d, 2H), 7.45-7.36 (m, 4H), 7.28-7.25 (m, 2H), 3.55-3.50 (m, 2H), 3.01-2.98 (m, 2H), 2.08 (s, 3H). MS (EI): 486.8 (MH+).

[01192] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-{[2-(trifluoromethyl)-phenyl]methyl}benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.81 (s, 1H), 9.07 (t, 1H), 8.53-8.49 (m, 2H), 8.19-8.17 (m, 2H), 7.96-7.94 (m, 1H), 7.75-7.72 (m, 2H), 7.55-7.39 (m, 6H), 4.68 (d, 2H), 2.08 (s, 3H). MS (EI): 506.5 (MH+).

[01193] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-{[3-(trifluoromethyl)-phenyl]methyl}benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.80 (s, 1H), 9.10 (t, 1H), 8.53-8.49 (m, 2H), 8.19-8.17 (m, 2H), 7.94-7.91 (m, 1H), 7.74 (d, 2H), 7.68-7.58 (m, 3H), 7.48-7.39 (m, 3H), 4.58 (d, 2H), 2.09 (s, 3H). MS (EI): 506.4 (MH+).

[01194] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-{[4-(trifluoromethyl)-phenyl]methyl}benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.80 (s, 1H), 9.10 (t, 1H), 8.52 (m, 2H), 8.18 (d, 2H), 7.91-7.89 (m, 1H), 7.75-7.69 (m, 4H), 7.55 (d, 2H), 7.49-7.38 (m, 3H), 4.58 (d, 2H), 2.08 (s, 3H). MS (EI): 506.5 (MH+).

[01195] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(2,4-difluorophenyl)-methyl]benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.79 (s, 1H), 8.98 (t,

1H), 8.52 (m, 2H), 8.18 (d, 2H), 7.91-7.89 (m, 1H), 7.54 (d, 2H), 7.47-7.38 (m, 4H), 7.27-7.22 (m, 1H), 7.09-7.04 (m, 1H), 4.48 (d, 2H), 2.09 (s, 3H). MS (EI): 474.4 (MH+).

[01196] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-ethyl-N-methylbenzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s, 1H), 9.80 (s, 1H), 8.53 (d, 1H), 8.13 (d, 2H), 7.76-7.74 (m, 2H), 7.40-7.32 (m, 3H), 6.94 (m,2H), 3.28-3.24 (m, 2H), 2.94 (m, 3H), 2.09 (s, 3H), 1.15-1.08 (m, 3H). MS (EI): 390.4 (MH+).

[01197] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-({4-[(trifluoromethyl)-oxy]phenyl}methyl)benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.79 (s, 1H), 9.04 (t, 1H), 8.52 (m, 2H), 8.18 (d, 2H), 7.91-7.88 (m, 1H), 7.75 (d, 2H), 7.48-7.39 (m, 4H), 7.34-7.32 (m, 2H), 4.51 (d, 2H), 2.09 (s, 3H). MS (EI): 522.5 (MH+).

[01198] N-{4-[2-({3-[(4-acetylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.82 (s, 1H), 8.53 (t, 1H), 8.19 (d, 2H), 8.14-8.12 (m, 2H), 7.84-7.84 (m, 1H), 7.75 (d, 2H), 7.40-7.38 (m, 2H), 3.53-3.44 (m, 8H), 2.09 (s, 6H). MS (EI): 459.5 (MH+).

[01199] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(cyclopropylmethyl)-benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.77 (s, 1H), 8.53-8.50 (m, 2H), 8.48 (d, 1H), 8.19(dd, 2H), 7.86-7.84 (m, 1H), 7.75 (d, 2H), 7.41-7.38 (m, 2H), 3.17-3.14 (m, 2H), 2.09 (s, 3H), 1.06 (m, 1H), 0.45-0.42 (m, 2H), 0.25-0.23 (m, 2H). MS (EI): 402.5 (MH+).

[01200] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[2-(2-fluorophenyl)-ethyl]benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.77 (s, 1H), 8.54-8.51 (m, 2H), 8.44 (m, 1H), 8.20-8.17 (m, 2H), 7.88-7.86 (m, 1H), 7.75 (d, 2H), 7.40-7.26 (m, 4H), 7.18-7.13 (m, 2H), 3.52-3.49 (m, 2H), 2.92-3.88 (m, 2H), 2.09 (s, 3H). MS (EI): 470.4 (MH+).

[01201] N-[4-(2-{[3-(pyrrolidin-1-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.78 (s, 1H), 8.53 (d, 1H), 8.20-8.12 (m, 4H), 7.83 (d, 1H), 7.76-7.73 (m, 2H), 7.39-7.35 (m, 2H), 3.50-3.40 (m, 4H), 2.09 (s, 3H), 1.95-1.80 (m, 4H). MS (EI): 402.5 (MH+).

[01202] N-{4-[2-({3-[(4-pyrimidin-2-ylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.83 (s, 1H), 8.53 (d, 2H), 8.39 (d, 1H), 8.14-8.12 (m, 2H), 8.04 (t, 1H), 7.89-7.87 (m, 1H), 7.74 (d, 1H), 7.43-7.38 (m, 2H), 7.03-7.01 (m, 1H), 6.67 (t, 2H), 3.81 (m, 4H), 3.73 (m, 4H), 2.08 (s, 3H). MS (EI): 495.6 (MH+).

[01203] N-{4-[2-({4-[4-(9H-fluoren-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.87 (t, 2H), 7.73 (d, 2H), 7.65 (d, 2H), 7.59-7.56 (m, 2H), 7.37-7.25 (m, 4H), 6.92 (d, 2H), 3.92 (s, 2H), 3.60 (s, 2H), 3.10 (m, 4H), 2.56 (m, 4H), 2.08 (s, 3H). MS (EI): 567.7 (MH+).

[01204] N-(4-{2-[(4-{4-[(3-methyl-2-thienyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.73 (d, 2H), 7.65 (d, 2H), 7.33 (d, 1H), 7.26 (d, 1H), 6.92 (d, 2H), 6.85 (d, 1H), 3.63 (s, 2H), 3.07 (m, 4H), 2.56 (m, 4H), 2.17 (s, 3H), 2.08 (s, 3H). MS (EI): 499.5 (MH+).

[01205] N-(4-{2-[(4-{4-[(5-ethylfuran-2-yl)methyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.73 (d, 2H), 7.64 (d, 2H), 7.26 (d, 1H), 6.92 (d, 2H), 6.18 (d, 1H), 6.01 (d, 1H), 3.48 (s, 2H), 3.07 (m, 4H), 2.62-2.56 (m, 6H), 2.09 (s, 3H), 1.16 (t, 3H). MS (EI): 497.6 (MH+).

[01206] N-(4-{2-[(4-{4-[(3-{[4-(1,1-dimethylethyl)phenyl]oxy}phenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.64 (d, 2H), 7.42-7.38 (m, 2H), 7.33 (t, 1H), 7.26 (d, 1H), 7.08 (d, 1H), 6.97-6.86 (m, 6H), 3.52 (s, 2H), 3.06 (m, 4H), 2.52 (m, 4H), 2.09 (s, 3H), 1.27 (s, 9H). MS (EI): 627.7 (MH+).

[01207] N-{4-[2-({4-[4-(3-thienylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.73 (d, 2H), 7.64 (d, 2H), 7.51-7.45 (m, 1H), 7.35 (d, 1H), 7.29-7.25 (m, 1H), 7.08-7.04 (m, 1H), 6.91 (d, 2H), 3.53 (s, 2H), 3.07 (m, 4H), 2.52 (m, 4H), 2.09 (s, 3H). MS (EI): 485.6 (MH+).

[01208] methyl 4-({4-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-phenyl]piperazin-1-yl}methyl)benzoate: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.94 (d, 2H), 7.73 (d, 2H), 7.65 (d, 2H), 7.50 (d, 2H), 7.26 (d, 1H), 6.92 (d, 2H), 3.85 (s, 3H), 3.61 (s, 2H), 3.09 (m, 4H), 2.54 (m, 4H), 2.09 (s, 3H). MS (EI): 537.7 (MH+).

[01209] N-(4-{2-[(4-{4-[3-(methylthio)propyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.26 (d, 1H), 6.92 (d, 2H), 3.34 (m, 4H),

3.07 (m, 4H), 2.39 (m, 4H), 2.09 (s, 3H), 2.03 (m, 3H), 1.75-1.68 (m, 2H). MS (EI): 477.5 (MH+).

[01210] N-(4-{2-[(4-{4-[(4-{[3-(dimethylamino)propyl]oxy}phenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.73 (d, 2H), 7.64 (d, 2H), 7.26-7.21 (m, 3H), 6.92-6.87 (m, 4H), 3.97 (t, 2H), 3.44 (m, 6H), 3.06 (m, 4H), 2.37 (t, 2H), 2.16 (s, 6H), 2.09 (s, 3H), 1.87-1.82 (m, 2H). MS (EI): 580.7 (MH+).

[01211] N-[4-(2-{[4-(4-{2-[(phenylmethyl)oxy]ethyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.38-7.26 (m, 6H), 6.92 (d, 2H), 4.50 (s, 2H), 3.59 (m, 3H), 3.07 (m, 3H), 2.58 (m, 6H), 2.09 (s, 3H). MS (EI): 523.5 (MH+).

[01212] N-(4-{2-[(4-{4-[(2-chloroquinolin-3-yl)methyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.37 (s, 1H), 8.49 (s, 1H), 8.44 (d, 1H), 8.13-8.09 (m, 3H), 7.96 (d, 1H), 7.83-7.79 (m, 1H), 7.74 (d, 1H), 7.69-7.65 (m, 3H), 7.26 (d, 2H), 6.95 (d, 2H), 3.78 (s, 2H), 3.15 (m, 4H), 2.69 (m, 4H), 2.09 (s, 3H). MS (EI): 565.1 (MH+).

[01213] N-{4-[2-({4-[4-(2,2'-bithien-5-ylmethyl)piperazin-1-yl]phenyl}amino)-pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.49 (dd, 1H), 7.27-7.25 (m, 2H), 7.15 (d, 1H), 7.09-7.07 (m, 1H), 6.96-6.92 (m, 3H), 3.73 (s, 2H), 3.10 (m, 4H), 2.59 (m, 4H), 2.09 (s, 3H). MS (EI): 567.6 (MH+).

[01214] N-[4-(2-{[4-(4-{[4-(2-thienyl)phenyl]methyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.73 (d, 2H), 7.66-7.62 (m, 4H), 7.54-7.50 (m, 2H), 7.38 (d, 2H), 7.26 (d, 1H), 7.15-7.13 (m, 1H), 6.92 (d, 2H), 3.54 (s, 2H), 3.09 (m, 4H), 2.55-2.52 (m, 4H), 2.09 (s, 3H). MS (EI): 561.6 (MH+).

[01215] N-(4-{2-[(4-{4-[(4-cyanophenyl)methyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.82 (d, 2H), 7.73 (d, 2H), 7.65 (d, 2H), 7.56 (d, 2H), 7.26 (d, 1H), 6.92 (d, 2H), 3.63 (s, 2H), 3.10-3.08 (m, 4H), 2.54-2.52 (m, 4H), 2.09 (s, 3H). MS (EI): 504.5 (MH+).

[01216] N-[4-(2-{[4-(4-{[2,5-bis(methyloxy)phenyl]methyl}piperazin-1-yl)phenyl]-amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H),

9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.26 (d, 1H), 6.95-6.90 (m, 4H), 6.81-6.78 (m, 1H), 3.74 (s, 3H), 3.70 (s, 3H), 3.50 (s, 2H), 3.09 (m, 4H), 2.55 (m, 4H), 2.09 (s, 3H). MS (EI): 539.7 (MH+).

[01217] N-{4-[2-({4-[4-(2,2-diphenylethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.82 (d, 2H), 7.65-7.59 (m, 6H), 7.50-7.46 (m, 4H), 7.26 (d, 1H), 7.21 (d, 2H), 6.92 (d, 2H), 4.45 (t, 1H), 3.61 (t, 2H), 3.09 (m, 4H), 2.54 (m, 4H), 2.09 (s, 3H). MS (EI): 569.6 (MH+).

[01218] N-{4-[2-({4-[4-(1H-pyrrol-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.71 (s, 1H), 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.73 (d, 2H), 7.64 (d, 2H), 7.26 (d, 1H), 6.91 (d, 2H), 6.65-6.63 (m, 1H), 5.94-5.90 (m, 2H), 3.44 (s, 2H), 3.06 (m, 4H), 2.48 (m, 4H), 2.09 (s, 3H). MS (EI): 468.6 (MH+).

[01219] N-[4-(2-{[4-(4-propylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.73 (d, 2H), 7.65 (d, 2H), 7.26 (d, 1H), 6.92 (d, 2H), 3.06 (m, 4H), 2.27 (m, 4H), 2.08 (s, 3H), 1.80 (s, 2H), 1.48 (m, 2H), 0.88 (t, 3H). MS (EI): 431.6 (MH+).

[01220] N-[4-(2-{[4-(4-butylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.12 (d, 2H), 7.74 (d, 2H), 7.64 (d, 2H), 7.25 (d, 1H), 6.92 (d, 2H), 3.07 (m, 4H), 2.31 (m, 4H), 2.09 (s, 3H), 1.87 (m, 2H), 1.44 (m, 2H), 1.30 (m, 2H), 0.90 (t, 3H). MS (EI): 445.6 (MH+).

[01221] N-{4-[2-({4-[4-(cyclopropylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.73 (d, 2H), 7.65 (d, 2H), 7.25 (d, 1H), 6.92 (d, 2H), 3.08 (m, 4H), 2.58 (m, 4H), 2.22 (d, 2H), 2.09 (s, 3H), 1.86 (s, 1H), 0.49 (m, 2H), 0.09 (m, 2H). MS (EI): 443.6 (MH+).

[01222] N-[4-(2-{[4-(4-pentanoylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.96 (d, 2H), 3.60 (m, 4H), 3.07 (m, 2H), 3.02 (m, 2H), 2.35 (t, 2H), 2.09 (s, 3H), 1.49 (m, 2H), 1.31 (m, 2H), 0.89 (t, 3H). MS (EI): 473.6 (MH+).

[01223] N-{4-[2-({4-[4-(pyridin-2-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.62

(d, 1H), 8.44 (d, 1H), 8.10 (d, 2H), 7.95 (t, 1H), 7.74 (d, 2H), 7.69 (d, 2H), 7.61 (d, 1H), 7.27 (d, 1H), 6.97 (d, 2H), 3.82 (t, 2H), 3.57 (t, 2H), 3.18 (t, 2H), 3.06 (t, 2H), 2.09 (s, 3H). MS (EI): 494.6 (MH+).

[01224] N-{4-[2-({4-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.68 (m, 2H), 8.44 (d, 1H), 8.10 (d, 2H), 7.89 (d, 1H), 7.74 (d, 2H), 7.69 (d, 2H), 7.51 (m, 1H), 7.28 (d, 2H), 3.80 (m, 2H), 3.49 (m, 2H), 3.18 (m, 2H), 3.09 (m, 2H), 2.09 (s, 3H). MS (EI): 494.6 (MH+).

[01225] N-{4-[2-({4-[4-(pyridin-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.69 (d, 2H), 8.44 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.44 (d, 2H), 7.28 (d, 1H), 6.96 (d, 2H), 3.79 (m, 2H), 3.41 (m, 2H), 3.18 (m, 2H), 3.07 (m, 2H), 2.09 (s, 3H). MS (EI): 494.6 (MH+).

[01226] N-{4-[2-({4-[4-(1H-pyrazol-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.10 (d, 2H), 7.75-7.68 (m, 4H), 7.28 (d, 2H), 6.97 (d, 3H), 3.75 (m, 4H), 3.11 (m, 4H), 2.09 (s, 3H). MS (EI): 483.5 (MH+).

[01227] N-(4-{2-[(4-{4-[(1-acetylpiperidin-4-yl)carbonyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.26 (d, 1H), 6.97 (d, 2H), 3.65 (m, 4H), 3.02 (m, 8H), 2.62 (m, 1H), 2.09 (s, 3H), 1.99 (s, 3H), 1.66 (m, 2H), 1.56 (m, 2H). MS (EI): 542.7 (MH+).

[01228] N-(4-(2-(4-(4-(2-cyclopropylacetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.10 (d, 2H), 7.54 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.96 (d, 2H), 3.59 (m, 4H), 3.04 (m, 4H), 2.30 (d, 2H), 2.09 (s, 3H), 0.97 (m, 1H), 0.45 (m, 2H), 0.14 (m, 2H). MS (EI): 471.6 (MH+).

[01229] N-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.68 (d, 2H), 7.27 (d, 1H), 6.95 (d, 2H), 3.58 (m, 6H), 3.23 (s, 3H), 3.08 (m, 2H), 3.02 (m, 2H), 2.62 (t, 2H), 2.09 (s, 3H). MS (EI): 475.6 (MH+).

[01230] N-{4-[2-({4-[4-(2-{[2-(methyloxy)ethyl]oxy}acetyl)piperazin-1-yl]phenyl}amino)-pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO):

10.23 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.68 (d, 1H), 7.27 (d, 1H), 6.96 (d, 2H), 4.20 (s, 2H), 3.58 (m, 6H), 3.47 (m, 2H), 3.25 (s, 3H), 3.06 (m, 4H), 2.09 (s, 3H). MS (EI): 505.6 (MH+).

[01231] N-(4-(2-(4-(4-(2-(pyridin-3-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.44 (m, 3H), 8.10 (d, 2H), 7.75 (d, 2H), 7.68 (d, 2H), 7.64 (m, 1H), 7.34 (m, 1H), 7.28 (d, 1H), 6.96 (d, 1H), 3.83 (s, 2H), 3.70 (m, 2H), 3.63 (m, 2H), 3.05 (m, 4H), 2.09 (s, 3H). MS (EI): 508.6 (MH+).

[01232] (2R,4S)-4-hydroxy-N-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.40 (s, 1H), 8.48 (d, 1H), 8.44 (d, 1H), 8.39 (dd, 1H), 8.11 (d, 1H), 7.74 (d, 2H), 7.69 (m, 3H), 7.28 (m, 3H), 6.94 (d, 2H), 3.59 (m, 4H), 3.01 (m, 4H), 2.86 (t, 2H), 2.73 (t, 2H), 2.09 (s, 3H). MS (EI): 522.6 (MH+).

[01233] N-{4-[2-({3-[4-(1,3-thiazol-2-ylmethyl)piperazin-1-yl]phenyl}amino)-pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.19 (s, 1H), 9.45 (s, 1H), 8.47 (d, 1H), 8.11 (d, 2H), 7.73 (d, 2H), 7.66 (d, 1H), 7.60 (s, 1H), 7.31 (d, 1H), 7.21 (d, 1H), 7.12 (t, 1H), 6.55 (dd, 1H), 3.90 (s, 2H), 3.17 (m, 4H), 2.66 (m, 4H), 2.07 (s, 3H). MS (EI): 486.6 (MH+).

[01234] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-5-oxo-L-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.33 (s, 1H), 9.40 (s, 1H), 8.45 (d, 1H), 8.14 (d, 2H), 7.93 (s, 1H), 7.79 (d, 2H), 7.67 (d, 2H), 7.29 (d, 1H), 6.93 (d, 2H), 4.23 (dd, 1H), 3.75 (m, 4H), 3.06 (m, 4H), 2.35 (m, 1H), 2.21 (m, 2H), 2.02 (m, 1H). MS (EI): 459.5 (MH+).

[01235] (3S)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyrrolidine-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.75 (s, 1H), 9.84 (s, 1H), 9.34 (m, 1H), 9.14 (m, 1H), 8.51 (d, 1H), 8.16 (d, 2H), 7.82 (d, 3H), 7.41 (d, 2H), 3.93 (m, 4H), 3.82 (m, 6H), 3.36 (m, 2H), 3.24 (m, 1H), 2.33-2.24 (m, 1H), 2.11-2.04 (m, 2H). MS (EI): 445.5 (MH+).

[01236] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-threoninamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.53 (s, 1H), 10.11 (s, 1H), 8.51 (d, 1H), 8.31 (d, 2H), 8.15 (d, 2H), 7.86 (t, 3H), 7.73 (d, 2H), 7.44 (d, 2H), 4.01 (m, 6H), 3.48 (m, 4H), 1.18 (s, 3H). MS (EI): 449.5 (MH+).

[01237] N-{4-[2-({4-[4-(N,N-diethyl-beta-alanyl)piperazin-1-yl]phenyl}amino)-pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.38 (s,

1H), 8.42 (d, 1H), 8.09 (d, 2H), 7.73 (d, 2H), 7.67 (d, 2H), 7.25 (d, 1H), 6.95 (d, 2H), 3.58 (m, 4H), 3.05 (m, 4H), 2.81 (t, 2H), 2.66-2.55 (m, 6H), 1.93 (s, 3H), 0.99 (t, 6H). MS (EI): 516.7 (MH+).

[01238] N^1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-glutamamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.36 (s, 1H), 8.42 (d, 2H), 8.11 (d, 3H), 7.80 (d, 2H), 7.66 (d, 2H), 7.26 (d, 2H), 6.92 (d, 3H), 3.72 (m, 4H), 3.32 (m, 1H), 3.02 (m, 4H), 1.93 (s, 2H), 1.82 (s, 2H). MS (EI): 476.6 (MH+).

[01239] (S)-1-ethyl-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.19 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.94 (d, 2H), 3.04 (m, 4H), 2.90 (m, 2H), 2.65 (m, 2H), 2.43 (m, 3H), 1.98 (m, 6H), 1.03 (t, 3H). MS (EI): 473.6 (MH+).

[01240] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-norvalinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.50 (s, 1H), 10.15 (s, 1H), 8.56 (m, 3H), 8.24 (d, 2H), 7.94 (d, 2H), 7.76 (m, 3H), 7.51 (d, 2H), 4.08 (m, 4H), 3.67 (d, 1H), 1.97 (m, 4H), 1.43 (m, 2H), 1.19 (m, 2H), 0.94 (m, 3H). MS (EI): 447.6 (MH+).

[01241] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-norleucinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.55 (s, 1H), 10.19 (s, 1H), 8.57 (d, 2H), 8.26 (d, 1H), 8.01 (m, 4H), 7.80 (m, 3H), 7.53 (d, 2H), 4.05 (m, 4H), 3.68 (d, 1H), 1.92 (m, 4H), 1.36 (m, 4H), 1.19 (m, 2H), 0.99 (d, 3H). MS (EI): 461.6 (MH+).

[01242] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-alloisoleucinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.32 (s, 1H), 10.01 (s, 1H), 8.56 (d, 2H), 8.44 (d, 3H), 8.21 (d, 2H), 7.89 (m, 3H), 7.46 (d, 2H), 4.02 (m, 4H), 3.56 (d, 1H), 1.99 (m, 4H), 1.63 (m, 1H), 1.17 (m, 2H), 1.00 (d, 3H), 0.91 (d, 3H). MS (EI): 461.6 (MH+).

[01243] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-leucinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.32 (s, 1H), 9.97 (s, 1H), 8.56 (d, 2H), 8.45 (d, 3H), 8.21 (d, 2H), 7.89 (m, 3H), 7.46 (d, 2H), 4.02 (m, 4H), 3.57 (d, 1H), 1.99 (m, 4H), 1.91 (m, 1H), 1.71 (t, 2H), 1.17 (t, 3H), 0.95 (t, 3H). MS (EI): 461.6 (MH+).

[01244] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(2-ethylphenyl)benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.85 (d, 2H), 8.59 (s, 1H), 8.53 (d, 1H), 8.18 (d, 2 H), 7.93 (m, 1H), 7.73 (d, 2H), 7.57 (d, 1H), 7.46 (t, 1H), 7.40 (d, 1H), 7.30-7.34 (m, 2H), 7.24-7.27 (m, 2H), 2.62-2.67 (m, 2H), 2.08 (s, 3H), 1.13-1.7 (t, 3H). MS (EI) for $C_{27}H_{25}N_5O_2$: 452.58 (MH^+).

[01245] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(phenylmethyl)-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.22 (s, 1H), 9.80 (s, 1H), 8.98-9.01 (t, 1H), 8.52 (d, 1H), 8.50 (s, 1H), 8.18 (d, 2H), 7.9 (dd, 1H), 7.76 (s,1H), 7.74 (s, 1H), 7.47 (d, 1H), 7.39-7.43 (m, 2H), 7.43 (s, 2H), 7.34 (d, 2H), 7.23-7.25 (m, 1H), 4.50(d, 2H), 2.09 (s, 3H). MS (EI) for $C_{26}H_{23}N_5O_2$: 438.48 (MH^+).

[01246] N-{4-[2-({3-[(4-cyclopentylpiperazin-1-yl) carbonyl] phenyl}amino) pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.23 (s, 1H), 9.82 (s, 1H), 8.53 (d, 1H), 8.12 (s, 2H), 8.05 (s, 1H), 7.81 (dd, 1H), 7.76 (d, 2H), 7.38 (t, 2H), 6.95 (d, 1H), 2.89 (s, 2H), 2.73 (s, 2H), 2.34-2.45 (m, 5H), 2.09 (s, 3H), 2.73-2.75 (m, 2H), 1.52-1.59 (m, 2H), 1.46-1.50 (m, 2H), 1.27-1.33 (m, 2H): MS (EI) for $C_{28}H_{32}N_6O_2$: 485.8 (MH^+).

[01247] N-{4-[2-({3-[(4-pyrazin-2-ylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.17 (s, 1H), 9.84 (s, 1H), 8.54 (d, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 8.06-8.10 (m, 2H), 7.86-7.88 (m, 2H), 7.73 (d, 2H), 7.42 (d, 1H), 7.39 (d, 1H), 7.02-7.04 (m, 1H), 3.69 (m, 4H), 3.57 (m, 4H), 2.08 (s, 3H). MS (EI) for $C_{27}H_{26}N_8O_2$: 495.7 (MH^+).

[01248] N-(4-{2-[(3-{[4-(3-chlorophenyl)piperazin-1-yl]carbonyl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.20 (s,1H), 9.84 (s, 1H), 8.53 (d, 1H), 8.13 (dd, 2H), 8.064 (t, 1H), 7.85-7.87 (m, 1H), 7.74 (d, 2H), 7.39-7.43 (m, 2H), 7.22 (t, 1H), 7.01-7.03 (m, 1H), 6.96 (t, 1H), 6.90 (dd, 1H), 6.81 (dd, 1H), 3.76 (m, 4H), 3.52 (m, 4H), 2.08 (s, 3H). MS (EI) for $C_{29}H_{27}ClN_6O_2$: 528.1 (MH^+).

[01249] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(1-methyl-1H-benzimidazol-2-yl)methyl]benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.23 (s, 1H), 9.80 (s, 1H), 9.01 (t, 1H), 8.52 (t, 2H), 8.17-8.19 (m, 2H), 7.91-7.93 (m, 1H), 7.75 (d, 2H), 7.50-7.59 (m, 3H), 7.39-7.43 (m, 2H), 7.16-7.26 (m, 2H), 4.80 (d, 2H), 3.86 (s, 3H), 2.10 (s, 3H). MS (EI) for $C_{28}H_{25}N_7O_2$: 492.4 (MH^+).

[01250] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-propylbenzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.22 (s. 1H), 9.77 (s, 1H), 8.52 (d, 1H), 8.46 (s, 1H), 8.40 (t, 1H), 8.18 (d, 2H), 7.83-7.86 (m, 1H), 7.75 (d, 2H), 7.38-7.40 (m, 3H), 3.21-3.26 (m, 2H), 2.09 (s, 3H), 1.52-1.58 (m, 2H), 089-0.93 (t, 3H). MS (EI) for $C_{22}H_{23}N_5O_2$: 390.7 (MH^+).

[01251] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-cyclopropylbenzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.24 (s 1H), 9.77 (s, 1H), 8.52 (d, 1H), 8.47 (s, 1H), 8.40 (d, 1H), 8.18 (d, 2H), 7.82-7.85 (m, 1H), 7.76 (d, 2H), 7.39 (d, 1H), 7.36-7.37 (m, 2H), 2.84-2.89 (m, 1H), 2.09 (s, 3H), 0.69-0.73 (m, 2H), 0.56-0.60 (m, 2H). MS (EI) for $C_{22}H_{21}N_5O_2$: 388.7 (MH^+).

[01252] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(3-fluorophenyl)-methyl]benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.22 (s, 1H), 9.80 (s, 1H), 9.04 (t, 1H), 8.53 (d, 1H), 8.50 (s, 1H), 8.17-8.20 (m, 2H), 7.90-7.93 (m, 1H), 7.74 (d, 2H), 7.46-7.50 (m, 1H), 7.36-7.43 (m, 3H), 7.08-7.19 (m, 3H), 4.51 (d, 2H), 2.09 (s, 3H). MS (EI) for $C_{26}H_{22}FN_5O_2$: 456.5 (MH^+).

[01253] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(naphthalen-1-ylmethyl)-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.21 (s, 1H), 9.79 (s, 1H), 9.03 (t, 1H), 8.52 (d, 2H), 8.15-8.23 (m, 3H), 7.95-7.97 (m, 1H), 7.90-7.93 (m, 1H), 7.85-7.87 (dd, 1H), 7.75 (d, 2H), 7.55-760 (m, 2H), 7.48-7.50 (m, 3H), 7.38-7.42 (m, 2H), 4.97 (d, 2H), 2.08 (s, 3H). MS (EI) for $C_{30}H_{25}N_6O_2$: 488.6 (MH^+).

[01254] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[2-(dimethylamino)ethyl]-N-methylbenzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.23 (s, 1H), 9.80 (s, 1H), 8.53 (d, 1H), 8.13 (d, 2H), 8.00 (d, 1H), 7.82 (s, 1H), 7.75 (d, 2H), 7.35-7.39 (m, 2H)6.93 (d, 1H), 3.39-3.419 (m, 2H), 2.94 (s, 3H), 2.21 (m, 2H), 2.09 (s, 6H), 1.95 (s, 3H). MS (EI) for $C_{24}H_{28}N_6O_2$: 433.7 (MH^+).

[01255] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(2-methylphenyl)-methyl]benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.22 (s, 1H), 9.79 (s, 1H), 8.56 (t, 1H), 8.52 (d,1H), 8.50 (s, 1H), 8.17-8.19 (m, 2H), 7.90-7.90 (m, 1H), 7.75 (d, 2H), 7.45-7.50 (s, 1H), 7.39-7.43 (m, 2H), 7.25-7.27 (1H), 7.14-7.18 (m, 3H), 4.47 (d, 2H), 2.34 (s, 3H), 2.09(s, 3H). MS (EI) for $C_{27}H_{25}N_5O_2$: 452.6 (MH^+).

[01256] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(3-chlorophenyl)methyl]-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.25 (s, 1H), 9.80 (s, 1H), 9.05 (t, 1H), 8.53 (d, 1H), 8.50 (s, 1H), 8.17-8.20 (m, 2H), 7.91-7.94 (m, 1H), 7.60 (s, 1H), 7.40 (s, 1H), 7.46-7.48 (m, 1H), 7.43 (d, 1H), 7.36-7.40 (m, 3H), 7.30-7.32 (m, 2H), 4.95 (d, 2H), 2.09 (s, 3H). MS (EI) for $C_{26}H_{22}ClN_5O_2$: 472.8 (MH^+).

[01257] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(2-phenylethyl)-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.22 (s, 1H), 9.78 (s, 1H), 8.51-8.53 (m, 2H), 8.46 (s, 1H), 8.19 (d, 2H), 7.85-7.88 (m, 1H), 7.76 (d, 2H), 7.37-7.38 (m, 3H), 7.27-7.32 (m, 4H), 7.19-7.23 (m, 1H), 3.47-3.52 (m, 2H), 2.84-2.88 (m, 2H), 2.08 (s, 3H). MS (EI) for $C_{27}H_{25}N_5O_2$: 452.6 (MH^+).

[01258] N-{4-[2-({3-[(4-methylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.24 (s, 1H), 9.82 (s, 1H), 8.53 (d, 1H), 8.12-8.15(m, 2H), 8.04(s, 1H), 7.80-7.82 (m, 1H), 7.76 (d, 2H), 7.36-7.40 (m, 2H), 6.94-6.96

(m, 1H), 2.94 (s, 2H), 2.78 (s, 2H), 2.37 (s, 2H), 2.27 (s, 2H), 2.18 (s, 3H), 2.09 (s, 3H). MS (EI) for $C_{24}H_{26}N_6O_2$: 431.6 (MH^+).

[01259] N-(4-{2-[(3-{[4-(2-fluorophenyl)piperazin-1-yl]carbonyl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.22 (s, 1H), 9.84 (s, 1H), 8.53 (d, 1H), 8.14 (d, 2H), 8.08 (m, 1H), 7.85 (d, 1H), 7.77 (d, 2H), 7.39-7.43 (m, 2H), 7.05-7.17 (m, 2H), 6.99-7.05 (m, 4H), 3.81(s, 2H), 3.55 (s, 2H), 3.09 (s, 2H), 2.98 (s, 2H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{27}FN_6O_2$: 511.7 (MH^+).

[01260] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[2-(phenyloxy)ethyl]-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.22 (s, 1H), 9.79 (s, 1H), 8.65 (t, 1H), 8.2 (d, 2H), 8.50 (s br, 1H), 8.9 (d, 2H), 7.88-7.90 (m, 1H), 7.76 (d, 2H), 7.38-7.45 (m, 3H), 7.27-7.30 (m, 2H), 6.91-6.98 (m, 3H), 4.11-4.14 (m, 2H), 3.63-3.78 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{27}H_{25}N_5O_3$: 468.4 (MH^+).

[01261] methyl 1-{[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]carbonyl}-piperidine-4-carboxylate: ^{1}H-NMR (400MHz, d_6-DMSO):10.23 (s, 1H), 9.82 (s, 1H), 8.53 (d, 1H), 8.14 (d, 2H), 7.97 (t, 1H), 7.86-7.88 (m, 1H), 7.75 (d, 2H), 7.36-7.70 (m, 2H), 6.94-6.96 (m, 1H), 3.61 (s, 3H), 3.30-3.36 (m, 2H), 2.77-3.29 (m, 2H), 2.65-2.70 (m, 1H), 2.09 (s, 3H), 1.99-2.19 (m, 2H), 1.79-1.88 (m, 2H). MS (EI) for $C_{26}H_{27}N_5O_4$: 474.6 (MH^+).

[01262] N-[4-(2-{[3-({4-[3-(methyloxy)phenyl]piperazin-1-yl}carbonyl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.21 (s, 1H), 9.83 (s, 1H), 8.53 (d, 1H), 8.14 (d, 2H), 8.04 (m, 1H), 7.86-7.89 (m, 1H), 7.75 (d, 2H), 7.39-7.43 (m, 2H), 7.12 (t, 1H), 7.00-7.03 (m, 1H), 6.53 (dd, 1H), 6.47 (t, 1H), 6.40 (dd, 1H), 3.78-3.80 (m, 2H), 3.71 (s, 3H), 3.20-3.24 (m, 2H), 3.12-3.19(m, 2H), 2.09 (s, 3H). MS (EI) for $C_{30}H_{30}N_6O_3$: 523.5 (MH^+).

[01263] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-{2-[2-(methyloxy)phenyl]-ethyl}benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.22 (s, 1H), 9.78 (s, 1H), 8.52-8.53 (m, 1H), 8.45 (s, 2H), 8.19 (d, 2H), 7.88 (s, 1H), 7.75 (d, 2H), 7.38-7.39(m, 3H), 7.17-7.23 (m, 2H), 6.97 (d, 1H), 6.87 (t, 1H), 3.78 (s, 3H), 3.45-3.47 (m, 2H), 2.84-2.87 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{28}H_{27}N_5O_3$: 482.7 (MH^+).

[01264] N-[4-(2-{[3-(1,3-dihydro-2H-isoindol-2-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)-phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.21 (s, 1H), 9.82 (s, 1H), 8.53 (d, 1H), 8.16 (s, 1H), 8.12-8.14 (m, 2H), 7.94-7.97 (m, 1H), 7.74 (s, 1H), 7.72 (s, 1H), 7.39-7.45 (m, 3H), 7.27-7.32 (m, 1H), 7.26 (d, 2H), 7.19-7.21 (m, 1H), 7.89 (s, 2H), 4.82 (s, 2H), 2.09 (s, 3H). MS (EI) for $C_{27}H_{23}N_5O_2$: 450.7 (MH^+).

[01265] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(biphenyl-4-ylmethyl)-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.23 (s, 1H), 9.80 (s, 1H), 9.04 (s br, 1H), 8.53 (d, 2H), 8.19 (d, 2H), 7.89 (d, 1H), 7.76 (d, 2H), 7.64 (m, 4H), 7.35-7.50 (m, 8H), 4.55 (s, 2H), 2.08 (s, 3H). MS (EI) for $C_{32}H_{27}N_5O_2$: 514.8 (MH^+).

[01266] N-(4-{2-[(3-{[4-(phenylcarbonyl)piperazin-1-yl]carbonyl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.25 (s, 1H), 9.83 (s, 1H), 8.53 (d, 1H), 8.14 (d, 2H), 8.04 (s, 1H), 7.86 (d, 1H), 7.76 (d, 2H), 7.44 (m, 5H), 7.39 (d, 2H), 7.00 (d, 1H), 3.56 (m, 8H) 2.09 (s, 3H). MS (EI) for $C_{30}H_{28}N_6O_3$: 521.6 (MH^+).

[01267] N-[4-(2-{[3-({4-[4-(methyloxy)phenyl]piperazin-1-yl}carbonyl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.83 (s, 1H), 8.53 (d, 1H), 8.13 (m, 2H), 8.05 (m, 1H), 7.86 (m, 1H), 7.75 (d, 2H), 7.37-7.43 (m, 2H), 7.01 (m, 1H), 6.90 (m, 2H), 6.82 (m, 2H), 3.77 (m, 2H), 3.68 (s, 3H), 3.53 (m, 2H), 3.08 (m, 2H), 2.97 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{30}H_{30}N_6O_3$: 523.7 (MH^+).

[01268] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-methyl-N-{[2-(methyloxy)-phenyl]methyl}benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.23 (s, 1H), 9.80 (s, 1H), 8.37 (m, 1H), 8.14 (d, 2H), 7.76 (m, 3H), 7.39 (d, 2H), 7.25-7.32 (m, 2H), 7.14-7.18 (m, 1H), 7.04 (m, 1H), 6.95 (d, 2H), 4.57 (d, 2H), 3.76 (d, 3H), 2.88 (s, 3H), 2.09 (s, 3H). MS (EI) for $C_{28}H_{27}N_5O_3$: 482.7 (MH^+).

[01269] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(2-fluorophenyl)methyl]-N-methylbenzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.23 (s, 1H), 9.08 (s, 1H), 8.52 (m, 1H), 8.14 (d, 2H), 8.01 (m, 1H), 7.89 (m, 1H), 7.75 (d, 2H), 7.38 (m, 4H), 7.21 (m, 2H), 7.01 (m, 1H), 4.67 (d, 2H), 2.91 (s, 3H), 2.09 (s, 3H). MS (EI) for $C_{27}H_{24}FN_5O_2$: 470.6 (MH^+).

[01270] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(2-pyridin-2-ylethyl)-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.78 (s, 1H), 8.51-8.54 (m, 3H), 8.46 (s, 1H), 8.18 (d, 2H), 7.86-7.88 (m, 1H), 7.76 (d, 2H), 7.69-7.73 (m, 1H), 7.37-7.40 (m, 3H), 7.31 (m, 1H), 7.21-7.24 (m, 1H), 3.61-3.66 (m, 2H), 3.02 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{26}H_{24}N_6O_2$: 453.6 (MH^+).

[01271] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(pyridin-2-ylmethyl)-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.81 (s, 1H), 9.06 (m, 1H), 8.52 (m, 2H), 8.19 (d, 2H), 7.91 (m, 1H), 7.73-7.79 (m, 3H), 7.51 (d, 1H), 7.40 (m, 2H), 7.30 (d, 1H), 7.25-7.27 (m, 1H), 4.59 (d, 2H), 2.09 (s, 3H). MS (EI) for $C_{25}H_{22}N_6O_2$: 439.8 (MH^+).

[01272] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(pyridin-3-ylmethyl)-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.22 (s, 1H), 9.78 (s, 1H), 8.52 (d, 1H), 8.45 (s br, 1H), 8.25 (d, 1H), 7.18 (d, 3H), 7.82-7.85 (m, 1H), 7.76 (d, 3H), 7.35-7.41 (m, 4H), 4.25 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{25}H_{22}N_6O_2$: 438.6 (MH^+).

[01273] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(pyridin-4-ylmethyl)-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.80 (s, 1H), 9.08 (t, 1H), 8.50-8.54 (m, 4H), 8.18 (d, 2H), 7.92 (d, 1H), 7.74 (d, 2H), 7.49 (d, 1H), 7.42 (t, 1H), 7.40 (d, 1H), 7.31 (d, 2H), 4.51 (d, 2H), 2.09 (s, 3H). MS (EI) for $C_{25}H_{22}N_6O_2$: 438.5 (MH^+).

[01274] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-methyl-N-(phenylmethyl)-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.23 (s, 1H), 9.81 (s, 1H), 8.53 (s br, 1H), 8.14 (d, 2H), 7.46 (d, 2H), 7.23-7.46 (m, 8H), 7.21 (s br, 1H), 7.02 (s br, 1H), 4.56 (d, 2H), 2.95 (s, 3H), 2.09 (s, 3H). MS (EI) for $C_{27}H_{25}N_5O_2$: 452.7 (MH^+).

[01275] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-cyclopentylbenzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.75 (s, 1H), 8.52 (d, 1H), 8.45 (s br, 1H), 8.25 (d, 1H), 8.17 (d, 2H), 7.84 (d, 1H) 7.75 (d, 2H), 7.35-7.42 (m, 3H), 4.22-4.27 (m, 1H), 2.09 (s, 3H), 1.88-1.93 (m, 2H), 1.70 (m, 2H), 1.49-1.59 (m, 4H). MS (EI) for $C_{24}H_{25}N_5O_2$: 416.8 (MH^+).

[01276] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(2-chlorophenyl)methyl]-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.80 (s, 1H), 9.00 (t, 1H), 8.53 (d, 1H), 8.50 (s br, 1H), 8.18 (d, 2H), 7.93 (d, 1H), 7.63 (d, 2H), 7.52 (d, 1H), 7.28-7.48 (m, 6H), 4.56 (d, 2H), 2.09 (s, 3H). MS (EI) for $C_{26}H_{22}ClN_5O_2$: 473.0 (MH^+).

[01277] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(4-chlorophenyl)methyl]-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.22 (s, 1H), 9.79 (s, 1H), 9.02 (t, 1H), 8.52 (d, 1H), 8.50 (s br, 1H), 8.18 (d, 2H), 7.90 (d, 1H), 7.74 (d, 2H), 7.46 (d, 1H), 7.41 (m, 2H), 7.38 (s, 2H), 7.36 (m, 2H), 4.48 (d, 2H), 2.09 (s, 3H). MS (EI) for $C_{26}H_{22}ClN_5O_2$: 473.1 (MH^+).

[01278] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(furan-2-ylmethyl)-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.78 (s, 1H), 8.91 (t, 1H), 8.52 (d, 1H), 8.48 (s br, 1H), 8.17 (d, 2H), 7.88 (d, 1H), 7.76 (d, 2H), 7.58 (m, 1H), 7.44 (d, 1H), 7.37-7.41 (m, 2H), 6.41 (m, 1H), 6.28 (dd, 1H), 4.48 (d, 2H), 2.09 (s, 3H). MS (EI) for $C_{24}H_{21}N_5O_3$: 428.6 (MH^+).

[01279] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-{[4-(methyloxy)phenyl]-methyl}benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.22 (s, 1H),

9.77 (s, 1H), 8.92 (t, 1H), 8.52 (d, 1H), 8.49 (s br, 1H), 8.19 (d, 2H), 7.88 (d, 1H), 7.76 (d, 2H), 7.45 (d, 1H), 7.37-7.41 (m, 2H), 7.27 (d, 2H), 6.89 (d, 2H), 4.42 (d, 2H), 3.72 (s, 3H), 2.08 (s, 3H). MS (EI) for $C_{27}H_{25}N_5O_3$: 468.4 (MH^+).

[01280] N-[4-(2-{[3-({4-[2-(methyloxy)phenyl]piperazin-1-yl}carbonyl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.82 (s, 1H), 8.53 (d, 1H), 8.14 (d, 2H), 8.06 (s, 1H) 7.86 (d, 1H), 7.76 (d, 2H), 7.40 (m, 2H), 7.01 (d, 1H), 6.59 (m, 2H), 6.88 (s, 2H), 3.78 (s, 3H), 3.55 (m, 2H), 3.03 (m, 2H), 2.94 (s, 2H), 2.79 (s, 2H), 2.09 (s, 3H). MS (EI) for $C_{30}H_{30}N_6O_3$: 523.5 (MH^+).

[01281] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[3-(methyloxy)propyl]-benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.76 (s, 1H), 8.52 (d, 1H), 8.46 (s br, 1H), 8.40 (t, 1H), 8.18 (d, 2H), 7.85-7.88 (m, 1H), 7.75 (d, 2H), 7.38-7.40 (m, 3H), 3.40 (m, 2H), 3.30 (m, 2H), 3.24 (s, 3H), 2.09 (s, 3H), 1.74-1.80 (m, 2H). MS (EI) for $C_{23}H_{25}N_5O_3$: 420.5 (MH^+).

[01282] N-(4-{2-[(3-{[(2R,6S)-2,6-dimethylmorpholin-4-yl]carbonyl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.23 (s, 1H), 9.81 (s, 1H), 8.53 (d, 1H), 8.13 (d, 2H), 7.99 (m, 1H), 7.86 (d, 1H), 7.76 (d, 2H), 7.37-7.41 (m, 2H), 6.98 (d, 1H), 2.94 (s, 2H), 2.79 (s, 2H), 2.09 (s, 3H), 1.96 (s, 1H), 1.16 (m, 3H), 0.99 (m, 3H). MS (EI) for $C_{25}H_{27}N_5O_3$: 445.5 (MH^+).

[01283] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-[(6-chloropyridin-3-yl)methyl]benzamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.22 (s, 1H), 9.79 (s, 1H), 9.06 (t, 1H), 8.52 (d, 1H), 8.49 (s, 1H), 8.40 (d, 1H), 8.18 (d, 2H), 7.91 (m, 2H), 7.81 (dd, 1H), 7.74 (d, 2H), 7.49 (d, 1H), 7.41-7.46 (m, 2H), 7.39 (d, 1H), 4.50 (d, 2H), 2.09 (s, 3H). MS (EI) for $C_{25}H_{21}ClN_6O_2$: 474.1 (MH^+).

[01284] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-butylbenzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.24 (s, 1H), 9.80 (s, 1H), 8.53 (d, 1H), 8.13 (d, 2H), 8.02 (s br, 1H), 7.78 (m, 1H), 7.75 (d, 2H), 7.39 (d, 1H), 7.35 (d, 1H), 6.91 (d, 2H), 3.26 (m, 2H), 2.09 (s, 3H), 1.62 (m, 2H), 1.32 (m, 2H), 1.08 (m, 3H). MS (EI) for $C_{23}H_{25}N_5O_2$: 404.5 (MH^+).

[01285] N-(4-{2-[(3-{[4-(2-chlorophenyl)piperazin-1-yl]carbonyl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.83 (s, 1H), 8.53 (d, 1H), 8.14 (d, 2H), 7.90 (s br, 1H), 7.85 (d, 1H), 7.76 (d 2H), 7.38-7.43 (m, 3H), 7.28 (m, 1H), 7.13 (dd, 1H), 7.07 (dd, 1H), 7.03 (m, 1H), 3.81 (m, 4H), 3.58 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{27}ClN_6O_2$: 528.1 (MH^+).

[01286] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-ethyl-N-[2-(methyloxy)-ethyl]benzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.80 (s, 1H), 8.53 (d, 1H), 8.13 (d, 2H), 7.99 (m, 2H), 7.82 (m, 1H), 7.76 (d, 2H), 7.39 (d, 2H), 7.36 (d, 2H), 6.92 (d, 1H), 3.57 (m, 2H), 3.12 (m, 2H), 2.94 (s, 3H), 2.09 (s, 3H), 1.10 (m, 3H). MS (EI) for $C_{24}H_{27}N_5O_3$: 434.4 (MH^+).

[01287] N-{4-[2-({4-[4-(phenylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.35 (d, 4H), 7.27 (d, 2H), 6.92 (d, 2H), 3.54 (s, 2H), 3.9 (m, 4H), 2.53 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{30}N_6O$: 479.7 (MH^+).

[01288] N-(4-{2-[(4-{4-[(5-methyl-3-phenylisoxazol-4-yl)methyl]piperazin-1-yl}phenyl)-amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.93-7.96 (m, 2H), 7.74 (d, 2H), 7.66 (d, 2H), 7.50-7.53 (m, 3H), 7.26 (d, 1H), 6.93 (d, 2H), 3.43 (s, 2H), 3.09 (m, 4H), 2.56 (m, 4H), 2.48 (s, 3H), 2.09 (s, 3H). MS (EI) for $C_{33}H_{33}N_7O_2$: 560.4 (MH^+).

[01289] N-(4-{2-[(4-{4-[(5-methyl-1-phenyl-1H-pyrazol-4-yl)methyl]piperazin-1-yl}-phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.56 (s, 1H), 7.53 (d, 4H), 7.40-7.45 (m, 1H), 7.26 (d, 1H), 6.92 (d, 2H), 3.43 (s, 2H), 3.09 (m, 4H), 2.56 (m, 4H), 2.31 (s, 3H), 2.09 (s, 3H). MS (EI) for $C_{33}H_{34}N_8O$: 559.7 (MH^+).

[01290] N-(4-{2-[(4-{4-[(2-phenyl-1,3-thiazol-4-yl)methyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.94 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.57 (s, 1H), 7.48-7.53 (m, 3H), 7.26 (d, 1H), 6.93 (d, 1H), 3.73 (s, 2H), 3.11 (m, 4H), 2.65 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{32}H_{31}N_7OS$: 562.5 (MH^+).

[01291] N-[4-(2-{[4-(4-{[6-(phenyloxy)pyridin-3-yl]methyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.23 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 8.07 (d, 1H), 7.81 (dd, 1H), 7.74 (d, 2H), 7.65 (d, 2H), 7.43 (t, 2H), 7.26 (d, 1H), 7.19-7.23 (m, 1H), 7.14 (d, 2H), 7.01 (d, 1H), 6.92 (d, 2H), 3.21 (s, 2H), 3.08 (m, 4H), 2.48 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{34}H_{33}N_7O_2$: 572.4 (MH^+).

[01292] N-{4-[2-({4-[4-(cyclohexylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.26 (d, 1H), 6.92 (d, 2H), 3.06 (m, 4H), 2.47

(m, 4H), 2.13 (d, 2H), 2.09 (s, 3H), 1.76 (d, 2H), 1.65 (m, 3H), 1.49-1.54 (m, 1H), 1.12-1.17 (m, 3H), 080-0.89 (m, 2H). MS (EI) for $C_{29}H_{36}N_6O$: 485.8 (MH^+).

[01293] N-(4-{2-[(4-{4-[(1S,4S)-bicyclo[2.2.1]hept-5-en-2-ylmethyl]piperazin-1-yl}phenyl)-amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.26 (d, 1H), 6.92 (d, 2H), 6.14-6.16 (m, 1H), 5.95-5.97 (m, 1H), 3.07 (m, 4H), 2.79 (d, 2H), 2.45 (m, 4H), 2.32-2.39 (m, 2H), 2.09 (s, 3H), 1.95-1.99 (m, 1H), 1.81-1.87 (m, 1H), 1.31 (m, 1H), 1.23 (m, 1H), 0.51 (m, 1H). MS (EI) for $C_{30}H_{34}N_6O$: 495.7 (MH^+)

[01294] N-[4-(2-{[4-(4-pentylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.26 (d, 1H), 6.92 (d, 2H), 3.07 (m, 4H), 2.55 (m, 4H), 2.307 (t, 2H), 2.09 (s, 3H), 1.43-1.49 (m, 2H), 1.22-1.34 (m, 4H), 0.88 (t, 3H). MS (EI) for $C_{27}H_{34}N_6O$: 459.7 (MH^+).

[01295] N-(4-{2-[(4-{4-[(2-chlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.21 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.66 (d, 2H), 7.54 (dd, 1H), 7.45 (dd, 1H), 7.29-7.39 (m, 2H), 7.26 (d, 1H), 6.93 (d, 2H), 3.64 (s, 2H), 3.10 (m, 4H), 2.60 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{29}ClN_6O$: 514.1 (MH^+).

[01296] N-[4-(2-{[4-(4-{[3,5-bis(methyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.26 (d, 1H), 6.93 (d, 2H), 6.51 (d, 2H), 6.39 (t, 1H), 3.75 (s, 6H), 3.46 (s, 2H), 3.09 (m, 4H), 2.61 (m, 4H), 2.09 (s. 3H). MS (EI) for $C_{31}H_{34}N_6O_3$: 539.8 (MH^+).

[01297] N-(4-{2-[(4-{4-[(4-fluorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.36-7.39 (m, 2H), 7.26 (d, 1H), 7.16 (t, 2H), 6.92 (d, 2H), 3.51 (S, 2H), 3.08 (m, 4H), 2.28 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{29}FN_6O$: 497.8 (MH^+).

[01298] N-(4-{2-[(4-{4-[(1-methyl-1H-pyrrol-2-yl)methyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.26 (d, 1H), 6.92 (d, 2H), 6.68 (t, 1H), 5.88-5.91 (m, 2H), 3.61 (s, 2H), 3.4 (s, 3H), 3.06 (m, 4H), 2.58 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{28}H_{31}N_7O$: 482.8 (MH^+).

[01299] N-[4-(2-{[4-(4-{[5-(3-chlorophenyl)furan-2-yl]methyl}piperazin-1-yl)phenyl]-amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.72-7.76 (m, 3H), 7.63-7.66 (m, 3H), 7.45 (t, 1H), 7.33 (d, 1H), 7.26 (d, 1H), 7.06 (d, 1H), 6.92 (d, 2H), 6.48 (d, 1H), 3.64 (s, 2H), 3.10 (m, 4H), 2.60 (m, 4H), 20.9 (s, 3H). MS (EI) for $C_{33}H_{31}ClN_6O$: 580.3 (MH^+).

[01300] N-[4-(2-{[4-(4-{[4-fluoro-2-(trifluoromethyl)phenyl]methyl}piperazin-1-yl)phenyl]-amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.37 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.84-7.88 (m, 1H), 7.74 (d, 2H), 7.66 (d, 2H), 7.54-7.72 (m, 2H), 7.26 (d, 1H), 6.93 (d, 2H), 3.66 (s, 2H), 3.10 (m, 4H), 2.56 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{30}H_{28}F_4N_6O$: 565.3 (MH^+).

[01301] N-[4-(2-{[4-(4-{[4-(1H-imidazol-1-yl)phenyl]methyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO):10.21 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.25 (t, 1H), 7.11 (d, 2H), 7.74 (d, 3H), 7.61-7.67 (m, 4H), 7.48 (d, 2H), 7.26 (d, 1H), 7.11 (t, 1H), 6.93 (d, 2H), 3.58 (s, 2H), 3.10 (m, 4H), 2.55 (m, 4H), 20.9 (s, 3H). MS (EI) for $C_{32}H_{32}N_8O$: 545.8 (MH^+).

[01302] N-[4-(2-{[4-(4-{[2,5-bis(trifluoromethyl)phenyl]methyl}piperazin-1-yl)phenyl]-amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 (s, 1H), 9.37 (s, 1H), 8.43 (d, 1H), 8.17 (s, 1H), 8.10 (d, 2H), 8.00 (d, 1H), 7.89 (d, 1H), 7.74 (d, 2H), 7.67 (d, 2H), 7.26 (d, 1H), 6.94 (d, 2H), 3.79 (s, 2H), 3.12 (m, 4H), 2.60 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{31}H_{28}F_6N_6O$: 615.7 (MH^+).

[01303] N-(4-{2-[(4-{4-[(2,6-dimethylphenyl)methyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.24 (d, 2H), 7.64 (d, 2H), 7.26 (d, 1H), 7.00-7.08 (m, 3H), 6.90 (d, 2H), 3.50 (s, 2H), 3.02 (m, 4H), 2.54 (m, 4H), 2.37 (s, 6H), 2.09 (s, 3H). MS (EI) for $C_{31}H_{34}N_6O$: 507.7 (MH^+).

[01304] N-(4-{2-[(4-{4-[(2,3-dimethylphenyl)methyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.74 (d 2H), 7.65 (d, 2H), 7.26 (d, 1H), 7.01-7.09 (m, 3H), 6.91 (d, 2H), 3.45 (s, 2H), 3.05 (m, 4H), 2.53 (m, 4H), 2.24 (d, 6H), 2.09 (s, 3H). MS (EI) for $C_{31}H_{34}N_6O$: 507.8 (MH^+).

[01305] N-[4-(2-{[4-(4-{[2,4-bis(ethyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.35 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.64 (d, 2H), 7.26 (d,

1H), 7.19 (d, 1H), 6.91 (d, 2H), 6.47-6.51 (m, 2H), 3.97-4.04 (m, 4H), 3.46 (s, 2H), 3.06 (m, 4H), 2.52 (m, 4H), 2.09 (s, 3H), 1.30-1.35 (m, 6H). MS (EI) for $C_{33}H_{38}N_6O_3$: 567.8 (MH^+).

[01306] N-[4-(2-{[4-(4-{[3-(ethyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.36 (s, 1H), 8.45 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.24 (t, 1H), 7.11-7.19 (m, 3H), 7.02-7.09 (m, 3H), 6.91 (d, 2H), 3.96-4.00 (m, 2H), 3.40 (s, 2H), 3.07 (m, 4H), 2.59 (m, 4H), 2.09 (s, 3H), 1.32-1.38 (m, 3H). MS (EI) for $C_{31}H_{34}N_6O_2$: 523.8 (MH^+).

[01307] N-{4-[2-({4-[4-(3-methylbutanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.23 (s, 1H), 9.04 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.27 (d, 1H), 6.96 (d, 2H) 3.67 (m, 4H), 3.06 (m, 2H), 3.02 (m, 2H), 2.24 (d, 2H), 2.09 (s, 3H), 1.97-2.09 (m, 1H), 0.92 (d, 6H). MS (EI) for $C_{27}H_{32}N_6O_2$: 473.8 (MH^+).

[01308] N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.27 (d, 1H), 6.95 (d, 2H), 3.59 (m, 2H), 3.46 (m, 2H), 3.39 (t, 1H), 3.02 (m, 4H), 2.11-2.23 (m, 4H), 2.09 (s, 3H), 1.89-1.92 (m, 1H), 1.72-1.78 (m, 1H). MS (EI) for $C_{27}H_{30}N_6O_2$: 470.7 (MH^+).

[01309] N-{4-[2-({4-[4-(cyclopentylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.27 (d, 1H), 6.96 (d, 2H), 3.63 (m, 4H), 3.04 (m, 4H), 2.98 (m, 1H), 2.09 (s, 3H), 1.74-2.09 (m, 2H), 1.51-1.72 (m, 6H). MS (EI) for $C_{28}H_{32}N_6O_2$: 485.5 (MH^+).

[01310] N-[4-(2-{[4-(4-{[2-(methyloxy)phenyl]carbonyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.68 (d, 2H), 7.42 (m, 1H), 7.27 (d, 1H), 7.22 (dd, 1H), 7.10 (d, 1H), 7.02 (m, 1H), 6.96 (d, 2H), 3.81 (s, 3H), 3.77 (m, 2H), 3.27 (m, 2H), 3.12 (m, 2H), 3.01 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{30}H_{30}N_6O_3$: 523.7 (MH^+).

[01311] N-(4-{2-[(4-{4-[(2-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.30-7.36 (m, 2H), 7.28 (d, 2H), 7.19-7.24 (m, 1H), 6.96 (d, 2H), 3.82 (m, 2H), 3.28 (m, 2H), 3.16 (m, 2H), 3.00 (m, 2H), 2.25 (s, 3H), 2.09 (s, 3H). MS (EI) for $C_{30}H_{30}N_6O_2$: 507.8 (MH^+).

[01312] N-[4-(2-{[3-(4-{[2-(methyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.21 (s, 1H), 9.46 (s,

1H), 8.49 (d, 1H), 8.12 (d, 2H), 7.73 (d, 2H), 7.63 (s, 1H), 7.36 (d, 1H), 7.32 (d, 1H), 7.21 (m, 2H), 7.10 (t, 1H), 6.98 (m, 2H), 6.55 (d, 1H), 3.80 (s, 3H), 3.54 (s, 2H), 3.16 (m, 4H), 2.57 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{30}H_{32}N_6O_2$: 509.6 (MH+).

[01313] N-{4-[2-({4-[(2R,6S)-2,6-dimethylmorpholin-4-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.44 (s, 1H), 10.07 (s, 1H), 8.74 (s, 1H), 8.57 (d, 1H), 8.21 (s, 2H), 7.90 (m, 4H), 7.73 (s, 2H), 7.48 (d, 1H), 4.49 (m, 1H), 4.24 (m, 2H), 4.02 (m, 1H), 3.57 (m, 3H), 3.29 (m, 2H), 1.99 (m, 4H), 1.18 (m, 7H). MS (EI) for $C_{27}H_{32}N_6O_2$: 473.5 (MH+).

[01314] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-5-oxo-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.33 (s, 1H), 9.39 (s, 1H), 8.45 (d, 1H), 8.14 (d, 2H), 7.93 (s, 1H), 7.79 (d, 2H), 7.67 (d, 2H), 7.28 (d, 1H), 6.93 (d, 2H), 4.23 (m, 1H), 3.75 (m, 4H), 3.05 (m, 4H), 2.35 (m, 1H), 2.21 (m, 2H), 2.03 (m, 1H). MS (EI) for $C_{25}H_{26}N_6O_3$: 459.5 (MH+).

[01315] N^1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-aspartamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.71 (s, 1H), 10.09 (s, 1H), 8.94 (s, 3H), 8.58 (d, 1H), 8.23 (d, 2H), 7.91 (m, 4H), 7.73 (s br, 2H), 7.49 (d, 1H), 4.52 (m, 4H), 4.05 (m, 5H), 3.33 (d, 1H), 3.29 (d, 1H). MS (EI) for $C_{24}H_{27}N_7O_3$: 462.5 (MH+).

[01316] N^1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-glutamamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.39 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.83 (d, 2H), 7.67 (d, 2H), 7.35 (s, 1H), 7.29 (d, 1H), 6.93 (d, 2H), 6.77 (s, 1H), 3.75 (m, 4H), 3.37 (t, 1H), 3.05 (m, 4H), 1.88 (m, 2H), 1.70 (m, 1H). MS (EI) for $C_{25}H_{29}N_7O_3$: 476.5 (MH+).

[01317] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-threoninamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.26 (s, 1H), 9.89 (s, 1H), 8.54 (d, 1H), 8.31 (s, 2H), 8.19 (d, 2H), 7.86 (d, 3H), 7.44 (m, 3H), 4.11 (m, 2H), 3.96 (m, 4H), 3.39 (m, 4H), 1.23 (d, 3H) . MS (EI) for $C_{24}H_{28}N_6O_3$: 449.5 (MH+).

[01318] N-(4-{2-[(3-chloro-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.43 (s, 1H), 9.99 (s, 1H), 8.55 (d, 1H), 8.20 (d, 2H), 8.03 (s, 1H), 7.89 (2H), 7.71 (dd, 1H), 7.46 (d, 2H), 7.20 (d, 1H), 4.49 (m, 1H), 3.76 (m, 4H), 3.28 (m, 2H), 2.96 (m, 4H), 1.97 (m, 4H). MS (EI) for $C_{25}H_{27}ClN_6O_2$: 479.9 (MH+).

[01319] N-(4-{2-[(3-chloro-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.55 (s, 1H), 10.15 (s, 1H), 8.56 (d, 1H), 8.21 (d, 2H), 8.01 (s, 1H), 7.89 (d, 2H), 7.71 (dd, 1H), 7.49 (d, 2H), 7.23 (d, 1H), 4.51 (m,

1H), 3.76 (m, 4H), 3.29 (m, 2H), 2.97 (m, 4H), 1.97 (m, 4H). MS (EI) for $C_{25}H_{27}ClN_6O_2$: 479.9 (MH+).

[01320] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-leucinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.41 (s, 1H), 10.05 (s, 1H), 8.56 (d, 1H), 8.60 (m, 3H), 8.25 (d, 2H), 7.96 (m, 3H), 7.69 (m, 2H), 7.47 (d, 1H),4.14 (m, 1H), 4.04 (m, 4H), 3.57 (m, 4H), 1.71 (m, 2H), 1.19 (m, 1H), 1.00 (s, 6H). MS (EI) for $C_{26}H_{32}N_6O_2$: 461.5 (MH+).

[01321] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-isoleucinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.41 (s, 1H), 10.10 (s, 1H), 8.56 (d, 1H), 8.47 (m, 2H), 8.20 (d, 2H), 7.92 (m, 3H), 7.73 (m, 2H), 7.47 (d, 1H), 4.12 (m, 4H), 3.57 (m, 4H), 1.65 (m, 2H), 1.18 (m, 2H), 1.00 (d, 3H), 0.89 (t, 3H). MS (EI) for $C_{26}H_{32}N_6O_2$: 461.5 (MH+).

[01322] (2R)-2-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-butanamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.57 (s, 1H), 10.20 (s, 1H), 8.56 (m, 3H), 8.24 (m, 2H), 7.97 (m, 4H), 7.82 (s, 1H), 7.54 (s, 1H), 4.05 (m, 5H), 1.96 (m, 4H), 1.10 (m, 5H). MS (EI) for $C_{24}H_{28}N_6O_2$: 433.5 (MH+).

[01323] N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)thiophene-2-carboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.5 (s, 1H), 9.40 (br s, 1H), 8.55 (d, 1H), 8.23 (d, 2H), 8.09 (dd, 1H), 7.96-7.91 (m, 5H), 7.53 (m, 1H), 7.45 (d, 1H), 7.32-7.25 (m, 3H), 6.74 (br s, 1H). MS (EI): 388.0 (MH+).

[01324] N-(3-{[4-(4-aminophenyl)pyrimidin-2-yl]amino}phenyl)-2,6-dichlorobenzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.7 (s, 1H), 9.67 (s, 1H), 8.37-8.35 (m, 2H), 8.01 (d, 2H), 7.61-7.58 (m, 2H), 7.51-7.49 (m, 1H), 7.44 (dt, 1H), 7.31-7.22 (m, 3H), 6.69 (d, 2H), 5.95 (br, 2H)); MS (EI): 450.0 (MH+).

[01325] 4-{[2-chloro-4-(methyloxy)phenyl]oxy}-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine: ^{1}H-NMR (400MHz, d6-DMSO): 9.37 (s, 1H), 8.31 (d, 1H), 7.33-7.23 (m, 4H), 7.02 (dd, 1H), 7.00 (br d, 2H), 6.41 (d, 1H), 3.83 (s, 3H), 3.73-3.71 (m, 4H), 2.98-2.96 (m, 4H). MS (EI): 412.8 (MH+).

[01326] N-[4-({2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}oxy)phenyl]acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.2 (s, 1H), 9.92 (br s, 1H), 8.33 (d, 1H), 7.66 (d, 2H), 7.42 (br s, 2H), 7.17 (d, 2H), 7.10 (br s, 2H), 6.50 (d, 1H), 3.86 (br s, 4H), 3.24 (br s, 4H), 2.08 (s, 3H); MS (EI): 406.1 (MH+).

[01327] N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-3-(methyloxy)propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.3 (s, 1H), 9.61 (br s, 1H),

8.46 (d, 1H), 8.16-8.12 (m, 4H), 7.78 (d, 2H), 7.72 (d, 2H), 7.34 (d, 1H), 7.12 (br s, 2H), 4.47-4.44 (m, 1H), 3.80 (br s, 4H), 3.64 (t, 2H), 3.64 (s, 3H), 3.07 (br s, 4H), 2.60 (t, 2H), 1.34 (d, 3H); MS (EI): 504.2 (MH+).

[01328] 3-(methyloxy)-N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.3 (s, 1H), 9.51 (s, 1H), 8.54 (m, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.77 (d, 2H), 7.71 (d, 2H), 7.31 (d, 1H), 7.04 (br d, 2H), 4.68 (m, 1H), 4.07 (br s, 4H), 3.64 (t, 2H), 3.25 (s, 3H), 3.17 (br s, 4H), 2.60 (t, 2H), 2.43-2.39 (m, 2H), 1.94-1.81 (m, 4H); MS (EI): 530.2 (MH+).

[01329] N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}cyclopropanecarboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.5 (s, 1H), 9.60 (br s, 1H), 8.46 (d, 1H), 8.12 (d, 2H), 7.78-7.76 (m, 4H), 7.34 (m, 1H), 7.13 (br s, 2H), 3.70 (m, 1H), 3.54 (br s, 4H), 3.41 (m, 1H), 3.16 (br s, 4H), 2.23-2.08 (m, 3H), 1.95-1.74 (m, 3H), 0.84-0.83 (m, 4H); MS (EI): 497.2 (MH+).

[01330] N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}cyclopropanecarboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.5 (s, 1H), 9.69 (br s, 1H), 8.47 (d, 1H), 8.13 (d, 2H), 7.77 (d, 4H), 7.36 (d, 2H), 7.23 (br s, 1H), 3.76 (br s, 4H), 3.25 (br s, 4H), 2.94 (septet, 1H), 1.84 (p, 1H), 1.03 (d, 6H), 0.84-0.83 (m, 4H). MS (EI): 485.1 (MH+).

[01331] 2,6-dichloro-N-{3-[(4-{4-[(cyclopropylcarbonyl)amino]phenyl}pyrimidin-2-yl)-amino]phenyl}benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.7 (s, 1H), 10.5 (s, 1H), 9.74 (s, 1H), 8.50 (d, 1H), 8.40 (s, 1H), 8.21 (d, 2H), 7.76 (d, 2H), 7.61-7.59 (m, 2H), 7.53-7.49 (m, 1H), 7.47-7.45 (m, 1H), 7.39 (d, 1H), 7.31-7.22 (m, 2H), 1.83 (p, 1H), 0.83-0.81 (m, 4H); MS (EI): 518.1 (MH+).

[01332] 2,6-dichloro-N-(3-{[4-(1H-indol-5-yl)pyrimidin-2-yl]amino}phenyl)benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 11.3 (s, 1H), 10.7 (s, 1H), 9.56 (s, 1H), 8.45 (s, 1H), 8.39 (d, 1H), 8.31 (s, 1H), 7.96 (dd, 1H), 7.54-7.52 (m, 2H), 7.46-7.41 (m, 3H), 7.37-7.34 (m, 2H), 7.21 (d, 2H), 6.48-6.48 (m, 1H). MS (EI): 474.0 (MH+).

[01333] N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)-2-morpholin-4-ylacetamide: ^{1}H-NMR (400MHz, d6-DMSO): 11.0 (s, 1H), 10.4 (br, 2H), 9.89 (s, 1H), 8.56 (d, 1H), 8.23 (d, 2H), 7.82-7.79 (m, 3H), 7.62 (br, 1H), 7.44 (d, 1H), 7.34 (br, 1H), 6.8 (br, 1H), 4.24 (s, 2H), 3.96-3.84 (m, 8H); MS (EI): 405.3 (MH+).

[01334] N-(4-phenylpyrimidin-2-yl)benzene-1,3-diamine: ^{1}H-NMR (400MHz, d6-DMSO): 9.37 (s, 1H), 8.51 (d, 1H), 8.19-8.16 (m, 2H), 7.57-7.53 (m, 3H), 7.37-7.36 (d, 1H), 7.10 (t, 1H), 7.00-6.91 (m, 2H), 6.22-6.20 (m, 1H), 5.00 (s, 2H). MS (EI): 263.3 (MH+).

[01335] N-[3-({4-[4-(acetylamino)-2-chlorophenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.7 (s, 1H), 10.3 (s, 1H), 9.78 (s, 1H), 8.52 (d, 1H), 8.13-8.12 (m, 1H), 7.93 (s, 1H), 7.71 (d, 1H), 7.30-7.21 (m, 5H), 7.30-7.21 (m, 2H), 7.11 (d, 1H), 2.07 (s, 3H). MS (EI): 527.9 (MH+).

[01336] 2,6-dichloro-N-{3-[(4-phenylpyrimidin-2-yl)amino]phenyl}benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.7 (s, 1H), 9.76 (s, 1H), 8.56 (d, 1H), 8.39 (s, 1H), 8.26-8.23 (m, 2H), 7.61-7.59 (m, 2H), 7.55-7.48 (m, 5H), 7.44 (d, 1H), 7.31-7.24 (m, 2H); MS (EI): 437.0 (MH+).

[01337] 4-(2,4-dichlorophenyl)-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine: ^{1}H-NMR (400MHz, d6-DMSO): 9.59 (s, 1H), 8.52 (d, 1H), 7.80 (d, 1H), 7.66 (d, 1H), 7.63-7.58 (m, 3H), 7.00 (d, 1H), 6.88 (d, 2H), 3.74-3.72 (m, 4H), 3.04-3.01 (m, 4H); MS (EI): 401.0 (MH+).

[01338] 4-(2,4-dichlorophenyl)-N-{3-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}pyrimidin-2-amine: ^{1}H-NMR (400MHz, d6-DMSO): 10.0 (s, 1H), 8.62 (d, 1H), 7.92 (s, 1H), 7.82 (d, 1H), 7.76 (dd, 1H), 7.70-7.68 (m, 1H), 7.62-7.59 (m, 1H), 7.34 (t, 1H), 7.13 (d, 1H), 6.96-6.94 (m, 1H), 3.59 (br s, 2H), 3.32 (br s, 2H), 2.37 (br s, 2H), 2.30 (q, 2H), 2.22 (br s, 2H), 0.99 (t, 3H); MS (EI): 456.0 (MH+).

[01339] 2,6-dichloro-N-(3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}phenyl)benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.7 (s, 1H), 9.89 (s, 1H), 8.59 (d, 1H), 8.14-8.13 (m, 1H), 7.80 (d, 1H), 7.77 (d, 1H), 7.59-7.48 (m, 5H), 7.32-7.23 (m, 2H), 7.14 (d, 1H); MS (EI): 504.9 (MH+).

[01340] N-(2-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 11.3 (s, 1H), 9.61 (s, 1H), 8.53 (d, 1H), 8.19 (d, 1H), 7.79 (d, 1H), 7.50 (d, 2H), 7.48-7.44 (m, 1H), 7.22 (td, 1H), 7.14 (d, 1H), 6.94 (d, 2H), 3.75-3.73 (m, 4H), 3.06-3.03 (m, 4H), 1.69 (s, 3H). MS (EI): 390.1 (MH+).

[01341] 4-[3-(methyloxy)phenyl]-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine: ^{1}H-NMR (400MHz, d6-DMSO): 9.45 (s, 1H), 8.49 (d, 1H), 7.73-7.66 (m, 4H), 7.45 (t, 1H), 7.34 (d, 1H), 7.13-7.10 (m, 1H), 6.92 (d, 2H), 3.86 (s, 3H), 3.75-3.35 (m, 4H), 2.51-2.50 (m, 4H). MS (EI): 363.1 (MH+).

[01342] 4-(2,3-dihydro-1,4-benzodioxin-6-yl)-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine: ^{1}H-NMR (400MHz, d6-DMSO): 9.36 (s, 1H), 8.41 (d, 1H), 7.69-7.64 (m, 4H), 7.25 (d, 1H), 6.99 (d, 1H), 6.92 (d, 2H), 4.33-4.30 (m, 4H), 3.75-3.73 (m, 4H), 3.06-3.03 (m, 4H); MS (EI): 391.1 (MH+).

[01343] 3-(methyloxy)-N-{4-[2-({4-[4-(piperazin-1-ylacetyl)piperazin-1-yl]phenyl}amino)-pyrimidin-4-yl]phenyl}propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.2 (s, 1H), 9.43 (s, 1H), 8.79 (br, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.77 (d, 2H), 7.69 (d, 2H), 7.29 (d, 1H), 6.98 (d, 2H), 3.64 (t, 2H), 3.59 (br s, 2H), 3.25 (s, 3H), 3.22 (br m, 8H), 3.13 (br m, 4H), 3.07 (br m, 4H), 2.60 (t, 2H). MS (EI): 559.3 (MH+).

[01344] N^2,N^2-dimethyl-N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]glycinamide • 1.3 AcOH: ^{1}H-NMR (400MHz, d_6-DMSO): 10.00 (s, 1H), 9.42 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.84 (d, 2H), 7.69 (d, 2H), 7.29 (d, 1H), 6.97 (d, 2H), 3.90 (m, 1H), 3.64 (m, 4H), 3.11 (s, 2H), 3.10-2.98 (m, 5H), 2.66 (m, 1H), 2.29 (s, 6H), 2.07-1.99 (m, 1H), 1.89 (s, 4H), 1.73-1.54 (m, 3H); MS (EI) $C_{29}H_{36}N_8O_2$: 529.2 (MH^+).

[01345] N^2,N^2-dimethyl-N-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]glycinamide • 1.4 AcOH: ^{1}H-NMR (400MHz, d_6-DMSO): 10.00 (s, 1H), 9.42 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.84 (d, 2H), 7.69 (d, 2H), 7.29 (d, 1H), 6.97 (d, 2H), 3.97 (m, 1H), 3.64 (m, 4H), 3.12 (s, 2H), 3.11-3.0 (m, 5H), 2.70 (m, 1H), 2.29 (s, 6H), 2.07-1.99 (m, 1H), 1.90 (s, 4H), 1.75-1.55 (m, 3H); MS (EI) $C_{29}H_{36}N_8O_2$: 529.2 (MH^+).

[01346] 2-(dimethylamino)-N-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide • 3 AcOH: ^{1}H-NMR (400MHz, d_6-DMSO): 10.01 (s, 1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.84 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.96 (d, 1H), 3.71 (m, 2H), 3.59 (m, 2H), 3.15 (s, 2H), 3.12 (s, 2H), 3.10 (m, 2H), 3.02 (m, 2H), 2.71 (m, 4H), 2.35 (m, 4H), 2.29 (s, 6H), 1.84 (s, 9H); MS (EI) $C_{30}H_{39}N_9O_2$: 558.5 (MH^+).

[01347] 1,1-dimethylethyl [(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)methyl]carbamate: ^{1}H NMR (400MHz, CDCl3): 8.20-8.22 (b, 1H), 8.05 (d, 2H), 7.65(d,1H), 7.50 (d, 2H), 7.25 (s, 1H), 7.23 (d, 2H), 7.05 (d, 2H), 5.01 (d, 1H), 4.40-4.44 (b, 2H), 3.90 (t, 4H), 3.20 (t, 4H), 1.50 (s, 9H); MS (EI) for $C_{26}H_{31}N_5O_3$: 462 (MH^+).

[01348] 4-(4-(aminomethyl)phenyl)-N-(4-morpholinophenyl)pyrimidin-2-amine: ^{1}H NMR (400MHz, CD3CN): 10.10-10-20(b,1H), 8.40 (d, 1H), 8.20(d,2H), 7.80 (d, 2H), 7.60 (d, 2H), 7.50 (d, 2H), 7.45(d,1H),7.20-7.22 (b, 2H), 4.40-4.44 (b, 2H), 3.90 (t, 4H), 3.20 (t, 4H); MS (EI) for $C_{21}H_{23}N_5O$: 362 (MH^+).

[01349] methyl 4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzoate: ^{1}H NMR (400MHz, CDCl3):8.45(s,1H), 8.20-8.30 (m, 4H), 7.65(d,1H), 7.25 (d, 2H), 7.15

(d, 2H), 6.85 (d, 1H), 4.01(s,3H), 3.90 (t, 4H), 3.20 (t, 4H),; MS (EI) for $C_{22}H_{22}N_4O_3$: 391 (MH^+).

[01350] 1-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-3-ethylurea: ^{1}H NMR (400MHz, d6-DMSO): 9.50-9.45 (b, 1H), 8.80(s,1H), 8.40(s,1H), 8.05 (d, 2H), 7.75-7.70 (m,4H), 7.30 (d, 1H), 7.05 (d, 2H),, 6.01 (d, 1H), 4.01(q,2H), 3.90 (m, 2H), 3.20 (m, 6H), 1.20 (s, 9H),1.10(t,3H); MS (EI) for $C_{28}H_{35}N_7O_2$: 502 (MH^+).

[01351] 1-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-3-ethylurea: ^{1}H NMR (400MHz, d6-DMSO): 9.45 (s, 1H), 8.80(s,1H), 8.40(s,1H), 8.05 (d, 2H), 7.75-7.70 (m, 4H), 7.30 (d, 1H), 7.05 (d, 2H),, 6.01 (d, 1H), 3.80 (m, 4H),3.50(q, 2H), 3.40 (m, 4H),3.30 (m, 1H),3.20 (m, 6H),1.10(t,3H); MS (EI) for $C_{28}H_{33}N_7O_2$: 500 (MH^+).

[01352] 1-ethyl-3-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}urea: ^{1}H NMR (400MHz, d6-DMSO): 9.45 (s, 1H), 8.80(s,1H), 8.40(s,1H), 8.05 (d, 2H), 7.75-7.70 (m, 4H), 7.30 (d, 1H), 7.05 (d, 2H),, 6.01 (d, 1H), 3.80 (m, 4H),3.30(q, 2H), 3.20 (m, 4H),3.10 (m, 1H),1.20 (m, 6H),1.10(t,3H); MS (EI) for $C_{27}H_{33}N_7O_2$: 488 (MH^+).

[01353] N-ethyl-4-(4-{[4-(4-{[(ethylamino)carbonyl]amino}phenyl)pyrimidin-2-yl]amino}-phenyl)piperazine-1-carboxamide: ^{1}H NMR (400MHz, d6-DMSO): 9.45 (s, 1H), 8.80(s,1H), 8.40(m,1H), 8.05 (d, 2H), 7.75-7.70 (m, 4H), 7.30 (d, 1H), 7.05 (d, 2H),6.50 (s, 1H), 6.20 (d, 1H),3.40-3.50(m, 4H),3.00-3.15 (m, 8H),1.10-1.20(m,6H); MS (EI) for $C_{26}H_{32}N_8O_2$: 489 (MH^+).

[01354] 1-ethyl-3-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-urea: ^{1}H NMR (400MHz, d6-DMSO): 10.20-10.25 (b, 1H), 9.45 (s, 1H), 8.40(m,1H), 8.05 (d, 2H), 7.75-7.60 (m, 6H), 7.30 (d, 1H), 7.00-6.90 (m, 2H),3.80-3.81 (m, 1H), 3.70-3.65(m, 4H),3.20-3.25 (m, 2H), 3.15-3.10 (m, 4H), 1.60-1.50 (m, 6H),1.10-1.20(m,3H); MS (EI) for $C_{28}H_{34}N_8O_2$: 515 (MH^+).

[01355] 1-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-3-ethyl-urea: ^{1}H NMR (400MHz, d6-DMSO): 9.70-9.65 (b, 1H), 9.25 (s, 1H), 8.40(m,1H), 8.05 (d, 2H), 7.75-7.60 (m, 4H), 7.30 (d, 1H), 7.00-6.90 (m, 2H), 6.80-6.75 (m, 1H),3.80-3.81 (m, 1H), 3.70-3.65(m, 4H),3.60-3.55 (b, 2H), 3.25-3.20 (m, 6H),,1.10-1.20(m,6H); MS (EI) for $C_{26}H_{32}N_8O_2$: 489 (MH^+).

[01356] 1-ethyl-3-{4-[2-({4-[4-(piperazin-1-ylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}urea: ^{1}H NMR (400MHz, d4-MeOH): 8.40 (m,

1H), 8.05 (d, 2H), 7.75-7.60 (m, 4H), 7.30 (d, 1H), 7.00-6.90 (m, 2H), 3.80-3.81 (m, 4H), 3.30-3.10(m, 16H), 2.80-2.90 (m, 4H),1.20(t,3H); MS (EI) for $C_{29}H_{37}N_9O_2$: 544 (MH^+).

[01357] 1-ethyl-3-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-urea: ^{1}H NMR (400MHz, d6-DMSO): 10.20-10.25 (b, 1H), 9.40-9.35 (b, 1H), 9.20 (s, 1H), 8.40(m,1H), 8.05 (d, 2H), 7.75-7.60 (m, 4H), 7.30 (d, 1H), 7.00-6.90 (m, 2H),6.80-6.75 (b, 1H), 3.80-3.81 (m, 1H), 3.70-3.65(m, 4H),3.20-3.25 (m, 2H), 3.15-3.10 (m, 4H), 1.60-1.50 (m, 6H),1.10-1.20(m,3H); MS (EI) for $C_{28}H_{34}N_8O_2$: 515 (MH^+).

[01358] 1-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-3-ethyl-urea: ^{1}H NMR (400MHz, d6-DMSO): 11.00-10.90 (b, 1H), 9.25 (s, 1H), 8.40(m,1H), 8.05 (d, 2H), 7.75-7.60 (m, 4H), 7.30 (d, 1H), 7.00-6.90 (m, 2H), 6.80-6.75 (m, 1H),3.80-3.81 (m, 1H), 3.70-3.65(m, 4H),3.60-3.55 (b, 2H), 3.25-3.20 (m, 6H),,1.10-1.20(m,6H); MS (EI) for $C_{26}H_{32}N_8O_2$: 489 (MH^+).

[01359] (R)-N-(4-(2-(4-(4-(2-ethoxyacetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)-phenyl)pyrrolidine-2-carboxamide: ^{1}H NMR (400MHz, d6-DMSO): 10.20-10.25 (b, 1H), 9.40 (s, 1H), 8.50 (d, 1H), 8.05 (d, 2H), 7.75-7.60 (m, 4H), 7.30 (d, 1H), 7.00-6.90 (m, 2H), 4.20 (s, 2H), 3.80-3.81 (m, 2H), 3.70-3.65(m, 1H),3.20-3.25 (m, 2H), 3.25-2.85 (m, 6H), 2.20 (m, 1H),1.80-1.60 (m, 6H),1.20(t, 3H); MS (EI) for $C_{29}H_{35}N_7O_3$: 530 (MH^+).

[01360] N-[4-(2-{[4-(4-formylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide: ^{1}H NMR (400MHz, CDCl3): 10.10-10.00 (b, 1H), 8.30 (d, 2H), 8.05 (s, 1H), 8.00 (d, 2H), 7.75-7.60 (m, 4H), 7.30 (d, 1H), 7.00-6.90 (m, 2H), 6.10-6.00 (b, 1H), 4.20 (m, 1H), 3.80-3.60 (m, 4H), 3.20-3.25 (m, 6H), 2.20 (m, 2H),1.90-1.80 (m, 2H); MS (EI) for $C_{26}H_{29}N_7O_2$: 472 (MH^+).

[01361] N-(4-{2-[(4-{4-[4-(dimethylamino)butanoyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H NMR (400MHz, d6-DMSO): 10.20-10.25 (b, 1H), 9.40 (s, 1H), 8.50 (d, 1H), 8.05 (d, 2H), 7.75-7.60 (m, 4H), 7.30 (d, 1H), 7.00-6.90 (m, 2H), 4.20 (m, 1H), 3.80-3.60 (m, 4H), 3.20-3.25 (m, 6H), 2.90-2.85 (m, 4H), 2.40 (s, 3H), 2.30-2.22 (m, 2H), 2.20 (m, 3H), 2.05 (s, 3H), 1.90-1.80 (m, 2H); MS (EI) for $C_{31}H_{40}N_8O_2$: 557 (MH^+).

[01362] N-(4-(2-(3-aminophenylamino)pyrimidin-4-yl)phenyl)-2-phenoxyacetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.41 (s, 1H), 12.4 (s, br, 1H), 8..56 (s, 1H), 8.19 (s, 1h), 7.97-7.82 (m, 3H), 7.61-7.26 (m, 5H), 7.07-7.02 (m, 3H), 6.98 (m, 1H), 4.79 (s, 2H). MS (EI): 412 (MH+).

[01363] N-(4-(2-(4-(4-acetylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide: ^{1}H NMR (400 MHz, d4-MeOH): 10.22 (s, 1H), 9.41 (m, 1H), 8.12 (m,

2H), 7.75 (m, 2H), 7.68 (m, 2H), 7.27 (m, 1H), 3.72 (m, 4H), 6.94 (m, 2H), 3.58 (m, 4H), 3.09 (m, 2H), 3.02 (m, 2H), 2.09 (s, 3H), 2.03 (s, 3H). MS (EI): 431 (MH+).

[01364] N-(4-(2-(3-amino-2,4,5,6-tetrafluorophenylamino)pyrimidin-4-yl)phenyl)acetamide: ^{1}H NMR (400 MHz, d4-MeOH): 8.26 (m, 1H), 8.07 (m, 2H), 7.82 (m, 2H), 7.41 (m, 1H), 2.18 (s, 3H). MS (EI): 392 (MH+).

[01365] N-(4-(2-(4-(piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide: MS (EI) for $C_{22}H_{24}N_6O$: 389 (MH+).

[01366] 1-amino-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)cyclopropane-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.27 (s 1H), 10.19 (s, 1H), 9.23 (m, 3H), 8.60 (m, 1H), 8.09 (m, 2H), 7.95 (m, 3H), 7.79 (m, 2H), 7.54 (m, 1H), 4.11 (m, 4H), 3.65 (m, 4H), 1.71 (m, 2H), 1.42 (m, 2H). MS (EI): 431 (MH+).

[01367] (S)-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)indoline-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.18 (s, 1H), 9.50 (m, 1H), 8.43 (m, 1H), 8.08 (m, 2H), 7.92 (m, 2H), 7.84 (m, 2H), 7.31 (m, 1H), 7.10-6.88 (m, 4H), 6.61 (m, 2H), 6.07 (m, 1H), 4.42 (m, 1H), 3.75 (m, 4H), 3.18-2.99 (m, 6H). MS (EI): 493 (MH+).

[01368] N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.34 (s, 1H), 9.39 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.77 (d, 2H), 7.67 (d, 2H), 7.28 (d, 1H), 6.93 (d, 2H), 3.95 (t, 1H), 3.82-3.69 (m, 7H), 3.25-3.16 (m, 1H), 3.05 (t, 4H), 2.13-2.06 (m, 2H). MS (EI): 446 (MH+).

[01369] N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(pyridin-3-yl)-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.53 (s, 1H), 9.34 (s, 1H), 8.54 (s, 1H), 8.47 (d, 1H), 8.33 (d,1H), 8.12 (d, 2H), 7.76 (d,3H), 7.67 (d, 2H), 7.37 (m, 1H), 7.28 (d, 1H), 6.93 (d, 2H), 3.76-3.73 (m, 6H), 3.06-3.03 (m,4H). MS (EI): 467 (MH+).

[01370] 1-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenyl-amino)pyrimidin-4-yl)phenyl)-3-ethylurea: ^{1}H NMR (400 MHz, d6-DMSO): 9.33 (s, 1H), 9.00 (s, 1H), 8.40 (d,1H), 8.04 (d, 2H), 7.66 (d, 2H), 7.55 (d, 2H), 7.23 (d, 1H), 6.93 (d, 2H), 6.39 (t, 1H), 3.17-3.08 (m, 10H), 2.85 (s, 6H), 2.74 (s, 4H), 1.08-1.04 (m, 9H). MS (EI): 531 (MH+).

[01371] (R)-N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 12.64 (s, 1H), 9.35 (s, 1H), 8.42 (d,1H), 8.10 (d, 2H), 7.69-7.63 (m, 4H), 7.28 (d, 1H), 6.89 (d, 2H), 3.30-3.23 (m, 1H), 3.15 (d, 2H), 3.10-3.04 (m, 4H), 2.62-2.58 (m, 4H), 2.34-2.28 (m, 1H), 2.21 (s, 6H), 2.18 (s, 2H), 2.10 (s, 2H), 1.82-1.64 (m, 4H), 0.84 (s, 6H). MS (EI): 557 (MH+).

[01372] (R)-2-amino-N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.35 (s, 1H), 8.42 (d,1H), 8.10 (d, 2H), 7.80 (d, 2H), 7.63 (d, 2H), 7.27 (d, 1H), 6.89 (d, 2H), 3.49-3.43 (m, 1H), 3.05-3.01 (m, 4H), 2.62-2.58 (m, 4H), 2.19 (s, 6H), 2.15 (s, 2H), 2.07 (s, 2H), 1.21 (d, 3H), 0.82 (s, 6H). MS (EI): 531 (MH+).

[01373] N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-methoxypropanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.31 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.78 (d, 2H), 7.66 (d, 2H), 7.27 (d, 1H), 6.93 (d, 2H), 3.63 (t, 2H), 3.34 (s, 4H), 3.25 (s, 3H), 3.13 (s, 4H), 2.84 (s, 6H), 2.74 (s, 4H), 2.60 (t, 2H), 1.05 (s, 6H). MS (EI): 546 (MH+).

[01374] 2-(dimethylamino)-N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.98 (s, 1H), 9.33 (s, 1H), 8.41 (d, 1H), 8.08 (d, 2H), 7.81 (d, 2H), 7.62 (d, 2H), 7.24 (d, 1H) 6.88 (d, 2H), 3.09 (s, 2H), 3.05-3.02 (m, 4H), 2.60-2.45 (m, 4H), 2.27 (s, 6H), 2.20 (s, 6H), 2.15 (s, 2H), 2.09 (s, 2H), 0.82 (s, 6H). MS (EI): 545 (MH+).

[01375] N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide: ^{1}H NMR (400 MHz, d6-DMSO): 10.18 (s, 1H), 9.36 (s, 1H), 8.41 (d, 1H), 8.08 (d, 2H), 7.75 (d, 2H), 7.64 (d, 2H), 7.26 (d, 1H), 6.92 (d, 2H), 3.12 (s, 4H), 3.07 (s, 4H), 2.84 (s, 6H), 2.73 (s, 4H), 2.31 (t, 2H), 1.66-1.58 (m, 2H), 1.03 (s, 6H), 0.91 (t, 3H). MS (EI): 530 (MH+).

[01376] (3S,7S)-7-(hydroxymethyl)-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)quinuclidine-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.25 (s, 1H), 9.39 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.27 (d, 1H), 6.93 (d, 2H), 3.74 (t, 4H), 3.65-3.58 (m, 2H), 3.45-3.37 (m, 3H), 3.05 (t, 4H), 2.94-2.88 (m, 3H), 2.71-2.67 (m, 1H), 2.17 (s, 1H), 1.68-1.63 (m, 2H), 1.50-1.46 (m, 1H), 1.27-1.21 (m, 1H). MS (EI): 515 (MH+).

[01377] (R)-N-(4-(2-(3-ethoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.45 (s, 1H), 10.04 (s, 1H), 8.59 (d, 1H), 8.21 (d, 2H), 7.87 (d, 2H), 7.49 (d, 1H), 7.44-7.41 (m, 2H), 7.32 (s, 1H), 7.19 (s, 1H), 4.51-4.45 (m, 2H), 4.28-4.25 (m, 4H), 4.09-4.01 (m, 4H), 3.68-3.52 (m, 3H), 3.33-3.23 (m, 2H), 2.49-2.42 (m, 1H), 2.03-1.91 (m, 3H), 1.49 (t, 3H). MS (EI): 489 (MH+).

[01378] N-{4-[2-({4-morpholin-4-yl-3-[(phenylmethyl)oxy]phenyl}amino)pyrimidin-4-yl]-phenyl}-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO):11.57 (s, 1H), 10.17 (s, 1H), 8.59 (d, 1H), 8.23 (d, 2H), 8.09 (s, 1H), 7.90 (m, 3H), 7.59 (m, 2H), 7.48 (m, 5H), 5.34 (s,

2H), 4.51 (m, 4H), 4.06 (m, 5H), 3.29 (m, 3H), 1.98 (m, 3H). MS (EI) for $C_{32}H_{34}N_6O_3$: 551.7 (MH+).

[01379] 4-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-piperazine-1-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.35 (s, 1H), 8.88 (s, 1H), 8.41 (d, 1H), 8.15 (s, 1H), 8.06 (d, 1H), 7.66 (m, 3H), 7.25 (d, 1H), 6.93 (d, 2H), 3.74 (m, 4H), 3.53 (m, 8H), 3.04 (m, 4H), 3.32 (m, 3H). MS (EI) for $C_{26}H_{31}N_7O_2$: 474.6 (MH+).

[01380] 1-[3-(dimethylamino)propyl]-3-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)urea: ^{1}H NMR (400 MHz, d6-DMSO): 9.34 (s, 1H), 9.22 (s, 1H), 8.40 (d, 1H), 8.05 (d, 2H), 7.67 (d, 2H), 7.57 (d, 2H), 7.24 (d, 1H), 6.93 (d, 2H), 6.66 (t, 1H), 3.74 (m, 4H), 3.17 (m, 2H), 3.05 (m, 4H), 2.90 (t, 2H), 2.62 (s, 6H), 1.78 (m, 2H). MS (EI) for $C_{26}H_{33}N_7O_2$: 476.6 (MH+).

[01381] 1-[3-(methyloxy)propyl]-3-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)urea: ^{1}H NMR (400 MHz, d6-DMSO): 9.3 (s, 1H), 8.87 (s, 1H), 8.40 (d, 1H), 8.05 (d, 2H), 7.67 (d, 2H), 7.55 (d, 2H), 7.24 (d, 1H), 6.93 (d, 2H), 6.37 (t, 1H), 3.74 (m, 4H), 3.38 (d, 2H), 3.25 (s, 3H), 3.15 (m, 2H), 3.04 (m, 4H), 1.68 (m, 2H). MS (EI) for $C_{25}H_{30}N_6O_3$: 463.6 (MH+).

[01382] 1-(2-morpholin-4-ylethyl)-3-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)urea: ^{1}H NMR (400 MHz, d6-DMSO): 9.34 (s, 1H), 9.00 (s, 1H), 8.40 (d, 1H), 8.17 (s, 1H), 8.05 (d, 2H), 7.68 (d, 2H), 7.55 (d, 2H), 7.24 (d, 1H), 6.93 (d, 2H), 6.25 (t, 1H), 3.74 (m, 4H), 3.60 (m, 4H), 3.22 (m, 2H), 3.04 (m, 4H), 2.40 (m, 5H). MS (EI) for $C_{27}H_{33}N_7O_3$: 504.5 (MH+).

[01383] 1-[2-(dimethylamino)ethyl]-3-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)urea: ^{1}H NMR (400 MHz, d6-DMSO): 9.33 (s, 1H), 9.06 (s, 1H), 8.40 (d, 1H), 8.21 (s, 1H), 8.04 (d, 2H), 7.67 (d, 2H), 7.55 (d, 2H), 7.23 (d, 1H), 6.93 (d, 2H), 6.33 (t, 1H), 3.74 (d, 4H), 3.21 (m , 2H), 3.05 (m, 1H), 2.38 (t, 2H), 2.12 (s, 6H). MS (EI) for $C_{25}H_{31}N_7O_2$: 462.5 (MH+).

[01384] 1-ethyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.53 (s, 1H), 9.40 (s, 1H), 8.45 (d, 1H), 8.14 (d, 2H), 7.85 (d, 2H), 7.67 (d, 2H), 7.29 (d, 1H), 6.93 (d, 1H), 3.75 (m, 4H), 3.21 (m, 1H), 3.09 (m, 4H), 2.65 (m, 1H), 2.54 (m, 2H), 2.35 (m, 1H), 2.14 (m, 1H), 1.79 (m, 3H), 1.08 (t, 3H). MS (EI) for $C_{27}H_{32}N_6O_2$: 473.6 (MH+).

[01385] 1-(2-hydroxyethyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.31 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.81 (d, 2H), 7.67 (d, 2H), 7.30 (d, 1H), 6.93 (d, 1H), 5.05 (s, br, 1H),

3.75 (m, 4H), 3.05 (m, 4H), 2.75 (m, 2H), 2.63 (m, 1H), 2.40 (m, 2H), 2.18 (m, 2H), 1.80 (m, 3H). MS (EI) for $C_{27}H_{32}N_6O_3$: 489.5 (MH+).

[01386] N-(4-{2-[(4-{4-[3-(dimethylamino)-2,2-dimethylpropyl]piperazin-1-yl}phenyl)-amino]pyrimidin-4-yl}phenyl)tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.39 (s, 1H), 9.39 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.79 (d, 2H), 7.66 (d, 2H), 7.28 (d, 1H), 6.93 (d, 2H), 3.94 (t, 1H), 3.75 (m, 4H), 3.15 (m, 8H), 2.80 (m, 9H), 2.09 (m, 2H), 1.03 (s, 7H). MS (EI) for $C_{32}H_{43}N_7O_2$: 558.7 (MH+).

[01387] (2R)-N-(4-{2-[(4-{4-[3-(dimethylamino)-2,2-dimethylpropyl]piperazin-1-yl}-phenyl)amino]pyrimidin-4-yl}phenyl)tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.88 (s, 1H), 9.34 (s, 1H), 8.52 (s, 1H), 8.38 (s, 1H), 8.00 (s, 1H), 7.56 (m, 2H), 7.22 (d, 1H), 6.96 (d, 2H), 4.43 (m, 1H), 4.00 (m, 1H), 3.86 (m, 1H), 3.05 (m, 7H), 2.60 (m, 7H), 2.20 (m, 10H), 0.85 (s, 6H). $C_{32}H_{43}N_7O_2$. MS (EI) for $C_{32}H_{43}N_7O_2$: 558.7 (MH+).

[01388] N-(4-{2-[(4-{4-[3-(dimethylamino)-2,2-dimethylpropyl]piperazin-1-yl}phenyl)-amino]pyrimidin-4-yl}phenyl)cyclopropanecarboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.47 (s, 1H), 9.36 (s, 1H), 8.42 (d, 1H), 8.10 (d, 2H), 7.75 (d, 2H), 7.64 (d, 2H), 7.26 (d, 1H), 6.90 (d, 2H), 3.05 (m, 4H), 2.61 (m, 4H), 2.21 (s, 6H), 2.17 (s, 2H), 2.10 (s, 2H), 1.90 (s, 1H), 1.82 (m, 1H), 0.84 (m, 9H). MS (EI) for $C_{31}H_{41}N_7O$: 528.6 (MH+).

[01389] (S)-N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenyl-amino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.95 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.88 (d, 2H), 7.67 (d, 2H), 7.29 (d, 1H), 6.93 (d, 2H), 4.44 (t, 1H), 4.01 (m, 1H), 3.85 (m, 1H), 3.14 (m, 6H), 2.86 (s, 6H), 2.77 (m, 4H), 2.21 (m, 2H), 2.01 (m, 2H), 1.90 (m, 2H), 1.05 (s, 6H). MS (EI) for $C_{32}H_{43}N_7O_2$: 558.7 (MH+).

[01390] N-(4-(2-(4-(4-(piperidine-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)-phenyl)tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.35 (s, 1H), 9.41 (s, 1H), 8.44 (s, 1H), 8.14 (d, 2H), 7.78 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.96 (d, 2H), 3.96 (m, 1H), 3.73 (m, 3H), 3.62 (m, 4H), 3.20 (m, 1H), 3.04 (m, 5H), 2.79 (m, 1H), 2.62 (t, 2H), 2.11 (m, 2H), 2.79 (m, 3H), 1.55 (m, 3H). MS (EI) for $C_{31}H_{37}N_7O_3$: 556.6 (MH+).

[01391] 1-(1-methylethyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.98 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.84 (d, 2H), 7.67 (d, 2H), 7.29 (d, 1H), 6.93 (d, 2H), 3.74 (m, 4H),

3.14 (m, 1H), 3.05 (m, 4H), 2.81 (1H), 2.54 (m, 2H), 2.08 (m, 1H), 1.77 (m, 1H), 1.75 (m, 2H), 1.05 (m, 6H). MS (EI) for $C_{28}H_{34}N_6O_2$: 487.6 (MH+).

[01392] 1-ethyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.95 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.85 (d, 2H), 7.67 (d, 2H), 7.29 (d, 1H), 6.95 (d, 2H), 3.74 (m, 4H), 3.20 (m, 1H), 3.07 (m, 5H), 2.64 (m, 1H), 2.54 (m, 1H), 2.35 (m, 1H), 2.14 (m, 1H), 1.79 (m, 3H), 1.08 (t, 3H). MS (EI) for $C_{27}H_{32}N_6O_2$: 473.5 (MH+).

[01393] 2-(2-fluorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.50 (s, 1H), 9.32 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.76 (d, 2H), 7.67 (d, 1H), 7.41 (m , 1H), 7.34 (m, 1H), 7.28 (d, 1H), 7.18 (m, 2H), 6.93 (d, 2H), 3.79 (s, 2H), 3.74 (m, 4H), 3.05 (m, 4H). MS (EI) for $C_{28}H_{26}FN_5O_2$: 484.5 (MH+).

[01394] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-4-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.76 (s, 1H), 9.42 (s, 1H), 8.82 (d, 2H), 8.47 (d, 1H), 8.20 (d, 2H), 7.96 (s, 2H), 7.89 (d, 2H), 7.68 (d, 2H), 7.32 (d, 1H), 6.95 (d, 2H), 3.75 (m, 4H), 3.07 (m, 4H). MS (EI) for $C_{26}H_{24}N_6O_2$: 453.5 (MH+).

[01395] (R)-N-(4-(5-methyl-2-(4-(4-((1-methyl-1H-imidazol-2-yl)methyl)piperazin-1-yl)-phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.19 (s, br, 1H), 9.25 (s, br, 1H), 8.31 (s, 1H), 7.81-7.58 (m, 6H), 7.09-6.76 (br m, 3H), 3.79 (m, 3H), 3.66 (s, 3H), 3.02-2.92 (m, 4H), 2.20 (m, 4H), 2.09 (m, 2H), 2.00 (m, 1H), 1.82 (m, 1H), 1.70 (m, 1H), 12.4 (s, 3H). MS (EI): 552 (MH+).

[01396] (R)-2-amino-N-(4-(5-methyl-2-(4-(4-((1-methyl-1H-imidazol-2-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, br, 1H), 9.24 (s, br, 1H), 8.31 (s, 1H), 7.80 (d, 2H), 7.66-7.69 (m, 4H), 7.09 (s, 1H), 6.85 (m, 2H), 6.76 (s, 1H), 3.80 (m, 3H), 3.66 (m, 3H), 3.00 (m, 4H), 2.95 (m, 4H), 2.22 (s, 3H), 1.24 (s, 3H). MS (EI): 526 (MH+).

[01397] (S)-2-amino-N-(4-(5-methyl-2-(4-(4-((1-methyl-1H-imidazol-2-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide: ^{1}H NMR (400 MHz, d6-DMSO):): 10.20 (s, br, 1H), 9.24 (s, br, 1H), 8.31 (s, 1H), 7.79 (d, 2H), 7.67-7.58 (m, 4H), 7.09 (s, 1H), 6.86 (m, 2H), 6.76 (s, 1H), 3.80 (m, 3H), 3.66 (m, 3H), 3.01 (m, 4H), 2.95 (m, 4H), 2.22 (s, 3H), 1.23 (s, 3H). MS (EI) for C29H35N9O: 526 (MH+).

[01398] *N*-[3-({2-[(4-morpholin-4-ylphenyl)amino]-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-yl}-amino)phenyl]acetamide: ^{1}H NMR (400MHz, d6-DMSO): 11.14 (s, 1H), 9.87 (s, 1H), 9.15 (s, 1H), 8.47 (s, 1H), 8.04 (s, 1H), 7.80-7.73 (m, 1H), 7.70-7.63 (m, 2H), 7.25-7.18 (m, 2H),

6.89-6.81 (m, 3H), 6.67-6.64 (m, 1H), 3.77-3.71 (m, 4H), 3.04-2.98 (m,4H), 2.06 (s, 3H). MS (EI) for C24H25N7O2: 444 (MH+).

[01399] N-(4-{2-[(2-methyl-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-acetamide: ^{1}H NMR (400 MHz, *d*6-DMSO): 10.36 (br s, 1H), 9.51 (br s, 1H), 8.34 (d, 1H), 8.08 (d, 2H), 7.74 (d, 2H), 7.39 (d, 2H), 7.05 (br d, 2H), 3.80 (s, 4H), 3.22 (s, 4H), 2.21 (s, 3H), 2.07 (s, 3H). MS (EI): (MH+).

[01400] N-(4-{2-[(4-pyrrolidin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, *d*6-DMSO): 10.33 (br s, 1H), 9.72 (br s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.77 (d, 2H), 7,69 (br s, 2H), 7.34 (d, 1H), 3.37 (m, 4H), 2.10 (s, 3H), 2.03 (s, 4H). MS (EI): 374 (MH+).

[01401] N-[4-(2-{[4-(diethylamino)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, *d*6-DMSO): 10.34 (br s), 9.99 (br s, 1H), 8.56 (d, 1H), 8.12 (d, 2H), 8.06 (d, 2H), 7.79 (d, 2H), 7.72 (d, 2H), 7.44 (d, 1H), 3.49 (q, 4H), 2.10 (s, 3H), 1.05 (dt, 6H). MS (EI): 376 (MH+).

[01402] N-(4-{2-[(4-azepan-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, *d*6-DMSO): 10.34 (br s), 9.99 (br s, 1H), 8.56 (d, 1H), 8.12 (d, 2H), 8.06 (d, 2H), 7.79 (d, 2H), 7.72 (d, 2H), 7.44 (d, 1H), 3.54 (m, 4H), 2.09 (s, 3H), 1.91 (m, 2H), 1.70 (m,2H), 1.64 (m, 4H), 1.44 (m, 2H), 1.37 (m, 2H). MS (EI): 402 (MH+).

[01403] N-{4-[2-({4-[methyl(2-phenylethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl} acetamide: ^{1}H NMR (400 MHz, *d*6-DMSO): 10.34 (br s, 1H), 9.95 (br s, 1H), 8.54 (d, 1H), 8.15 (d, 2H), 7.98 (m, 1H), 7.79 (d, 2H), 7.43 (d, 1H), 7.31 (m, 3H), 7.23 (m, 4H), 3.71 (m, 2H), 3.13 (m, 2H), 2.10 (s, 1H), 1.99 (s, 3H). MS (EI): 438 (MH+).

[01404] N-[4-(2-{[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)phenyl]amino}pyrimidin-4-yl)phenyl] acetamide: ^{1}H NMR (400 MHz, *d*6-DMSO): 10.34 (br s), 9.99 (br s, 1H), 8.56 (d, 1H), 8.12 (d, 2H), 8.06 (d, 2H), 7.79 (d, 2H), 7.72 (d, 2H), 7.44 (d, 1H),3.90 (s, 4H), 2.70 (t, 4H), (2.10 (s, 3H), 1.76 (t, 4H). MS (EI): 446 (MH+).

[01405] N-[4-(2-{[4-(2-oxopiperidin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.32 (br s, 1H), 9.86 (br s 1H), 8.51 (d, 1H), 8.14 (d, 2H), 7.85 (t, 4H), 7.40 (d, 1H), 7.22 (d, 2H), 3.59 (m, 2H), 2.38 (t, 2H), 2.09 (s, 3H), 1.85 (m, 4H). MS (EI): 402 (MH+).

[01406] N-[4-(2-{[4-(2-methylpiperidin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (br s, 1H), 9.36 (br s, 1H), 8.43 (s, 1H), 8.27 (s, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.26 (s, 1H), 6.92 (d, 2H), 2.09 (s, 3H), 3.41 (m, 3H), 1.60 (m, 6H), 0.88 (d, 3H). MS (EI): 402 (MH+).

[01407] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-valinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.51 (br s, 1H), 10.16 (br s, 1H), 8.57 (s, 1H), 8.48 (m, 2H), 8.20 (m, 2H), 7.93 (m, 3H), 7.78 (m, 1H), 7.50 (s, 1H), 5.45 (br s, 4H), 4.07 (s, 4H), 3.53 (s, 4H), 3.35 (m, 1H), 2.25 (m, 1H), 1.03 (m, 6H). MS (EI): 447 (MH+).

[01408] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-valinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.51 (br s, 1H), 10.16 (br s, 1H), 8.57 (s, 1H), 8.48 (m, 2H), 8.20 (m, 2H), 7.93 (m, 3H), 7.78 (m, 1H), 7.50 (s, 1H), 5.45 (br s, 4H), 4.07 (s, 4H), 3.53 (s, 4H), 3.35 (m, 1H), 2.25 (m, 1H), 1.03 (m, 6H). MS (EI): 447 (MH+).

[01409] 2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-alaninamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.68 (br s,1H), 10.02 (br s, 1H), 8.53 (m, 2H), 8.18 (d, 2H), 7.95 (d, 2H), 7.89 (d, 2H), 7.66 (m, 1H), 7.47 (d, 1H), 5.20 (br s, 4H), 4.01 (s, 4H), 3.44 (s,4H), 1.66 (6H). MS (EI): 433 (MH+).

[01410] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)tryptophanamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.37 (s, 1H), 10.07 (s, 1H), 10.03 (s, 1H), 8.56 (d, 1H), 8.42 (d, 2H), 8.19 (d, 2H), 7.91 (d, 2H), (d, 2H), 7.73 (d, 1H), 7.66 (1H), 7.46 (d, 1H), 7.35 (d, 1H), 7.28 (d, 1H), 7.07 (t, 1H), 6.95 (t, 1H), 4.70 (br s, 4H), 4.34 (m, 1H), 4.03 (s, 4H), 3.49 (s, 4H), 3.36 (dq, 2H). MS (EI): 534 (MH+).

[01411] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.43 (br s, 1H), 10.07 (br s, 2H), 8.73 (d, 1H), 8.57 (d, 1H), 8.21 (d, 2H), 7.91 (d, 2H), 7.98 (d, 2H), 7.71 (br s, 2H), 7.48 (d, 1H), 4.48 (m, 1H), 4.08 (s, 4H), 3.74 (m, 4H), 3.42 (m, 1H), 3.36 (m, 1H), 3.04 (m, 4H), 2.22 (m 1H), 1.90 (m, 2H), 1.82 (m, 2H). MS (EI): 445 (MH+).

[01412] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1,2,3,4-tetrahydro-isoquinoline-1-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO):11.30 (br d, 1H), 10.04 (br s, 1H), 8.56 (d, 1H), 8.39 (s, 3H), 8.20 (d, 2H), 7.90 (m, 2H), 7.87 (m, 2H), 7.67 (m, 3H), 7.47 (d, 1H), 5.00 (br s, 3H), 4.65 (s, 1H), 4.20 (m, 2H), 4.03 (s, 4H), 3.97 (m, 1H), 3.94 (m, 2H), 3.80 (m, 1H), 3.49 (s, 4H). MS (EI): 507 (MH+).

[01413] O-(1,1-dimethylethyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)-L-serinamide: ^{1}H NMR (400 MHz, d6-DMSO): 12.11 (br s, 1H), 10.65 (br s, 1H), 10.12 (s, 1H), 9.60 (s, 1H), 8.58 (d, 1H), 8.23 (d, 2H), 7.95 (d, 2H),, 7.79 (s, 1H), 7.56 (d, 1H), 7.49 (d, 1H), 7.31 (s, 2H), 5.14 (br s, 4H), 4.06 (s, 4H), 3.79 (m, 1H), 3.54 (s, 4H), 3.45 (m, 1H), 3.15 (q, 1H), 1.21 (s, 9H). MS (EI): 491 (MH+).

[01414] 3-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl) tetrahydro-furan-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.89 (br s, 1H),

9.92 (br s , 1H), 8.83 (s, 2H), 8.55 (d, 1H), 8.21 (d, 2H), 7.94 (d, 2H), 7.87 (d, 1H), 7.53 (s, 1H), 7.43 (d, 1H), 4.30 (br s, 4H), 4.21 (d, 1H), 4.07 (d, 1H), 4.05 (m, 1H), 4.02 (m, 1H), 3.97 (s, 4H), 3.42 (s, 4H), 2.79 (m, 1H), 2.28 (m, 1H). MS (EI): 461 (MH+).

[01415] bis(1,1-dimethylethyl) (2R)-2-{[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]carbonyl}piperazine-1,4-dicarboxylate: ^{1}H NMR (400 MHz, d6-DMSO): 10.41 (br s, 1H), 9.35 (s, 1H), 8.42 (d, 1H), 8.14 (d, 2H), 8.76 (d, 2H), 7.67 (d, 2H), 7.28 (d, 1H), 6.93 (d, 2H), 4.51 (m, 1H), 3.90 (m, 2H), 3.74 (m, 4H), 3.66 (t, 4H), 3.04 (t, 4H), 1.41 (s, 3H), 1.33 (s, 9H), 1.17 (s, 6H). MS (EI): 660 (MH+).

[01416] N-(4-{2-[(4-{4-[2-(2-fluorophenyl)acetyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.70 (d, 2H), 7.29 (m, 3H), 7.16 (m, 2H), 6.98 (d, 2H), 3.80 (s, 2H), 3.69 (m, 2H), 3.63 (m, 2H), 3.09 (m, 2H), 3.04 (m, 2H), 2.09 (s, 3H). MS (EI): 525.5 (MH+).

[01417] N-(4-{2-[(4-{4-[2-(2-methylphenyl)acetyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.69 (d, 2H), 7.28 (d, 1H), 7.12 (m, 4H), 6.97 (d, 2H), 3.74 (s, 2H), 3.65 (m, 4H), 3.05 (m, 4H), 2.20 (s, 3H), 2.09 (s, 3H). MS (EI): 521.6 (MH+).

[01418] N-(4-{2-[(4-{4-[2-(3-fluorophenyl)acetyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.69 (d, 2H), 7.35 (m, 1H), 7.28 (d, 1H), 7.08 (m, 3H), 6.96 (d, 2H), 3.81 (s, 2H), 3.64 (m, 4H), 3.02 (m, 4H), 2.09 (s, 3H). MS (EI): 525.4 (MH+).

[01419] N-{4-[2-({4-[4-(3-thienylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.83 (m, 1H), 7.75 (d, 2H), 7.70 (d, 2H), 7.64 (m, 1H), 7.25 (m, 2H), 6.98 (d, 2H), 3.68 (m, 4H), 3.11 (m, 4H), 2.09 (s, 3H). MS (EI): 499.4 (MH+).

[01420] N-(4-{2-[(4-{4-[(6-chloropyridin-3-yl)carbonyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.41 (s, 1H), 8.53 (m, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.98 (dd, 1H), 7.75 (d, 2H), 7.70 (d, 2H), 7.65 (d, 1H), 7.28 (d, 1H), 6.98 (d, 2H), 3.78 (m,2H), 3.48 (m, 2H), 3.17 (m, 2H), 3.08 (m, 2H), 2.09 (s, 3H). MS (EI): 529.1 (MH+).

[01421] N-(4-{2-[(4-{4-[(3-methylfuran-2-yl)carbonyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.41 (s,

1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.75-7.68 (m, 5H), 7.28 (d, 1H), 6.98 (d, 2H), 6.52 (d, 1H), 3.73 (m, 4H), 3.11 (m, 4H), 2.17 (s, 3H), 2.09 (s, 3H). MS (EI): 497.6 (MH+).

[01422] N-(4-{2-[(4-{4-[(3-fluoro-2-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: MS (EI) for $C_{30}H_{29}FN_6O_2$: 525.5 (MH+).

[01423] N-(4-{2-[(4-{4-[(imidazol-4-yl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: MS (EI) for $C_{26}H_{26}N_8O_2$: 483.5 (MH+).

[01424] N-(4-{2-[(4-{4-[(2-methoxypyridin-3-yl)carbonyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.26 (dd, 1H), 8.12 (d, 2H), 7.75-7.67 (m, 5H), 7.28 (d, 1H), 7.09 (dd, 1H), 6.97 (d, 2H), 3.90 (s, 3H), 3.77 (m, 2H), 3.29 (m, 2H), 3.14 (m, 2H), 3.04 (m, 2H), 2.09 (s, 3H). MS (EI): 524.6 (MH+).

[01425] N-(4-{2-[(4-{4-[(4-fluoro-3-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: MS (EI) for $C_{30}H_{29}FN_6O_2$: 525.5 (MH+).

[01426] N-{4-[2-({4-[4-(naphthalen-2-ylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.37 (s, 1H), 8.50 (d, 1H), 8.42 (d, 1H), 8.22 (dd, 2H), 8.09 (dd, 3H), 7.82-7.71 (m, 5H), 7.64 (d, 2H), 7.26 (d, 1H), 6.89 (d, 2H), 3.14 (m, 4H), 3.11 (m, 4H), 2.08 (s, 3H). MS (EI): 579.6 (MH+).

[01427] N-{4-[2-({4-[4-(quinolin-8-ylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.37 (s, 1H), 9.10 (dd, 1H), 8.56 (dd, 1H), 8.42 (m, 2H), 8.34 (dd, 1H), 8.10 (d, 2H), 7.79 (m, 1H), 7.73 (m, 3H), 7.65 (d, 2H), 7.27 (d, 1H), 6.90 (d, 2H), 3.45 (m, 4H), 3.08 (m, 4H), 2.09 (s, 3H). MS (EI): 580.8 (MH+).

[01428] N-[4-(2-{[4-(4-{[4-(1,1-dimethylethyl)phenyl]sulfonyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.20 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.70 (m, 4H), 7.66 (d, 2H), 7.27 (d, 1H), 6.91 (d, 2H), 3.16 (m, 4H), 3.01 (m, 4H), 2.08 (s, 3H), 1.32 (s, 9H). MS (EI): 585.5 (MH+).

[01429] N-[4-(2-{[4-(4-{[5-bromo-2-(methyloxy)phenyl]sulfonyl}piperazin-1-yl)phenyl]-amino}pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.09 (dd, 2H), 7.84 (m, 2H), 7.74 (d, 2H), 7.68 (d,

2H), 7.28 (d, 2H), 6.94 (d, 2H), 3.92 (s, 3H), 3.27 (m, 4H), 3.11 (m, 4H), 2.09 (s, 3H). MS (EI) for C29H29BrN6O4S: 638.6 (MH+).

[01430] N-(4-{2-[(4-{4-[(phenylmethyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.69 (d, 2H), 7.42 (m, 5H), 7.28 (d, 1H), 6.96 (d, 2H), 4.50 (s, 2H), 3.20 (m, 4H), 3.06 (m, 4H), 2.08 (s, 3H). MS (EI): 543.6 (MH+).

[01431] N-[4-(2-{[4-(4-{[3-(trifluoromethyl)phenyl]sulfonyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.39 (s, 1H), 8.44 (d, 1H), 8.18-8.08 (m, 4H), 8.02 (s, 1H), 7.97 (d, 1H), 7.74 (d, 2H), 7.67 (d, 2H), 7.27 (d, 1H), 6.92 (d, 2H), 3.15 (m, 4H), 3.10 (m, 4H), 2.09 (s, 3H). MS (EI): 597.7 (MH+).

[01432] N-(4-{2-[(4-{4-[(2-methylphenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.43 (d, 1H), 8.09 (dd, 2H), 7.85 (dd, 1H), 7.74 (d, 2H), 7.67-7.59 (m, 3H), 7.47 (m, 2H), 7.27 (d, 1H), 6.94 (d, 2H), 3.17 (m, 4H), 3.13 (m, 4H), 2.61 (s, 3H), 2.09 (s, 3H). MS (EI): 543.7 (MH+).

[01433] N-(4-{2-[(4-{4-[(3-fluorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.39 (s, 1H), 8.43 (d, 1H), 8.10 (dd, 2H), 7.73 (m, 3H), 7.67-7.62 (m, 5H), 7.27 (d, 1H), 6.92 (d, 2H), 3.14 (m, 4H), 3.08 (m, 4H), 2.09 (s, 3H). MS (EI): 547.7 (MH+).

[01434] N-(4-{2-[(4-{4-[(2,4-difluorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: MS (EI) for $C_{28}H_{26}F_2N_6O_3S$: 565.6 (MH+).

[01435] N-{4-[2-({3-[4-({4-[(trifluoromethyl)oxy]phenyl}methyl)piperazin-1-yl]phenyl}-amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.47 (s, 1H), 8.49 (d, 1H), 8.14 (dd, 2H), 7.75 (d, 2H), 7.64 (s, 1H), 7.48 (dd, 2H), 7.33 (m, 3H), 7.22 (m, 1H), 7.13 (m, 1H), 6.56 (dd, 1H), 3.57 (s, 2H), 3.16 (m, 4H), 2.54 (m, 4H), 2.09 (s, 3H). MS (EI): 563.6 (MH+).

[01436] N-(4-{2-[(3-{4-[(1-methyl-1H-imidazol-2-yl)methyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.45 (s, 1H), 8.49 (d, 1H), 8.13 (dd, 2H), 7.75 (d, 2H), 7.58 (s, 1H), 7.33 (d, 1H), 7.25 (dd, 1H), 7.15-7.09 (m, 2H), 6.77 (d, 1H), 6.56 (dd, 1H), 3.68 (s, 3H), 3.58 (s, 2H), 3.12 (m, 4H), 2.54 (m, 4H), 2.09 (s, 3H). MS (EI): 483.5 (MH+).

[01437] N-{4-[2-({3-[4-({2-[(trifluoromethyl)oxy]phenyl}methyl)piperazin-1-yl]phenyl}-amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.47 (s, 1H), 8.50 (d, 1H), 8.13 (dd, 2H), 7.75 (d, 2H), 7.64-7.62 (m, 2H), 7.44-7.36 (m, 4H), 7.23 (dd, 1H), 7.14 (m, 1H), 6.55 (dd, 1H), 3.62 (s, 2H), 3.16 (m, 4H), 2.57 (m, 4H), 2.09 (s, 3H). MS (EI): 563.6 (MH+).

[01438] N-(4-{2-[(3-{4-[(3-chlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.69 (d, 2H), 7.44-7.38 (m, 4H), 7.28 (d, 1H), 6.96 (d, 2H), 4.48 (s, 2H), 3.27 (m, 4H), 3.09 (m, 4H), 2.09 (s, 3H). MS (EI): 514.1 (MH+).

[01439] N-{4-[2-({3-[4-(2,3-dihydroxypropyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s, 1H), 9.46 (s, 1H), 8.49 (d, 1H), 8.14 (d, 2H), 7.75 (d, 2H), 7.63 (s, 1H), 7.33 (d, 1H), 7.22 (d, 1H), 7.13 (m, 1H), 6.56 (dd, 1H), 3.67 (s, 2H), 3.14 (m, 5H), 2.60 (m, 4H), 2.45 (m, 1H), 2.30 (m, 1H), 2.09 (s, 3H). MS (EI): 463.6 (MH+).

[01440] N-{4-[2-({3-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.46 (s, 1H), 8.49 (d, 1H), 8.12 (m, 2H), 7.75 (d, 2H), 7.62 (s, 1H), 7.33 (d, 1H), 7.23 (dd, 1H), 7.12 (t, 1H), 6.90-6.85 (m, 2H), 6.79 (m, 1H), 6.55 (dd, 1H), 5.99 (s, 2H), 3.44 (s, 2H), 3.15 (m, 4H), 2.52 (m, 4H), 2.09 (s, 3H). MS (EI): 523.5 (MH+).

[01441] N-{4-[2-({3-[4-(pyridin-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.47 (s, 1H), 8.52-8.49 (m, 2H), 8.13 (m, 2H), 7.81-7.72 (m, 3H), 7.63 (s, 1H), 7.50 (d, 1H), 7.33 (d, 1H), 7.30-7.21 (m, 2H), 7.13 (t, 1H), 6.57 (dd, 1H), 3.67 (s, 2H), 3.17 (m, 4H), 2.60 (m, 4H), 2.09 (s, 3H). MS (EI): 480.6 (MH+).

[01442] N-{4-[2-({3-[4-(pyridin-3-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.47 (s, 1H), 8.54 (d, 1H), 8.49 (d, 2H), 8.12 (m, 2H), 7.78-7.73 (m, 3H), 7.63 (s, 1H), 7.40-7.37 (m, 1H), 7.33 (d, 1H), 7.23 (d, 1H), 7.13 (t, 1H), 6.55 (dd, 1H), 3.58 (s, 2H), 3.16 (m, 4H), 2.55 (m, 4H), 2.10 (s, 3H). MS (EI): 480.5 (MH+).

[01443] N-{4-[2-({3-[4-(pyridin-4-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.47 (s, 1H), 8.53 (dd, 2H), 8.49 (d, 1H), 8.14 (d, 2H), 7.75 (d, 2H), 7.64 (s, 1H), 7.38 (dd, 2H), 7.33 (d, 1H),

7.23 (d, 1H), 7.13 (t, 1H), 6.56 (dd, 1H), 3.59 (s, 2H), 3.18 (m, 4H), 2.56 (m, 4H), 2.09 (s, 3H). MS (EI): 480.7 (MH+).

[01444] N-{4-[2-({3-[4-(1H-pyrrol-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.45 (s, 1H), 8.49 (d, 1H), 8.12 (m, 2H), 7.75 (d, 2H), 7.61 (s, 1H), 7.33 (d, 1H), 7.21 (d, 1H), 7.12 (t, 1H), 6.64 (m, 1H), 6.55 (dd, 1H), 5.92 (m, 2H), 3.46 (s, 2H), 3.14 (m, 4H), 2.51 (m, 4H), 2.09 (s, 3H). MS (EI): 468.6 (MH+).

[01445] 4-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-N-(phenylmethyl)-piperazine-1-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.62 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.70 (d, 2H), 7.48 (dd, 2H), 7.28-7.21 (m, 3H), 7.00 (d, 2H), 6.94 (t, 1H), 4.41 (s, 2H), 3.60 (m, 4H), 310 (m, 4H), 2.09 (s, 3H). MS (EI): 522.4 (MH+).

[01446] N-[4-(2-{[3-(4-{[2-(methyloxy)phenyl]carbonyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.50 (s, 1H), 8.50 (d, 1H), 8.13 (d, 2H), 7.74 (d, 2H), 7.64 (s, 1H), 7.41 (m, 1H), 7.34 (d, 1H), 7.29 (d, 1H), 7.23 (dd, 1H), 7.16 (t, 1H), 7.10 (d, 1H), 7.01 (t, 1H), 6.59 (dd, 1H), 3.79 (s, 3H), 3.21 (m, 4H), 3.07 (m, 4H), 2.09 (s, 3H). MS (EI): 523.5 (MH+).

[01447] N-{4-[2-({3-[4-(1H-pyrazol-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 13.22 (s, 1H), 10.22 (s, 1H), 9.51 (s, 1H), 8.50 (d, 1H), 8.14 (d, 3H), 7.76 (d, 3H), 7.66 (s, 1H), 7.34 (d, 1H), 7.29 (d, 1H), 7.17 (t, 1H), 6.59 (dd, 1H), 3.78 (m, 4H), 3.20 (m, 4H), 2.09 (s, 3H). MS (EI): 483.5 (MH+).

[01448] N-{4-[2-({3-[4-(3-pyridin-3-ylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.24 (s, 1H), 9.50 (s, 1H), 8.50 (d, 2H), 8.39 (dd, 1H), 8.14 (d, 2H), 7.76 (d, 2H), 7.69 (dd, 2H), 7.34-7.24 (m, 3H), 7.15 (t, 1H), 6.58 (dd, 1H), 3.61 (m, 4H), 3.10 (m, 4H), 2.86 (t, 2H), 2.74 (t, 2H), 2.09 (s, 3H). MS (EI): 522.7 (MH+).

[01449] N-(4-{2-[(3-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.50 (s, 1H), 8.50 (d, 1H), 8.14 (d, 2H), 7.76 (d, 2H), 7.66 (s, 1H), 7.34 (d, 1H), 7.27 (d, 1H), 7.16 (t, 1H), 6.59 (dd, 1H), 3.63 (m, 4H), 3.58 (t, 2H), 3.23 (s, 3H), 3.12 (m, 4H), 2.63 (t, 2H), 2.09 (s, 3H). MS (EI): 475.6 (MH+).

[01450] N-[4-(2-{[3-(4-{2-[(4-fluorophenyl)oxy]acetyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s, 1H), 9.51 (s,

1H), 8.50 (d, 1H), 8.14 (d, 2H), 7.76 (d, 2H), 7.66 (s, 1H), 7.34 (d, 1H), 7.29 (d, 1H), 7.19-7.10 (m, 3H), 6.96 (m, 2H), 6.60 (dd, 1H), 4.88 (s, 2H), 3.64 (m, 4H), 3.17 (m, 4H), 2.09 (s, 3H). MS (EI): 541.5 (MH+).

[01451] N-{4-[2-({3-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.24 (s, 1H), 9.50 (s, 1H), 8.50 (d, 1H), 8.14 (d, 2H), 7.76 (d, 2H), 7.69 (s, 1H), 7.34 (d, 1H), 7.24 (d, 1H), 7.15 (t, 1H), 6.58 (dd, 1H), 3.61 (m, 2H), 3.48 (m, 2H), 3.41 (t, 1H), 3.10 (m, 4H), 2.18 (m, 2H), 2.09 (s, 3H) 1.92 (m, 2H), 1.75 (m, 2H). MS (EI): 471.4 (MH+).

[01452] N-{4-[2-({3-[4-(pyridin-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.51 (s, 1H), 8.69 (dd, 2H), 8.50 (d, 1H), 8.14 (d, 2H), 7.74 (d, 2H), 7.66 (s, 1H), 7.45 (dd, 2H), 7.34 (d, 1H), 7.28 (d, 1H), 7.16 (t, 1H), 6.60 (d, 1H), 3.81 (m, 2H), 3.43 (m, 2H), 3.27 (m, 2H), 3.14 (m, 2H), 2.10 (s, 3H). MS (EI): 494.6 (MH+).

[01453] N-{4-[2-({3-[4-(pyridin-2-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.50 (s, 1H), 8.61 (d, 1H), 8.50 (d, 1H), 8.14 (d, 2H), 7.95 (t, 1H), 7.74 (d, 2H), 7.66 (d, 2H), 7.50 (t, 1H), 7.34 (d, 1H), 7.29 (d, 1H), 7.16 (t, 1H), 6.60 (d, 1H), 3.84 (m, 2H), 3.59 (m, 2H), 3.26 (m, 2H), 3.14 (m, 2H), 2.09 (s, 3H). MS (EI): 494.6 (MH+).

[01454] N-(4-{2-[(3-{4-[(2-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s, 1H), 9.49 (s, 1H), 8.49 (d, 1H), 8.13 (d, 2H), 7.74 (d, 2H), 7.63 (s, 1H), 7.34-7.16 (m, 7H), 6.59 (d, 1H), 3.84 (m, 2H), 3.28 (m, 2H), 3.25 (m, 2H), 3.06 (m, 2H), 2.24 (s, 3H), 2.09 (s, 3H). MS (EI): 507.6 (MH+).

[01455] N-{4-[2-({3-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.51 (s, 1H), 8.50 (dd, 1H), 8.14 (d, 2H), 7.76 (d, 2H), 7.68 (s, 1H), 7.34 (d, 1H), 7.26 (d, 1H), 7.16 (t, 1H), 6.59 (d, 1H), 3.72 (m, 4H), 3.13 (m, 4H), 2.09 (s, 3H), 1.23 (s, 9H). MS (EI): 473.5 (MH+).

[01456] N-{4-[2-({3-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s, 1H), 9.51 (s, 1H), 8.67 (m, 2H), 8.50 (d, 1H), 8.13 (m, 2H), 7.90 (m, 1H), 7.75 (d, 2H), 7.66 (s, 1H), 7.50 (m, 1H), 7.34 (d, 1H), 7.29 (dd, 1H), 7.17 (t, 1H), 6.60 (dd, 1H), 3.82 (m, 2H), 3.50 (m, 2H), 3.29 (m, 2H), 3.16 (m, 2H), 2.09 (s, 3H). MS (EI): 494.7 (MH+).

[01457] N-{4-[2-({3-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.24 (s, 1H), 9.51 (s, 1H), 8.50 (d, 1H), 8.14 (dd, 2H), 7.76 (d, 2H), 7.69 (s, 1H), 7.34 (d, 1H), 7.26 (dd, 1H), 7.16 (t, 1H), 6.60 (dd, 1H), 3.66 (m, 4H), 3.11 (m, 4H), 2.90 (m, 1H), 2.09 (s, 3H), 1.03 (s, 6H). MS (EI): 459.6 (MH+).

[01458] N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]-tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.32 (s, 1H), 9.48 (s, 1H), 8.48 (d, 1H), 8.16 (d, 2H), 7.78 (d, 2H), 7.67 (s, 1H), 7.32 (d, 1H), 7.29 (dd, 1H), 6.87 (d, 1H), 3.95 (t, 2H), 3.81 (s, 3H), 3.78 (m, 2H), 3.71 (m, 4H), 3.29-3.17 (m, 1H), 2.91 (m, 4H), 2.13-2.07 (m, 2H). MS (EI): 476.5 (MH+).

[01459] (2R)-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)-phenyl]tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.94 (s, 1H), 9.48 (s, 1H), 8.48 (d, 1H), 8.16 (d, 2H), 7.89 (d, 2H), 7.66 (s, 1H), 7.33 (d, 1H), 7.30 (dd, 1H), 6.87 (d, 1H), 4.43 (dd, 1H), 4.01 (m, 1H), 3.86 (m, 1H), 3.81 (s, 3H), 3.72 (m, 4H), 2.91 (m, 4H), 2.22-2.19 (m, 1H), 2.03-1.98 (m, 1H), 1.89 (m, 2H). MS (EI): 476.4 (MH+).

[01460] (2S)-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)-phenyl]tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.94 (s, 1H), 9.48 (s, 1H), 8.48 (d, 1H), 8.16 (d, 2H), 7.89 (d, 2H), 7.66 (s, 1H), 7.33 (d, 1H), 7.30 (dd, 1H), 6.87 (d, 1H), 4.43 (dd, 1H), 4.01 (m, 1H), 3.86 (m, 1H), 3.81 (s, 3H), 3.72 (m, 4H), 2.91 (m, 4H), 2.24-2.19 (m, 1H), 2.03-1.98 (m, 1H), 1.89 (m, 2H). MS (EI): 476.5 (MH+).

[01461] N-(4-{2-[(4-{4-[(2-fluorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.85-7.77 (m, 2H), 7.74 (d, 2H), 7.68 (d, 2H), 7.56-7.46 (m, 2H), 7.28 (d, 1H), 6.93 (d, 2H), 3.18-3.16 (m, 8H), 2.09 (s, 3H). MS (EI): 547.7 (MH+).

[01462] N-(4-{2-[(3-{4-[(3,5-dichlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.24 (s, 1H), 9.51 (s, 1H), 8.50 (d, 1H), 8.14 (d, 2H), 7.73 (m, 3H), 7.64 (s, 1H), 7.54 (d, 2H), 7.34 (d, 1H), 7.29 (d, 1H), 7.16 (t, 1H), 6.60 (dd, 1H), 3.79 (m, 2H), 3.46 (m, 2H), 3.26 (m, 2H), 3.15 (m, 2H), 2.09 (s, 3H). MS (EI): 562.5 (MH+).

[01463] ethyl 3-(4-(2-(4-morpholinophenylamino(pyrimidin-4-yl)phenylamino)-3-oxopropanoate: ^{1}H NMR (400 MHz, d6-DMSO): 10.46 (s, 1H), 9.35 (s, 1H), 8.42 (d, 1H), 8.11 (d, 2H), 7.71 (d, 2H), 7.64 (d, 2H), 7.26 (d, 1H), 6.92 (d, 2H), 4.11 (q, 2H), 3.72 (m, 2H), 3.37 (m, 4H), 3.02 (m, 4H), 1.19 (t, 3H). MS (EI): 462 (MH+).

[01464] N-(4-(2-(4-(4-isobutyrylpiperazin-1-yl)penylamino)pyrimidin-4-yl)phenyl)-tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.30 (s, 1H), 9.43 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.97 (m, 2H), 3.96 (t, 1H), 3.76 (m, 2H), 3.63 (m, 4H), 3.19 (m, 2H), 3.06 (m, 4H), 2.93 (m, 1H), 2.10 (m, 2H), 1.02 (d, 6H). MS (EI): 515 (MH+).

[01465] N-(4-(2-(4-(4-(cyclobutanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.30 (s, 1H), 9.42 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.96 (d, 2H), 3.96 (t, 1H), 3.76 (m, 3H), 3.59 (m, 2H), 3.41 (m, 3H), 3.19 (m, 1H), 3.03 (m, 4H), 2.41 (m, 6H), 1.90 (m, 1H), 1.75 (m, 1H). MS (EI): 527 (MH+).

[01466] N-ethyl-4-(4-(4-(4-(tetrahydrofuran-3-carboxamido)phenyl)pyrimidin-2-yl-amino(phenyl)piperazine-1-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.30 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.77 (d, 2H), 7.67 (d, 2H), 7.28 (d, 1H), 6.96 (d, 2H), 6.59 (t, 1H), 3.96 (t, 1H), 3.75 (m, 3H), 3.42 (m, 4H), 3.19 (m, 1H), 3.05 (m, 6H), 2.10 (q, 2H), 1.02 (t, 3H). MS (EI): 516 (MH+).

[01467] N-(4-(2-(4-(4-((R)-2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.31 (s, 1H), 9.42 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.77 (d, 2H), 7.69 (d, 2H), 7.29 (d, 1H), 6.97 (d, 2H), 3.96 (dd, 1H), 3.89 (m, 1H), 3.76 (m, 4H), 3.63 (m, 4H), 3.18 (m, 2H), 3.07 (m, 4H), 2.09 (m, 2H), 1.13 (d, 3H). MS (EI): 516 (MH+).

[01468] N-(4-(2-(4-(4-((S)-2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.31 (s, 1H), 9.42 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.97 (d, 2H), 3.96 (t, 1H), 3.85 (q, 1H), 3.76 (m, 3H), 3.63 (m, 4H), 3.19 (m, 1H), 3.07 (m, 4H), 2.10 (m, 2H), 1.11 (d, 3H). MS (EI): 516 (MH+).

[01469] N-(4-(2-(4-(4-((R)-pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.31 (s, 1H), 9.42 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.77 (d, 2H), 7.69 (d, 2H), 7.29 (d, 1H), 6.97 (d, 2H), 3.97 (m, 2H), 3.76 (m, 3H), 3.64 (m, 4H), 3.19 (m, 1H), 3.06 (m, 6H), 2.73 (m, 1H), 2.09 (m, 2H), 1.67 (m, 4H). MS (EI): 542 (MH+).

[01470] N-(4-(2-(4-(4-((S)-pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.31 (s, 1H), 9.42 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.77 (d, 2H), 7.69 (d, 2H), 7.29 (d, 1H), 6.97 (d, 2H), 3.96 (t, 1H), 3.86 (m, 1H), 3.76 (m, 3H), 3.64 (m, 4H),

3.18 (m, 1H), 3.05 (m, 6H), 2.64 (m, 1H), 2.10 (m, 1H), 2.00 (m, 1H), 1.62 (m, 4H). MS (EI): 542 (MH+).

[01471] N-{4-[2-(1H-benzimidazol-6-ylamino)-5-methylpyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.25 (s, 1H), 8.97 (s, 1H), 8.78 (s, 1H), 8.21(d, 2H), 7.86 (d, 2H), 7.80 (d, 2H), 6.96 (s, 1H), 6.78 (dd, 2H), 2.44 (s, 3H), 2.11 (s, 3H); MS (EI) $C_{20}H_{18}N_6O$: 359.3 $(M+H)^+$.

[01472] 4-(4-furan-2-ylphenyl)-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine: ^{1}H-NMR (400MHz, d_6-DMSO): 9.46 (s, 1H), 8.49 (d, 1H), 8.22 (d, 2H), 7.87 (d, 2H), 7.84 (dd, 1H), 7.68 (d, 2H), 7.37 (d, 1H), 7.12 (t, 1H), 6.94 (d, 2H), 6.66 (dd, 1H), 3.75 (t, 4H), 3.05 (t, 4H) ; MS (EI) $C_{24}H_{22}N_4O_2$: 399.3 $(M+H)^+$.

[01473] N-(4-morpholin-4-ylphenyl)-4-[4-(pyrimidin-2-ylamino)phenyl]pyrimidin-2-amine: ^{1}H-NMR (400MHz, d_6-DMSO): 10.01 (s, 1H), 9.35 (s, 1H), 8.56 (d, 2H), 8.42 (d, 1H), 8.11 (dd, 2H), 7.95 (dd, 2H), 7.69 (d, 2H), 7.27 (d, 1H), 6.96-6.92 (m, 3H), 3.75 (t, 4H), 3.06 (t, 4H); MS (EI) $C_{24}H_{23}N_7O$: 426.3 $(M+H)^+$.

[01474] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-methylpyrimidin-4-yl)phenyl]-cyclopropanecarboxamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.40 (s, 1H), 9.41 (bs, 1H), 9.30 (s, 1H), 8.30 (s, 1H), 7.23-7.70 (m, 2H), 7.65-7.62 (m, 3H), 6.91 (d, 2H), 3.70-3.50 (bs, 2H), 3.21-2.87 (m, 8H), 2.20 (s, 3H), 1.80 (p, 1H), 1.18 (bs, 3H), 0.81 (d, 4H); MS (EI) $C_{24}H_{23}N_7O$: 457.4 $(M+H)^+$.

[01475] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-cyclopropanecarboxamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.48 (s, 1H), 9.37 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.76 (d, 2H), 7.65 (d, 2H), 7.27 (d, 1H), 6.93 (d, 2H), 3.09 (bs, 4H), 2.60-2.35 (m, 6H), 1.83 (p, 1H), 1.06 (t, 3H), 0.84-0.82 (m, 4H); MS (EI) $C_{26}H_{30}N_6O$: 443.4 $(M+H)^+$.

[01476] N-(4-{2-[(3,5-dimorpholin-4-ylphenyl)amino]-5-methylpyrimidin-4-yl}phenyl)-N^2,N^2-dimethylglycinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.04 (s, 1H), 9.25 (s, 1H), 8.37 (s, 1H), 7.81 (d, 2H), 7.74 (d, 2H), 7.12 (s, 2H), 6.11 (s, 1H), 3.73 (t, 8H), 3.20 (bs, 2H), 3.06 (t, 8H), 2.34 (s, 6H), 2.28 (s, 3H); MS (EI) $C_{29}H_{37}N_7O_3$: 532.4 $(M+H)^+$.

[01477] N^2,N^2-dimethyl-N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)glycinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.43 (s, 1H), 9.28 (s, 1H), 8.33 (s, 1H), 7.77 (d, 2H), 7.69 (d, 2H), 7.63 (d, 2H), 6.88 (d, 2H), 3.73 (t, 4H), 3.35 (bs, 2H), 3.01 (t, 4H), 2.65 (s, 6H), 2.21 (s, 3H); MS (EI) $C_{25}H_{30}N_6O_2$: 447.4 $(M+H)^+$.

[01478] N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.15 (s, 1H), 9.28 (s, 1H), 8.32 (s, 1H),

7.82-7.79 (m, 2H), 7.64 (t, 4H), 6.88 (d, 2H), 3.75-3.72 (t, 5H), 3.01 (t, 4H), 2.91 (t, 2H), 2.22 (s, 3H), 2.11-2.02 (m, 1H), 1.84-1.75 (m, 1H), 1.70-1.63 (m, 2H); MS (EI) $C_{26}H_{30}N_6O_2$: 459.4 $(M+H)^+$.

[01479] N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.25 (s, 1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.83 (d, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 6.96 (d, 2H), 3.80-3.77 (m, 1H), 3.65-3.41 (m, 4H), 3.08-3.02 (m, 4H), 2.96-2.89 (m, 3H), 2.13-2.08 (m, 1H), 1.84-1.78 (m, 1H), 1.73-1.68 (m, 2H), 1.02 (d, 6H); MS (EI) $C_{29}H_{35}N_7O_2$: 514.4 $(M+H)^+$.

[01480] N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.85 (s, 1H), 9.41 (s, 1H), 8.47 (d, 1H), 8.18 (d, 2H), 7.78 (d, 2H), 7.68 (d, 2H), 7.31 (d, 1H), 6.96 (d, 2H), 4.40-4.34 (m, 1H), 3.70 (t, 4H), 3.32-3.25 (m, 2H), 3.05 (t, 4H), 2.44-2.38 (m, 1H), 2.05-1.94 (m, 3H), 1.23 (s, 9H); MS (EI) $C_{30}H_{37}N_7O_2$: 528.4 $(M+H)^+$.

[01481] N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.19 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.84 (d, 2H), 7.67 (d, 2H), 7.30 (d, 1H), 6.95 (d, 2H), 3.74-3.70 (m, 1H), 3.60-3.46 (m, 4H), 3.04-3.00 (m, 4H), 2.91 (t, 2H), 2.22-2.02 (m, 6H), 1.95-1.87 (m, 1H), 1.82-1.73 (m, 2H), 1.70-1.64 (m, 2H); MS (EI) $C_{30}H_{35}N_7O_2$: 526.2 $(M+H)^+$.

[01482] N-ethyl-4-[4-({4-[4-(D-prolylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-piperazine-1-carboxamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.19 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.84 (d, 2H), 7.67 (d, 2H), 7.29 (d, 1H), 6.96 (d, 2H), 6.59 (t, 1H), 3.74-3.71 (m, 1H), 3.42 (t, 4H), 3.10-3.05 (m, 2H), 3.01 (t, 4H), 2.91 (t, 2H), 2.22 (s, 3H), 2.09-2.02 (m, 1H), 1.84-1.76 (m, 1H), 1.70-1.63 (m, 2H), 1.02 (t, 3H); MS (EI) $C_{28}H_{34}N_8O_2$: 515.5 $(M+H)^+$.

[01483] N-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 (s, 1H), 9.42 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.84 (d, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 6.97 (d, 2H), 3.92-3.89 (m, 1H), 3.75-3.71 (m, 1H), 3.65-3.59 (m, 4H), 3.09-2.98 (m, 5H), 2.91 (t, 2H), 2.69-2.63 (m, 1H), 2.09-2.02 (m, 2H), 1.84-1.76 (m, 1H), 1.70-1.54 (m, 5H); MS (EI) $C_{30}H_{36}N_8O_2$: 541.4 $(M+H)^+$.

[01484] N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 (s, 1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.84 (d, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 6.96 (d, 2H), 3.92-3.89 (m, 1H), 3.75-3.71 (m, 1H), 3.65-3.59 (m, 4H), 3.09-2.98 (m, 5H), 2.91 (t, 2H), 2.69-2.63 (m, 1H), 2.09-2.02 (m, 2H), 1.84-1.76 (m, 1H), 1.70-1.56 (m, 5H); MS (EI) $C_{30}H_{36}N_8O_2$: 541.4 $(M+H)^+$.

[01485] 1-Methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-prolinamide: ^{1}H NMR (400 MHz, d_6-DMSO): 9.93 (s, 1H), 9.39 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.87 (d, 2H), 7.67 (d, 2H), 7.29 (d, 1H), 6.93 (d, 2H), 3.74 (m, 4H), 3.12 (m, 1H), 3.05 (m, 4H), 2.95 (m, 1H), 2.36 (m, 4H) 2.17 (m, 1H), 1.80 (m, 3H); MS (EI) for $C_{26}H_{30}N_6O_2$: 459 (MH^+).

[01486] 1-Methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-2-carboxamide: ^{1}H NMR (400 MHz, d_6-DMSO): 9.97 (s, 1H), 9.39 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.85 (d, 2H), 7.67 (d, 2H), 7.28 (d, 1H), 6.93 (d, 2H), 3.74 (m, 4H), 3.05 (m, 4H), 2.92 (m, 1H), 2.60 (dd, 1H), 2.16 (s, 3H) 2.03 (m, 1H), 1.76 (m, 2H), 1.60 (m, 3H), 1.25 (m, 1H); MS (EI) for $C_{27}H_{32}N_6O_2$: 473 (MH^+).

[01487] N-{4-[2-({4-[4-(Piperidin-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, d_6-DMSO): 10.25 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.36 (s, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.28 (d, 1H), 6.97 (d, 2H), 3.64 (m, 4H), 3.17 (m, 2H), 3.06 (m, 4H), 2.93 (m, 1H), 2.81 (m, 2H), 2.09 (s, 3H) 1.60-1.75 (m, 4H); MS (EI) for $C_{28}H_{33}N_7O_2$: 500 (MH^+).

[01488] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-pyridin-4-ylacetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.53 (s, 1H), 9.38 (s, 1H), 8.53 (d, 2H), 8.44 (d, 1H), 8.12 (d, 2H), 7.95 (d, 1H), 7.76 (d, 2H), 7.67 (d, 2H), 7.35 (d, 1H), 6.92 (d, 2H), 3.75 (m, 6H), 3.04 (m, 4H). MS (EI): 467 (MH+).

[01489] 2-(3-fluorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.44 (s, 1H), 9.36 (s, 1H), 8.42 (m, 1H), 8.09 (d, 2H), 7.74 (d, 2H), 7.64 (d, 2H), 7.35 (m, 1H), 7.24 (m, 1H), 7.15 (d, 2H), 7.07 (m, 1H), 6.90 (d, 2H), 3.71 (m, 6H), 3.04 (m, 4H). MS (EI): 484 (MH+).

[01490] 3-(4-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.19 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.73 (d, 2H), 7.68 (d, 2H), 7.35 (d, 2H), 7.26 (m, 3H), 6.93 (d, 2H), 3.74 (m, 4H), 3.04 (m, 4H), 2.92 (t, 2H), 2.67 (t, 2H). MS (EI): 515 (MH+).

[01491] 2-(3-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.47 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.66 (d, 2H), 7.43 (s, 1H), 7.32 (m, 4H), 6.93 (d, 2H), 3.74 (m, 6H), 3.04 (m, 4H). MS (EI): 500 (MH+).

[01492] 2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-phenyl-propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.12 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.09 (d, 2H), 7.72 (d, 2H), 7.67 (d, 2H), 7.25 (m, 4H), 7.17 (m, 2H), 6.93 (d, 2H), 3.74

(m, 4H), 3.06 (m, 4H), 2.99 (m, 1H), 2.81 (m, 1H), 2.64 (m, 1H), 1.12 (d, 3H). MS (EI): 494 (MH+).

[01493] trans-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenyl-cyclopropanecarboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.53 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.77 (d, 2H), 7.67 (d, 2H), 7.28 (m, 3H), 7.21 (m, 3H), 6.93 (d, 2H), 3.74 (m, 4H), 3.04 (m, 4H), 2.39 (m, 1H), 2.11 (m, 1H), 1.53 (m, 1H), 1.42 (m, 1H). MS (EI): 492 (MH+).

[01494] 2-(4-fluorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.44 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.65 (d, 2H), 7.38 (m, 2H), 7.27 (d, 1H), 7.18 (dd, 2H), 6.93 (d, 2H), 3.71 (m, 4H), 3.69 (s, 2H), 3.04 (m, 4H). MS (EI): 484 (MH+).

[01495] 3-(2-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.67 (d, 2H), 7.45 (dd, 1H), 7.40 (dd, 1H), 7.25 (m, 3H), 6.93 (d, 2H), 3.74 (m, 4H), 3.04 (m, 6H), 2.70 (t, 2H). MS (EI): 515 (MH+).

[01496] 3-(3-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.19 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.67 (d, 2H), 7.27 (m, 5H), 6.93 (d, 2H), 3.74 (m, 4H), 3.04 (m, 4H), 2.94 (t, 2H), 2.69 (t, 2H). MS (EI): 515 (MH+).

[01497] 3-(2-fluorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.73 (d, 2H), 7.67 (d, 2H), 7.35 (t, 1H), 7.26 (d, 2H), 7.11 (m, 2H), 6.93 (d, 2H), 3.74 (m, 4H), 3.04 (m, 4H), 2.95 (t, 2H), 2.68 (t, 2H). MS (EI): 498 (MH+).

[01498] Nalpha,Nalpha-dimethyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]-pyrimidin-4-yl}phenyl)-L-phenylalaninamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.04 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.09 (d, 2H), 7.74 (d, 2H), 7.67 (d, 2H), 7.24 (m, 5H), 7.17 (m, 1H), 6.93 (d, 2H), 3.74 (m, 4H), 3.48 (dd, 1H), 3.06 (m, 5H), 2.86 (dd, 1H), 2.49 (s, 6H). MS (EI): 523 (MH+).

[01499] 2-(2-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.54 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.76 (d, 2H), 7.67 (d, 2H), 7.46 (m, 2H), 7.33 (m, 2H), 7.29 (d, 1H), 6.93 (d, 2H), 3.89(s, 2H), 3.74 (m, 4H), 3.04 (m, 4H). MS (EI): 500 (MH+).

[01500] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-pyridin-2-yl-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.51 (s, 1H), 9.35 (s, 1H), 8.49 (d, 1H),

8.41 (d, 1H), 8.10 (d, 2H), 7.77 (m, 3H), 7.64 (d, 2H), 7.39 (d, 1H), 7.26 (m, 2H), 6.92 (d, 2H), 3.87 (s, 2H), 3.71 (m, 4H), 3.02 (m, 4H). MS (EI): 467 (MH+).

[01501] 2-(4-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.47 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.66 (d, 2H), 7.39 (m, 4H), 7.26 (m, 1H), 6.93 (d, 2H), 3.74 (m, 4H), 3.70 (s, 2H), 3.04 (m, 4H). MS (EI): 500 (MH+).

[01502] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-{4-[(trifluoro-methyl)oxy]phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.50 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.12 (d, 2H), 7.75 (d, 2H), 7.66 (d, 2H), 7.47 (d, 2H), 7.35 (d, 2H), 7.27(d, 1H), 6.93 (d, 2H), 3.74 (m, 6H), 3.04 (m, 4H). MS (EI): 550 (MH+).

[01503] 2-[2-(methyloxy)phenyl]-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.34 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.76 (d, 2H), 7.67 (d, 2H), 7.26 (m, 3H), 7.00 (d, 1H), 6.91 (m, 3H), 3.77 (s, 3H), 3.74 (m, 4H), 3.67 (s, 2H), 3.04 (m, 4H). MS (EI): 496 (MH+).

[01504] 2-[3-(methyloxy)phenyl]-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.44 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.76 (d, 2H), 7.67 (d, 2H), 7.26 (m, 2H), 6.93 (m, 4H), 6.82 (dd, 1H), 3.74 (m, 7H), 3.55 (s, 2H), 3.04 (m, 4H). MS (EI): 496 (MH+).

[01505] 2-[4-(methyloxy)phenyl]-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.38 (s, 1H), 9.38 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.75 (d, 2H), 7.67 (d, 2H), 7.26 (m, 3H), 6.93 (m, 4H), 3.74 (m, 7H), 3.60 (s, 2H), 3.04 (m, 4H). MS (EI): 496 (MH+).

[01506] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-alaninamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.35 (s, 1H), 8.43 (d, 1H), 8.13 (d, 2H), 7.82 (d, 2H), 7.63 (d, 2H), 7.28 (d, 1H), 6.92 (d, 2H), 3.48 (m, 1H), 2.35 (q, 2H), 1.86 (br s, 8H), 1.24 (d, 3H), 1.03 (t, 3H). MS (EI): 446 (MH+).

[01507] N-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.21 (s, 1H), 9.39 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.75 (d, 2H), 7.67 (d, 2H), 7.28 (d, 1H), 6.96 (d, 2H), 3.68 (m, 4H), 3.10 (s, 2H), 3.07 (m, 4H), 2.18 (s, 6H), 2.09 (s, 3H). MS (EI): 474 (MH+).

[01508] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-3-(methyloxy)propanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.23 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.11 (d, 2H), 7.75 (d, 2H), 7.65 (d, 2H), 7.25 (d, 1H), 6.92 (d, 2H), 3.63 (t, 2H), 3.25 (s, 3H), 3.09 (m, 4H), 2.60 (t, 2H), 2.58 (m, 6H), 1.05 (t, 3H). MS (EI): 461 (MH+).

[01509] (2R)-2-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenylethanamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.37 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.80 (d, 2H), 7.66 (d, 2H), 7.49 (d, 2H), 7.34 (t, 2H), 7.26 (m, 2H), 6.92 (d, 2H), 4.56 (s, 1H), 3.75 (m, 4H), 3.04 (m, 4H). MS (EI): 481 (MH+).

[01510] N'2',N'2'-dimethyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)-D-alaninamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.02 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.84 (d, 2H), 7.66 (d, 2H), 7.28 (d,1H), 6.92 (d, 2H), 3.75 (m, 4H), 3.21 (q, 1H), 3.04 (m, 4H), 2.25 (s, 6H), 1.19 (d, 3H). MS (EI): 447 (MH+).

[01511] 1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.94 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.87 (d, 2H), 7.67 (d, 2H), 7.30(d,1H), 6.94 (d, 2H), 3.76 (m, 4H), 3.12 (m, 1H), 3.05 (m, 4H), 2.95 (m, 1H), 2.36 (s, 3H), 2.30 (m, 1H), 2.18 (m, 1H), 1.78 (m, 3H). MS (EI): 459 (MH+).

[01512] N'2',N'2'-dimethyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)-L-alaninamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.03 (s, 1H), 9.39 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.84 (d, 2H), 7.67 (d, 2H), 7.28 (d,1H), 6.92 (d, 2H), 3.75 (m, 4H), 3.21 (q, 1H), 3.05 (m, 4H), 2.25 (s, 6H), 1.19 (d, 3H). MS (EI): 447 (MH+).

[01513] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1-phenyl-cyclopropanecarboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.38 (s, 1H), 8.43 (d, 1H), 8.09 (d, 2H), 7.72 (d, 2H), 7.65 (d, 2H), 7.40 (m, 4H), 7.28 (m, 2H), 6.92 (d, 2H), 3.74 (m, 4H), 3.04 (m, 4H), 1.74 (dd, 2H), 1.15 (dd, 2H). MS (EI): 492 (MH+).

[01514] 2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-butanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.12 (s, 1H), 9.38 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.78 (d, 2H), 7.67 (d, 2H), 7.27 (d,1H), 6.93 (d, 2H), 3.75 (m, 4H), 3.04 (m, 4H), 2.46 (q, 1H), 1.65 (m, 1H), 1.41 (m, 1H), 1.10 (d, 3H), 0.87 (t, 3H). MS (EI): 432 (MH+).

[01515] (2S)-1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-azetidine-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.88 (s, 1H), 9.39 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.89 (d, 2H), 7.67 (d, 2H), 7.29 (d,1H), 6.93 (d, 2H), 3.74 (m, 4H), 3.56 (t, 1H), 3.36 (m, 1H), 3.04 (m, 4H), 2.93 (q, 1H), 2.33 (s, 3H), 2.30 (m, 1H), 2.12 (m, 1H). MS (EI): 445 (MH+).

[01516] 2,4,6-trichloro-N-(3-{[4-(4-methyl-2-thienyl)pyrimidine-2-yl]amino}propyl)-benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.68 (br s, 1H), 8.24 (d, 1H), 7.72-7.70 (m, 3H), 7.29 (s, 1H), 7.17 (t, 1H), 6.98 (d, 1H), 3.37-3.35 (m, 2H), 3.28-3.27 (m, 2H), 2.22 (s, 3H), 1.77 (br t, 2H). MS (EI): 457.0 (MH+).

[01517] N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}cyclopropanecarboxamide: MS (EI) $C_{29}H_{34}N_6O_2$: 499 (MH+)

[01518] 4-{4-[(4-{4-[(cyclopropylcarbonyl)amino]phenyl}pyrimidin-2-yl)amino]phenyl}-N-ethylpiperazine-1-carboxamide: MS (EI) $C_{27}H_{31}N_7O_2$: 486 (MH+)

[01519] N-[3-({4-[3,4-bis(mehtyloxy)phenyl]pyrimidine-2-yl}amino)propyl]-2,6-dichloro-benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.67 (br s, 1H), 8.26 (d, 1H), 7.69-7.67 (m, 2H), 7.49-7.35 (m, 3H), 7.14-7.09 (m, 2H), 7.03 (d, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.42 (m, 2H), 3.32 (m, 2H), 1.80 (m, 2H). MS (EI): 461.2 (MH+).

[01520] 2,6-dichloro-N-[3-({4-[(4-morpholino-4-ylphenyl)amino]pyrimidin-2-yl}amino)-propyl]benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.85 (br s, 1H), 8.63 (t, 1H), 7.69 (d, 1H), 7.48 (d, 2H), 7.44 (d, 1H), 7.42 (s, 1H), 7.37-7.33 (m, 1H), 6.81 (d, 2H), 6.59 (br s, 1H), 5.83 (d, 1H), 3.67-3.65 (m, 4H), 3.23-3.20 (m, 4H), 2.97-2.94 (m, 4H), 1.70 (t, 2H). MS (EI): 501.2 (MH+).

[01521] 2,6-dichloro-N-(3-{[4-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-fluoropyrimidin- 2-yl]amino}proypyl)benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.62 (t, 1H), 8.29 (d, 1H), 7.49-7.42 (m, 4H), 7.37-7.33 (m, 1H), 7.15 (t, 1H), 6.94-6.92 (m, 1H), 4.27-4.21 (m, 4H), 3.33-3.22 (m, 4H), 1.74 (t, 2H); MS (EI): 477.1 (MH+).

[01522] 2,6-dichloro-N-{3-[(4-{3-[(dimethylamino)methyl]phenyl}pyrimidin-2-yl)amino]propyl}benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.68 (t, 1H), 8.31 (d, 1H), 8.01-7.95 (m, 2H), 7.49-7.38 (m, 5H), 7.23 (br s, 1H), 7.10 (d, 1H), 3.43 (m, 2H), 3.33-3.29 (m, 4H), 2.14 (s, 6H), 1.82 (t, 2H); MS (EI): 460.2 (MH+).

[01523] 2,6-dichloro-N-[3-({4-[3-(1-methylethyl)phenyl]pyrimidin- 2-yl}amino)-propyl]-benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.66 (t, 1H), 8.31 (d, 1H), 7.95-7.88 (m, 2H), 7.55 (br s, 1H), 7.45-7.43 (m, 2H), 7.40-7.34 (m, 3H), 7.20 (br s, 1H), 3.30 (br s, 2H), 3.29-3.25 (m, 2H), 2.92 (septet, 1H), 1.78 (m, 2H), 1.18 (d, 6H); MS (EI): 443.0 (MH+).

[01524] 2,6-dichloro-N-{3-[(4-{4-[(1-methylethyl)oxy]phenyl}pyrimidin-2-yl)amino]propyl}-benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.68 (t, 1H), 8.25 (d, 1H), 8.03 (d, 2H), 7.49-7.47 (m, 2H), 7.42-7.38 (m, 1H), 7.10 (t, 1H), 7.03 (d, 1H), 6.98 (d, 2H), 4.69 (septet, 1H), 3.42 (m, 2H), 3.30 (m, 2H), 1.80 (t, 2H), 1.27 (d, 6H); MS (EI): 459.0 (MH+).

[01525] N-[3-({4-[3-(acetylamino)phenyl]pyrimidin- 2-yl}amino)propyl]-2,6-dichloro-benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.1 (s, 1H), 8.70 (t, 1H), 8.33-8.27 (m, 2H),

7.70 (m, 2H), 7.49-7.46 (m, 2H), 7.42-7.37 (m, 2H), 7.37 (br s, 1H), 7.01 (d, 1H), 3.43 (m, 4H), 2.02 (s, 3H), 1.97 (m, 2H). MS (EI): 458.2 (MH+).

[01526] 2,6-dichloro-N-[3-({4-[(E)-2-phenylethenyl]pyrimidin-2-yl}amino)propyl]-benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.71 (t, 1H), 8.27 (d, 1H), 7.76 (d, 1H), 7.67-7.65 (m, 2H), 7.51-7.49 (m, 2H), 7.44-7.34 (m, 4H), 7.12-7.06 (m, 2H), 6.72 (d, 1H), 3.36 (m, 2H), 3.33 (m, 2H), 1.81 (t, 2H). MS (EI): 427.0 (MH+).

[01527] phenyl (4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)carbamate: ^{1}H-NMR (400MHz, d6-DMSO): 8.59 (d, 1H), 7.90 (d, 2H), 7.69 (d, 1H), 7.44-7.40 (m, 2H), 7.28-7.20 (m, 5H), 6.97 (d, 2H), 6.62 (d, 2H), 5.90 (s, 2H), 3.74-3.72 (m, 4H), 3.13-3.11 (m, 4H). MS (EI): 468.1 (MH+).

[01528] phenylmethyl (4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-carbamate: ^{1}H-NMR (400MHz, d6-DMSO): 8.55 (d, 1H), 7.85 (d, 2H), 7.64 (d, 1H), 7.33-7.30 (m, 5H), 7.13 (d, 2H), 6.92 (d, 2H), 6.62 (d, 2H), 5.88 (s, 2H), 5.88 (s, 2H), 3.74-3.71 (m, 4H), 3.11-3.09 (m, 4H). MS (EI): 428.3 (MH+).

[01529] N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-3-(methyloxy)propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.2 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.95 (d, 2H), 3.71-3.69 (m, 4H), 3.65 (t, 2H), 3.25 (s, 3H), 3.06-3.03 (m, 4H), 2.59 (t, 2H), 1.23 (s, 9H). MS (EI): 517.4 (MH+).

[01530] N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-3-(methyloxy)propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.2 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.96 (d, 2H), 3.65-3.60 (m, 4H), 3.47-3.37 (m, 4H), 3.25 (s, 3H), 3.03-3.02 (m, 3H), 2.60 (t, 2H), 2.21-2.07 (m, 4H), 1.94-1.87 (m, 1H), 1.78-1.73 (m, 1H). MS (EI): 515.2 (MH+).

[01531] 3-(methyloxy)-N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)-pyrimidin-4-yl]phenyl}propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.2 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.76 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.96 (d, 2H), 3.65-3.62 (m, 6H), 3.25 (s, 3H), 3.08-3.02 (m, 4H), 2.92 (m, 1H), 2.59 (t, 2H), 1.02 (d, 6H). MS (EI): 503.4 (MH+).

[01532] N-ethyl-4-(4-{[4-(4-{[3-(methyloxy)propanoyl]amino}phenyl)pyrimidin-2-yl]-amino}phenyl)piperazine-1-carboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.2 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.12 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.28 (d, 1H), 6.97 (d, 2H), 6.59 (t, 1H), 3.64 (t, 2H), 3.43 (m, 4H), 3.25 (s, 3H), 3.10-3.03 (m, 6H), 2.61 (t, 2H), 1.02 (t, 3H). MS (EI): 504.4 (MH+).

[01533] N-(4-(2-(4-(4-ethylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-2-phenyl-acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.45 (s, 1H), 9.36 (s, 1H), 8.43 (d, 1H), 8.12 (d, 2H), 7.76 (d, 2H), 7.64 (d, 2H), 7.38-7.33 (m, 3H), 7.27 (d, 1H), 6.92 (d, 2H), 3.69 (s, 2H), 3.10-3.04 (m, 4H), 2.35 (q, 3 H), 1.89 (s, 2H), 1.03 (t, 2H); MS (EI): 493.1 (MH+).

[01534] 1-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidin-2-one: ^{1}H-NMR (400MHz, d6-DMSO): 8.26 (d, 1H), 8.14 (d, 2H), 7.77 (d, 2H), 7.65 (d, 2H), 7.36 (d, 1H), 7.25 (d, 2H), 3.92-3.84 (m, 5H), 3.82-3.74 (m, 1H), 3.74-3.60 (m, 1H), 3.42-3.30 (m, 4H), 3.06-3.02 (m, 1H), 2.16-2.06 (m, 2H); MS (EI): 416.1 (MH+).

[01535] (R)-2-amino-N-(4-(2-(4-(4-(cyclobutanecarbonyl)piperazin-1-yl)phenylamino)-pyrimidin-4-yl)phenyl)propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.41 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.82 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.95 (d, 2H), 3.63-3.56 (m, 2H), 3.43-3.37 (m, 3H), 3.18 (d, 1H), 3.07-2.98 (m, 4H), 2.25-2.02 (m, 4H), 1.98-1.83 (m, 1H), 1.82-1.70 (m, 1H), 1.23 (d, 3H); MS (EI): 500.2 (MH+).

[01536] (R)-2-amino-N-(4-(2-(4-(4-pivaloylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.41 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.82 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.95 (d, 2H), 3.73-3.67 (m, 4H), 3.52-4.42 (m, 1H), 3.08-3.02 (m, 4H), 1.25 (s, 3H), 1.23 (d, 3H); MS (EI): 502.4 (MH+).

[01537] (S)-2-hydroxy-3-methyl-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)-phenyl)butanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.90 (s, 1H), 9.39 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.90 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.94 (d, 2H), 5.76 (d, 1H), 3.86 (dd, 1H), 3.78-3.73 (m, 4H), 3.08-3.02 (m, 4H), 0.96 (d, 3H), 0.87 (d, 3H); MS (EI): 448.3 (MH+).

[01538] (R)-2-hydroxy-3-methyl-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)-phenyl)butanamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.90 (s, 1H), 9.39 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.90 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.94 (d, 2H), 5.76 (d, 1H), 3.86 (dd, 1H), 3.78-3.73 (m, 4H), 3.08-3.02 (m, 4H), 0.96 (d, 3H), 0.87 (d, 3H); MS (EI): 448.3 (MH+).

[01539] N-{4-[2-({4-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}-D-alaninamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.17 (s, 1H), 10.04 (s, 1H), 8.58 (s, 1H), 8.40 (s, 2H), 8.11-8.09 (m, 2H), 7.96-7.82 (m, 3H), 7.76-7.65 (m, 1H), 7.45 (d, 1H), 4.05 (t, 4H), 3.75-3.70 (m, 1H), 3.50 (t, 4H), 2.10-2.00 (m, 1H), 1.45 (d, 3H), 0.82-0.72 (m, 4H). MS (EI): 486 (MH+).

[01540] (2S)-2-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenylethanamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.73 (s, 1H), 10.08 (s, 1H), 8.99 (s, br, 3H), 8.58 (s, 1H), 8.19 (d, 2H), 7.96-7.83 (m, 3H), 7.76-7.65 (m, 3H), 7.45-7.40 (m, 3H), 5.40 (s, br, 1H), 3.85 (s, br, 4H), 3.50 (s, br, 4H). MS (EI): 481 (MH+).

[01541] 2-amino-2-(4-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.80 (s, 1H), 10.00 (s, 1H), 9.00 (s, 2H), 8.57 (d, 1H), 8.20 (d, 2H), 7.95-7.83 (m, 4H), 7.80-7.60 (m, 3H), 7.58 (d, 2H), 7.43 (d, 1H), 5.50 (s, 1H), 4.00 (t, 4H), 3.50 (t, 4H). MS (EI): 515 (MH+).

[01542] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)morpholine-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.60 (s, 1H), 10.20 (s, 1H), 10.00 (s, 1H), 9.40 (s, br, 1H), 8.58 (d, 1H), 8.20 (d, 2H), 7.95-7.88 (m, 3H), 7.60-7.20 (m, 4H), 4.42-4.30 (m, 2H), 4.05-3.90 (m, 2H), 3.85-3.70 (m, 4H), 3.60-3.45 (m, 4H), 3.25-3.10 (m, 3H). MS (EI): 461 (MH+).

[01543] 1-ethyl-3-[4-(2-{[4-(4-ethylpiperazin-1-yl)-3-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]urea: ^{1}H NMR (400 MHz, d6-DMSO): 9.40 (s, 1H), 8.90 (s, 1H), 8.42 (d, 1H), 8.20 (s, 1H), 8.05 (d, 2H), 7.56 (d, 2H), 7.28 (d, 2H), 6.83 (d, 1H), 6.36 (t, 1H), 3.80 (s, 3H), 3.12 (q, 2H), 2.98 (s, br, 4H), 2.58 (s, br, 4H), 2.42 (q, 2H), 1.08-1.00 (m, 6H). MS (EI): 476 (MH+).

[01544] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)-3-(methyloxy)phenyl]amino} pyrimidin-4-yl)-phenyl]-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.23 (s, 1H), 11.05 (s, 1H), 10.18 (s, br, 1H), 10.00 (s, 1H), 8.75 (s, br, 1H), 8.57 (d, 1H), 8.21 (d, 2H), 7.85 (d, 2H), 7.63 (s, 1H), 7.44 (d, 1H), 7.33 (dd, 1H), 7.03 (d, 1H), 4.55-4.50 (m, 1H), 3.82 (s, 3H), 3.80-3.60 (m, 4H), 3.35-3.05 (m, 7H), 2.50-2.45 (m, 2H), 2.02-1.95 (m, 3H), 1.30 (t, 3H). MS (EI): 502 (MH+).

[01545] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)-3-(methyloxy)phenyl]amino} pyrimidin-4-yl)-phenyl]acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.22 (s, 1H), 9.40 (s, 1H), 8.44 (s, 1H), 8.15 (d, 2H), 7.80-7.60 (m, 3H), 7.33 (d, 2H), 6.85 (d, 1H), 3.80 (s, 3H), 2.90 (s, br, 4H), 2.35 (q, 2H), 2.05 (s, 4H), 1.95 (s, 3H), 1.00 (s, 3H). MS (EI): 447 (MH+).

[01546] 1-(2,6-dichlorophenyl)-3-(3-{[4-(4-methyl-2-thienyl)pyrimidin-2-yl]amino}propyl)-urea: ^{1}H NMR (400 MHz, d_6-DMSO): 8.26 (d, 1H), 8.02 (br, 1H), 7.71 (s, 1H), 7.48 (d, 2H), 7.31 (s, 1H), 7.26 (t, 1H), 7.16 (t, 1H), 6.99 (d, 1H), 6.39 (t, 1H), 3.38 (t, 2H), 3.15 (t, 2H), 2.21 (s, 3H), 1.65 (m, 2H). MS (EI) for $C_{19}H_{19}Cl_2N_5OS$: 436 (MH^+)

[01547] 1-[2-fluoro-5-(trifluoromethyl)phenyl]-3-(3-{[4-(4-methyl-2-thienyl)pyrimidin-2-yl]amino}propyl)urea: ^{1}H NMR (400 MHz, d_6-DMSO): 8.65 (d, 2H), 8.23 (s, 1H), 7.7 (s, 1H), 7.4 (t, 1H), 7.38-7.15 (m, 3H), 7.0 (s, 1H), 6.8 (t, 1H), 3.38 (t, 2H), 3.2 (t, 2H), 2.21 (s, 3H), 1.75 (m, 2H). MS (EI) for $C_{20}H_{19}F_4N_5OS$: 454 (MH^+)

[01548] 2,6-dichloro-N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]-benzenesulfonamide: ^{1}H NMR (400 MHz, d_6-DMSO): 8.16 (d, 1H), 8.12 (t, 1H), 7.94 (d, 2H), 7.58 (d, 2H), 7.48 (t,1H), 6.97 (d, 1H), 6.92 (t, 6.76 (d, 2H)3.28 (m, 2H), 3.022.96 (m, 8H), 1.68 (m, 2H). MS (EI) for $C_{21}H_{23}Cl_2N_5O_2S$: 480 (MH^+)

[01549] N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2,6-difluoro-benzenesulfonamide: ^{1}H NMR (400 MHz, d_6-DMSO): 8.25 (T, 1H), 8.16 (d, 1H), 7.94 (d, 2H), 7.66 (m, 1H), 7.24 (t, 2H), 6.98 (d, 1H), 6.95 (t, 1H), 6.76 (d, 2H), 3.33(t, 2H), 3.0 (t, 2H), 2.98 (s, 6H), 1.68 (m, 2H). MS (EI) for $C_{21}H_{23}F_2N_5O_2S$: 448 (MH^+)

[01550] N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]naphthalene-2-sulfonamide: ^{1}H NMR (400 MHz, d_6-DMSO): 8.42 (br, 1H), 8.15-8.06 (m, 3H), 8.02 (d, 1H), 7.94 (d, 2H), 7.8 (dd, 1H), 7.74-7.62 (m, 3H), 6.96 (d, 1H), 6.92 (t, 1H), 6.74 (d, 2H), 3.3 (t, 2H), 2.98 (s, 6H), 2.83 (t, 2H), 1.63 (m, 2H). MS (EI) for $C_{25}H_{27}N_5O_2S$: 462 (MH^+)

[01551] N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]-3,4-bis(methyloxy)benzenesulfonamide: ^{1}H NMR (400 MHz, d_6-DMSO): 8.17 (d, 1H), 7.94 (d, 2H), 7.46 (t, 1H), 7.34 (dd, 1H), 7.27 (d, 1H), 7.06 (d, 1H), 6.97 (d, 1H), 6.93 (t, 1H), 6.76 (d, 2H), 3.8 (s, 6H), 3.3 (t, 2H), 2.98 (s, 6H), 2.8 (t, 2H), 1.65 (m, 2H). MS (EI) for $C_{23}H_{29}N_5O_4S$: 472 (MH^+)

[01552] 3-chloro-N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]propane-1-sulfonamide: ^{1}H NMR (400 MHz, d_6-DMSO): 8.2 (s, 1H), 7.98 (d, 2H), 7.2 (t, 1H), 7.0 (t, 2H), 6.8-6.7 (m, 2H), 3.7 (t, 2H), 3.1-2.9 (m, 10H), 2.05 (t, 2H), 1.7 (m, 2H), 1.2 (m, 2H). MS (EI) for $C_{18}H_{26}ClN5O_2S$: 412 (MH^+)

[01553] N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]propane-1-sulfonamide: ^{1}H NMR (400 MHz, d_6-DMSO): 8.2 (d, 1H), 7.96 (d, 2H), 7.0-6.95 (m, 3H), 6.76 (d, 2H), 3.38 (t, 2H), 3.0-2.9 (m, 10H), 1.75 (t, 2H), 1.6 (q, 2H), 0.95 (t, 3H). MS (EI) for $C_{18}H_{27}N_5O_2S$: 378 (MH^+).

[01554] methyl (3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}propyl)carbamate: ^{1}H MR (400 MHz, d_6-DMSO): 8.4 (d, 1H), 7.75 (s, 1H), 7.63-7.55 (m, 2H), 7.35 (t, 1H), 7.12 (t, 1H), 6.8 (d, 1H), 3.5 (s, 3H), 3.28 (t, 2H), 3.03 (t, 2H), 1.65 (m, 2H). MS (EI) for $C_{15}H_{16}Cl_2N_4O_2$: 355 (MH^+).

[01555] 1-methylethyl (3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}propyl)-arbamate: ^{1}H NMR (400 MHz, d_6-DMSO): 8.38 (d, 1H), 7.75 (s, 1H), 7.63-7.55 (m, 2H),7.35 (t, 1H), 7.0 (t, 1H), 6.8 (d, 1H), 4.72 (m, 1H), 3.28 (q, 2H), 3.0 (q, 2H), 1.65 (p, 2H), 1.12 (d, 6H). MS (EI) for $C_{17}H_{20}Cl_2N_4O_2$: 383 (MH^+).

[01556] phenylmethyl (3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}propyl)carbamate: ^{1}H NMR (400 MHz, d_6-DMSO): 8.46 (d, 1H), 8.2 (br, 1H), 7.8 (d, 1H), 7.66 (br, 1H), 7.6 (dd, 1H), 7.4-7.28 (m, 5H), 7.04 (br, 1H), 5.0 (s, 2H), 3.4 (t, 2H), 3.1 (t, 2H), 1.7 (m, 2H). MS (EI) for $C_{21}H_{20}Cl_2N_4O_2$: 431 (MH^+).

[01557] N-{4-[2-({[3-(3-chlorophenyl)isoxazol-5-yl]methyl}amino)pyrimidin-4-yl]-henyl}acetamide:^{1}H NMR (400 MHz, d_6-DMSO): 10.18 (s, 1H), 8.37 (d, 1H), 8.06 (d, 2H), 7.92 (t, 1H), 7.88-7.82 (m, 2H), 7.7 (d, 2H), 7.56-7.48 (m, 2H), 7.2 (d, 1H), 7.0 (s, 1H), 4.7 (s, 2H), 2.05 (s, 3H). MS (EI) for $C_{22}H_{18}ClN_5O_2$: 420 (MH^+).

[01558] ethyl 4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)piperidine-1-carboxylate: ^{1}H MR (400 MHz, d_6-DMSO): 10.18 (s, 1H), 8.3 (d, 1H), 8.04 (d, 2H), 7.7 (d, 2H), 7.13 (d, 1H), 7.06 (d, 1H), 4.05 (q, 3H), 3.95 (br, 2H), 2.96 (br, 2H), 2.08 (s, 3H), 1.9 (br, 2H), 1.4 (q, 2H), 1.2 (t, 3H). MS (EI) for $C_{20}H_{25}N_5O_3$: 384 (MH^+).

[01559] 1,1-dimethylethyl 4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)piperidine-1-carboxylate: ^{1}H NMR (400 MHz, d_6-DMSO): 10.18 (s, 1H), 8.3 (d, 1H), 8.05 (d, 2H), 7.7 (d, 2H), 7.2 (br, 1H), 7.1 (d, 1H), 3.92 (br, 3H), 2.9 (br, 2H), 2.08 (s, 3H), 1.87 (br, 2H), 1.46-1.36 (m, 11H). MS (EI) for $C_{22}H_{29}N_5O_3$: 412 (MH^+).

[01560] N-{4-[2-(3,5-diamino-1H-1,2,4-triazol-1-yl)pyrimidin-4-yl]phenyl}acetamide: ^{1}H MR (400 MHz, d_6-DMSO): 10.28 (s, 1H), 8.7 (d, 1H), 8.16 (d, 2H), 7.78 (d, 2H), 7.7 (d, 1H), 7.58 (s, 2H), 2.03(s, 3H). MS (EI) for $C_{14}H_{14}N_8O$: 311 (MH^+).

[01561] N-{4-[2-({5-[(4-ethylpiperazin-1-yl)carbonyl]pyridin-2-yl}amino)pyrimidin-4-yl]-henyl}acetamide:^{1}H NMR (400 MHz, d_6-DMSO): 10.26 (s, 1H), 10.12 (s, 1H), 8.6 (d, 1H), 8.46 (d, 1H), 8.36 (d, 1H), 8.18 (d, 2H), 7.9 (dd, 1H), 7.77 (d, 2H), 7.54 (d, 1H), 2.46-2.32 (m, 6H), 2.1 (s, 3H), 1.0 (t, 3H). MS (EI) for $C_{24}H_{27}N_7O_2$: 446 (MH^+).

[01562] N-(4-{2-[(4-cyanophenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H MR (400 MHz, d_6-DMSO): 10.24 (d, 2H), 8.6 (d, 1H), 8.17 (d, 2H), 8.06 (d, 2H), 7.78 (d, 4H), 7.5 (d, 1H), 2.05 9s, 3H). MS (EI) for $C_{19}H_{15}N_5O$: 330 (MH^+).

[01563] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyridin-4-yl}phenyl)acetamide: ^{1}H MR (400 MHz, d_6-DMSO): 10.14 (s, 1H), 8.82 (s, 1H), 8.12 (d, 1H), 7.72 9d, 2H), 7.62 (d, 2H), 7.53 (d, 2H), 6.97-6.92 (m, 2H), 6.9 (d, 2H), 3.74 (t, 4H), 3.02 (t, 4H), 2.07 (s, 3H). MS (EI) for $C_{23}H_{24}N_4O_2$: 389 (MH^+).

[01564] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-methylpyrimidin-4-yl)phenyl]-3-(methyloxy)propanamide: ^{1}H NMR (400 MHz, d_6-DMSO): 10.18 (s, 1H), 9.25 (s, 1H), 8.3 (s, 1H), 7.75 (d, 2H), 7.63 (d, 2H), 7.61 (d, 2H), 6.86 (d, 2H), 3.64 (t, 2H), 3.25 (s, 3H), 3.03 (t, 4H), 2.6 (t, 2H), 2.38 (br, 2H), 2.2 (s, 3H), 1.03 (t, 3H). MS (EI) for $C_{72}H_{34}N_6O_2$: 475 (MH^+).

[01565] tert-butyl 1-(4-(4-(4-acetamidophenyl)pyrimidin-2-ylamino)phenyl)piperidin-4-ylcarbamate: ^{1}H NMR (400 MHz, d_6-DMSO): 10.21 (s, 1H), 9.38 (s, br, 1H), 8.43 (s, 1H), 8.08 (m, 2H), 7.74 (m, 2H), 7.62 (m, 2H), 7.23 (m, 1H), 6.98 (m, 3H), 3.77 (m, 2H), 3.63 (m, 2H), 2.09 (s, 3H), 1.80 (m, 2H), 1.49 (m, 2H), 1.30 (s, 9H). MS (EI) for $C_{28}H_{34}N_6O_3$: 503 (MH^+).

[01566] 4-(4-aminophenyl)-N-(4-(4-aminopiperidin-1-yl)phenyl)pyrimidin-2-amine: ^{1}H MR (400 MHz, d_6-DMSO): 9.19 (s, 1H), 8.3 (m, 1H), 7.87 (m, 2H), 7.63 (m, 2H), 7.14 (m, 1H), 6.92 (m, 2H), 6.62 (m, 2H), 5.74 (m, 2H), 3.57 (m, 2H), 2.67 (m, 2H), 1.81 (m, 2H), 1.38 (m, 2H). MS (EI) for $C_{21}H_{24}N_6$: 361 (MH^+).

[01567] N-(1-(4-(4-(4-acetamidophenyl)pyrimidin-2-ylamino)phenyl)piperidin-4-yl)-acetamide: ^{1}H NMR (400 MHz, d_6-DMSO): 10.26 (s, 1H), 9.34 (s, 1H), 8.43 (d, 1H), 8.1 (d, 2H), 7.85 (d, 1H), 7.75 (d, 2H), 7.64 (d, 2H), 7.27 (d, 1H), 6.94 (d, 2H), 3.67 (m, 1H), 3.55 (m, 2H), 2.72 (t, 2H), 2.09 (s, 3H), 1.88-1.76 (m, 5H), 1.48 (m, 2H). MS (EI) for $C_{25}H_{28}N_6O_2$: 445 (MH^+).

[01568] N-(4-(2-(4-(4-(cyclopropanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)-phenyl)cyclopropanecarboxamide: ^{1}H NMR (400 MHz, d_6-DMSO): 10.51 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.87 (d, 2H), 7.69 (d, 2H), 7.28 (d, 1H), 6.97 (d, 2H), 3.82 (m, 2H), 3.61 (m, 2H), 3.25-2.99 (m, 4H), 2.04 (m, 1H), 1.83 (m, 1H), 0.89-0.68 (m, 8H).. MS (EI) for $C_{28}H_{30}N_6O_2$: 483 (MH^+).

[01569] N-(4-(2-(4-(4-isobutyrylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, d_6-DMSO): 9.94 (s, 1H), 9.42 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.87 (d, 2H), 7.68 (d, 2H), 7.31 (d, 1H), 6.96 (d, 2H), 4.42 (m, 1H), 3.99 (m, 1H), 3.85 (m, 1H), 3.62 (m, 4H), 3.08 (m, 2H), 3.02 (m, 2H), 2.92 (m, 1H) 2.21 (m, 1H), 2.01 (m, 1H), 2.73 (m, 2H), 1.03 (d, 6H). MS (EI) for $C_{29}H_{34}N_6O_3$: 515 (MH^+).

[01570] N-(4-(2-(4-(4-(cyclobutanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, d_6-DMSO): 9.94 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.13 (d, 2H), 7.87 (d, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 6.95 (d, 2H), 4.43 (m, 1H), 3.99 (m, 1H), 3.84 (m, 1H), 3.59 (m, 2H), 3.43 (m, 2H), 3.01 (m, 4H), 2.28-1.69 (m, 10H). MS (EI) for $C_{30}H_{34}N_6O_3$: 527 (MH^+).

[01571] N-(4-(2-(4-(4-pivaloylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, d_6-DMSO): 9.95 (s, 1H), 9.42 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.88 (d, 2H), 7.69 (d, 2H), 7.30 (d, 1H), 6.95 (d, 2H), 4.43 (m, 1H), 4.0 (m, 1H), 3.84 (m, 1H), 3.7 (m, 4H), 3.04 (m, 4H), 2.22 (m, 1H), 2.02 (m, 1H), 1.86 (m, 2H), 1.23 (s, 9H). MS (EI) for $C_{30}H_{36}N_6O_3$: 529 (MH^+).

[01572] N-cyclopropyl-4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.51 (s, br, 1H), 8.58 (s, br, 1H), 8.52 (d, 1H), 8.21 (d, 2H), 7.96 (d, 2H), 7.67 (d, 2H), 7.39 (d, 1H), 6.93 (d, 2H), 3.76 (m, 4H), 3.05 (m, 4H), 2.89 (m, 1H), 0.71 (m, 2H), 0.60 (m, 2H). MS (EI): 416 (MH+).

[01573] N-(2-methoxyethyl)-4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.51 (s, br, 1H), 8.68 (s, br, 1H), 8.52 (d, 1H), 8.23 (d, 2H), 8.00 (d, 2H), 7.67 (d, 2H), 7.40 (d, 1H), 6.94 (d, 2H), 3.75 (m, 4H), 3.47 (m, 4H), 3.28 (s, 3H), 3.05 (m, 4H). MS (EI): 434 (MH+).

[01574] 2,6-dichloro-n-{3-[(4-pyridin-3-ylpyrimidin-2-yl)amino]propyl}-benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 9.25 (br s, 1H), 8.68-8.66 (m, 2H), 8.37 (m, 2H), 7.49-7.47 (m, 3H), 7.42-7.38 (m, 1H), 7.32 (m, 1H), 7.21-7.20 (m, 1H), 3.44 (m, 2H), 3.29 (m, 2H), 1.82 (m, 2H). MS (EI): 402.0 (MH+).

[01575] 2,6-dichloro-n-(3-{[4-(4-methyl-3,4-dihydro-2h-1,4-benzoxazin-7-yl)pyrimidin-2-yl]amino}propyl)benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.69 (t, 1H), 8.18 (d, 1H), 7.58 (dd, 1H), 7.51-7.40 (m, 4H), 7.02-6.97 (m, 2H), 6.73 (d, 1H), 4.25-4.23 (m, 2H), 3.41 (m, 2H), 3.32-3.29 (m, 4H), 2.91 (s, 3H), 1.81 (t, 2H). MS (EI): 472.3 (MH+).

[01576] 2,6-dichloro-n-(3-{[4-(2,3-dihydro-1,4-benzodioxin-6-yl)-6-methyl-pyrimidin-2-yl]amino}propyl)benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.68 (t, 1H), 7.62-7.59 (m, 2H), 7.51-7.49 (m, 2H), 7.44-7.40 (m, 1H), 7.02 (t, 1H), 6.97-6.92 (m, 2H), 4.30-4.28 (m, 4H), 3.44-3.43 (m, 2H), 3.32-3.29 (m, 2H), 2.27 (s, 3H), 1.80 (t, 2H); MS (EI): 473.3 (MH+).

[01577] N-(4-{2-[(3-{[(2,6-dichlorophenyl)carbonyl]amino}propyl)-amino]pyrimidin-4-yl}phenyl)morpholine-4-carboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 8.69 (m, 2H), 8.33 (d, 1H), 8.18 (m, 1H), 7.60 (m, 2H), 7.51-7.49 (m, 2H), 7.44-7.34 (m, 2H), 7.20 (m, 1H), 7.01 (d, 1H), 3.62-3.61 (m, 4H), 3.43 (m, 6H), 3.32 (m, 2H), 1.83 (m, 2H). MS (EI): 529.1 (MH+).

[01578] 2,6-dichloro-n-{3-[(4-{4-[(cyclopropylcarbonyl)amino]-phenyl}pyrimidin-2-yl)amino]propyl}benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.4 (s, 1H), 8.72 (t, 1H),

8.36-8.33 (m, 2H), 7.73 (m, 2H), 7.51-7.39 (m, 4H), 7.24 (m, 1H), 7.03 (d, 1H), 3.45 (m, 2H), 3.33 (m, 4H), 1.84-1.78 (m, 2H), 0.81-0.78 (m, 3H). MS (EI): 484.0 (MH+).

[01579] N-(4-{2-[(3-{[(2,6-dichlorophenyl)carbonyl]amino}propyl)-amino]pyrimidin-4-yl}phenyl)thiophene-2-carboxamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.4 (s, 1H), 8.72 (t, 1H), 8.44 (t, 1H), 8.37 (d, 1H), 8.05 (s, 1H), 7.90-7.81 (m, 3H), 7.50-7.39 (m, 4H), 7.25-7.23 (m, 2H), 7.07 (d, 1H), 3.47 (m, 2H), 3.34 (m, 2H), 1.85 (m, 2H). MS (EI): 526.0 (MH+).

[01580] 2,6-dichloro-n-(3-{[4-(4-{[n-(2-morpholin-4-ylethyl)glycyl]-amino}phenyl)pyrimidin-2-yl]amino}propyl)benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.0 (br s, 1H), 8.72 (t, 1H), 8.35-8.32 (m, 2H), 7.82-7.75 (m, 2H), 7.51-7.40 (m, 4H), 7.22 (s, 1H), 7.05 (d, 1H), 3.56 (m, 4H), 3.45 (m, 2H), 3.30 (m, 3H), 2.64 (m, 2H), 2.41-2.35 (m, 8H), 1.84 (br s, 2H). MS (EI): 586.1 (MH+).

[01581] 1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-ethanone: ^{1}H-NMR (400MHz, d6-DMSO): 8.50 (d, 1H), 8.26-8.24 (m, 2H), 8.12-8.10 (m, 2H), 7.30 (s, 1H), 7.64-7.62 (m, 2H), 7.31 (d, 1H), 7.00-6.98 (m, 2H), 3.82-3.80 (m, 4H), 3.12-3.10 (m, 4H), 2.64 (s, 3H). MS (EI): 375.1 (MH+).

[01582] (1e)-1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)ethanone oxime: ^{1}H-NMR (400MHz, d6-DMSO): 11.4 (s, 1H), 9.82 (br s, 1H), 8.55 (d, 1H), 8.20 (d, 2H), 7.85-7.82 (m, 4H), 7.45 (d, 1H), 7.36 (br s, 1H), 4.69 (br, 1H), 3.91 (m, 4H), 3.34 (m, 4H), 2.21 (s, 3H). MS (EI): 388.1 (MH-).

[01583] N-{4-[2-({4-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}-amino)pyrimidin-4-yl]phenyl}-2-phenylacetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.4 (s, 1H), 9.43 (br s, 1H), 8.42 (d, 1H), 8.10 (d, 2H), 7.75 (d, 2H), 7.67 (d, 2H), 7.33-7.20 (m, 2H), 7.07 (s, 2H), 6.97-6.95 (m, 4H), 3.82 (m, 4H), 3.67 (s, 2H), 3.03 (m, 4H), 2.07 (m, 1H), 0.75-0.69 (m. 4H). MS (EI): 533.2 (MH+).

[01584] N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-bromobenzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.14 ppm (s, 1H), 8.42 ppm (t, 1H), 8.29 ppm (d, 1H), 8.06 ppm (d, 1H), 7.70 ppm (d,2H), 7.65 ppm (m, 1H), 7.39 ppm (m, 3H), 7.12 ppm (t, 1H), 7.07 ppm (d, 1H), 3.33 ppm (br. m, 2H), 3.31 ppm (m, 2H), 2.07 ppm (s, 3H), 1.81 ppm (m, 2H); MS (EI) $C_{22}H_{22}BrN_5O_2$: 468 (MH^+).

[01585] N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-fluorobenzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.17 ppm (s, 1H), 8.37 ppm (t, 1H), 8.30 ppm (d, 1H), 8.06 ppm (d, 2H), 7.70 ppm (d,2H), 7.61 ppm (m, 1H), 7.50 ppm (m, 1H), 7.26 ppm (m, 2H), 7.16 ppm (t, 1H), 7.08 ppm (d, 1H), 3.41 ppm (br. m, 2H), 3.33 ppm (m, 2H), 2.08 ppm (s, 3H), 1.81 ppm (br. m, 2H); MS (EI) $C_{22}H_{22}FN_5O_2$: 408 (MH^+).

[01586] N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-chlorobenzamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.14 ppm (s, 1H), 8.45 ppm (t, 1H), 8.28 ppm (d, 1H), 8.04 ppm (d, 2H), 7.68 ppm (d,2H), 7.68 ppm (d, 2H), 7.47 ppm (m, 1H), 7.41 ppm (m, 2H), 7.35 ppm (m, 1H), 7.13 ppm (t, 1H). 7.06 ppm (d, 1H), 3.42 ppm (br. m, 2H), 3.29 ppm (m, 2H), 2.05 ppm (s, 3H), 1.78 ppm (br m, 2H); MS (EI) $C_{22}H_{22}BrN_5O_2$: 468 (MH^+).

[01587] N-[4-(2-{[3-(morpholin-4-ylsulfonyl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.23 ppm (s, 1H), 10.12 ppm (s, 1H), 8.74 ppm (s, 1H), 8.58 ppm (d, 1H), 8.21 ppm (d,2H), 7.93 ppm (m, 1H), 7.76 ppm (d, 2H), 7.60 ppm (t, 1H), 7.47 ppm (d, 1H), 7.30 ppm (m, 1H), 3.64 ppm (m, 4H), 2.90 ppm (m, 4H), 2.10 ppm (s, 3H); MS (EI) $C_{22}H_{23}N_5O_4S$: 454 (MH^+).

[01588] N-{4-[2-({3-[(cyclohexylmethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl}-acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.43 ppm (s, 1H), 9.32 ppm (s, 1H), 8.46 ppm (d, 1H), 8.13 ppm (d, 2H), 7.77 ppm (d,2H), 7.30 ppm (d, 2H), 7.17 ppm (s, 1H), 6.94 ppm (m, 2H), 6.22 ppm (m, 1H), 5.56 ppm (t, 1H), 2.87 ppm (t, 2H), 2.09 ppm (s, 3H), 1.85 ppm (br d, 2H), 1.69 ppm (br m, 2H),1.64 ppm (br m, 1H), 1.19 ppm (m, 3H), 0.94 ppm (m, 2H); MS (EI) $C_{25}H_{29}N_5O$: 416 (MH^+).

[01589] N-(4-{2-[(3-{[(5-bromo-2-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.21 ppm (s, 1H), 9.37 ppm (s, 1H), 8.45 ppm (d, 1H), 8.12 ppm (d, 2H), 7.74 ppm (d, 2H), 7.55 ppm (m, 1H), 7.47 ppm (m, 1H), 7.31 ppm (d, 1H), 7.20 ppm (m, 1H), 7.05 ppm (m, 1H), 7.00 ppm (t, 1H), 6.28 ppm (t, 1H), 6.22 ppm (m, 1H), 4.32 ppm (d, 2H), 2.09 ppm (s, 3H); MS (EI) $C_{25}H_{21}BrFN_5O$: 507 (MH^+).

[01590] N-(4-{2-[(3-{[(2,5-dimethylphenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.20 ppm (s, 1H), 9.33 ppm (s, 1H), 8.45 ppm (d, 1H), 8.13 ppm (d, 2H), 7.73 ppm (d, 2H), 7.30 ppm (d, 1H), 7.16 ppm (m, 2H), 7.06 ppm (d, 1H), 6.97 ppm (m, 3H), 6.23 ppm (m, 1H), 5.99 ppm (t, 1H), 4.17 ppm (d, 2H), 2.28 ppm (s, 3H), 2.21 ppm (s, 3H), 2.08 ppm (s, 3H); MS (EI) $C_{27}H_{27}N_5O$: 438 (MH^+).

[01591] N-(4-{2-[(3,4-dimorpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.22 ppm (s, 1H), 9.43 ppm (s, 1H), 8.46 ppm (d, 1H), 8.14 ppm (d, 2H), 7.74 ppm (d, 2H), 7.65 ppm (s, 1H), 7.34 ppm (m, 2H), 7.29 ppm (d, 2H), 6.88 ppm (d, 1H), 3.75 ppm (m, 8H), 3.15 ppm (br s, 4H), 3.05 ppm (br s, 4H), 2.09 ppm (s, 3H); MS (EI) $C_{26}H_{30}N_6O_3$: 475 (MH^+).

[01592] N-{4-[2-({4-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}cyclopropanecarboxamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.47 ppm (s, 1H), 9.41 ppm (s, 1H), 8.67 ppm (m, 2H), 8.44 ppm (d, 1H), 8.11 ppm (d, 2H), 7.89 ppm (m, 1H), 7.76 ppm (d, 2H), 7.69 ppm (d, 2H), 7.51 ppm (m, 1H), 7.28 ppm (d, 1H), 6.97 ppm (d, 2H), 3.80 ppm (s, 2H), 3.49 ppm (s, 2H), 3.13 ppm (br d, 4H), 1.83 ppm (m, 1H), 0.84 ppm (m, 4H); MS (EI) $C_{30}H_{29}N_7O_2$: 520 (MH^+).

[01593] N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}butanamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.16 ppm (s, 1H), 9.41 ppm (s, 1H), 8.44 ppm (d, 1H), 8.11 ppm (d, 2H), 7.77 ppm (d, 2H), 7.68 ppm (d, 2H), 7.28 ppm (d, 1H), 6.96 ppm (d, 2H), 3.63 ppm (m, 4H), 3.05 ppm (m, 4H), 2.92 ppm (m, 1H), 2.33 ppm (t, 1H), 1.63 ppm (m, 2), 1.02 ppm (d, 6H), 0.93 ppm (t, 3H); MS (EI) $C_{28}H_{34}N_6O_2$: 487 (MH^+).

[01594] N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}butanamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.15 ppm (s, 1H), 9.41 ppm (s, 1H), 8.44 ppm (d, 1H), 8.11 ppm (d, 2H), 7.77 ppm (d, 2H), 7.68 ppm (d, 2H), 7.28 ppm (d, 1H), 6.95 ppm (d, 2H), 3.70 ppm (m, 4H), 3.05 ppm (m, 4H), 2.33 ppm (t, 2H), 1.63 ppm (m, 2H), 1.23 ppm (s, 9H), 0.93 ppm (t, 3H); MS (EI) $C_{29}H_{36}N_6O_2$: 501 (MH^+).

[01595] N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}butanamide: ^{1}H-NMR (400MHz, d_6-DMSO): 10.28 ppm (s, 1H), 9.41 ppm (s, 1H), 8.44 ppm (d, 1H), 8.11 ppm (d, 2H), 7.79 ppm (d, 2H), 7.68 ppm (d, 2H), 7.28 ppm (d, 1H), 6.95 ppm (d, 2H), 3.59 ppm (m, 2H), 3.46 ppm (m, 2H), 3.40 ppm (m, 1H), 3.02 ppm (m, 4H), 2.35 ppm (t, 2H), 2.14 ppm (m, 4H), 1.91 ppm (m, 1H), 1.75 ppm (m, 1H), 1.63 ppm (m 2H), 0.93 ppm (t, 3H); MS (EI) $C_{29}H_{34}N_6O_2$: 499 (MH^+).

[01596] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-2-carboxamide: 1H-NMR (400MHz, d6-DMSO): 10.91 (s, 1H), 9.41 (s, 1H), 8.78 (d, 1H), 8.47 (d, 2H), 8.17 (m, 4H), 7.69 (m, 2H), 7.33 (d, 1H), 6.95 (d, 2H), 6.80 (s, 2H), 3.75 (m, 4H), 3.06 (m, 4H). MS (EI) for $C_{26}H_{24}N_6O_2$: 453.5(MH+).

[01597] 2-hydroxy-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-benzamide: 1H-NMR (400MHz, d6-DMSO): 10.39 (s, 1H), 9.51 (s, 1H), 8.47 (s, 1H), 8.16 (d, 2H), 7.91 (d, 2H), 7.17 (m, 3H), 7.53 (t, 1H), 7.34 (s, 2H) 7.20 (d, 1H), 7.07 (m, 3H), 3.91 (m, 4H), 3.12 (m, 4H). MS (EI) for $C_{27}H_{25}N_5O_3$: 468.5(MH+).

[01598] 3-(methyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-benzamide: 1H-NMR (400MHz, d6-DMSO): 10.49 (s, 2H), 8.19 (m, 3H), 7.97

(m, 3H), 7.55 (m, 2H), 7.50 (m, 3H), 7.20 (dd, 3H), 3.86 (m, 8H), 3.77 (s, 3H). MS (EI) for $C_{28}H_{27}N_5O_3$: 482.6(MH+).

[01599] 4-(methyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-benzamide: 1H-NMR (400MHz, d6-DMSO): 10.35 (s, 1H), 9.40 (s, 1H), 8.45 (s, 1H), 8.16 (d, 2H), 7.98 (m, 4H), 7.68 (d, 2H), 7.31 (d, 1H), 7.09 (d, 2H), 6.94(d, 2H), 3.83 (s, 3H), 3.75 (m, 4H), 3.05 (m, 4H). MS (EI) for $C_{28}H_{27}N_5O_3$: 482.6(MH+).

[01600] 4-chloro-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-benzamide: 1H-NMR (400MHz, d6-DMSO):10.58 (s, 1H), 9.41 (s, 1H), 8.46 (s, 1H), 8.17 (d, 2H), 8.01 (d, 2H), 7.95 (d, 2H), 7.66 (m, 4H), 7.32 (d, 1H), 6.94 (d, 2H), 3.75 (m, 4H), 3.05 (m, 4H). MS (EI) for $C_{27}H_{24}ClN_5O_2$: 487.0(MH+).

[01601] (2R)-N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-tetrahydrofuran-2-carboxamide: 1H-NMR (400MHz, d6-DMSO):9.95 (s, 1H), 9.38 (s, 1H), 8.45 (s, 1H), 8.12 (d, 2H), 7.89 (d, 2H), 7.66 (d, 2H), 7.29 (s, 1H), 6.92 (d, 2H), 4.44 (t, 2H), 4.00 (m, 2H), 3.85 (m, 2H), 2.41 (m, 4H), 2.20 (m, 2H), 2.02 (m, 2H), 1.88 (m, 2H), 1.05 (m, 4H). MS (EI) for $C_{27}H_{32}N_6O_2$: 473.6(MH+).

[01602] (2S)-N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-tetrahydrofuran-2-carboxamide: 1H-NMR (400MHz, d6-DMSO):9.94 (s, 1H, 9.38 (s, 1H), 8.44 (s, 1H), 8.12 (d, 2H), 7.87 (d, 2H), 7.65 (d, 2H), 7.29 (s, 1H), 6.99 (d, 2H), 4.43 (m, 2H), 3.99 (m, 2H), 3.86 (m, 2H), 2.43 (m, 2H), 2.22 (m, 2H), 2.02 (m, 2H), 1.88 (m, 3H), 1.05 (m, 5H) . MS (EI) for $C_{27}H_{32}N_6O_2$: 473.6(MH+).

[01603] 1-(2-hydroxyethyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}-phenyl)-L-prolinamide: 1H-NMR (400MHz, d6-DMSO): 10.31 (s, 1H), 9.39 (s, 1H), 8.44 (d, 1H), 8.14 (d, 2H), 7.81 (d, 2H), 7.67 (d, 2H), 7.29 (d, 1H), 6.95 (d, 2H), 5.05 (s, br, 1H), 3.74 (m, 4H), 3.59 (m, 1H), 3.49 (m, 1H), 3.23 (m, 2H), 3.05 (m, 4H), 2.77 (m, 1H), 2.63 (m, 1H), 2.41 (m, 1H), 2.16 (m, 1H), 1.80 (m, 3H). MS (EI) for $C_{27}H_{32}N_6O_3$: 489.6(MH+).

[01604] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)thiophene-2-carboxamide: 1H-NMR (400MHz, d6-DMSO): 10.47 (s, 1H), 9.45 (s, 1H), 8.47 (s, 1H), 8.17 (d, 2H), 8.08 (s, 1H), 7.92 (m, 3H), 7.70 (s, 2H), 7.32 (s, 1H), 7.26 (t, 1H), 6.99 (s, 2H), 3.76 (m, 4H), 3.09 (m, 4H). MS (EI) for $C_{25}H_{23}N_5O_2S$: 458.6(MH+).

[01605] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-tetrahydrofuran-3-carboxamide: 1H-NMR (400MHz, d6-DMSO): 10.31 (s, 1H), 9.37 (s, 1H), 8.44 (s, 1H), 8.14 (m, 2H), 7.79 (d, 2H), 7.65 (d, 2H), 7.27 (d, 1H), 6.92 (d, 2H), 3.96 (t, 1H), 3.76 (m, 3H), 3.19 (m, 1H), 3.09 (m, 4H), 2.55 (m, 4H), 2.42 (m, 2H), 2.10 (m, 2H), 1.05 (t, 3H). MS (EI) for $C_{27}H_{32}N_6O_2$: 473.6(MH+).

[01606] N-(4-{2-[4-(4-nicotynoylpiperazin-1-yl)phenylamino]pyrimidin-4-yl}phenyl)-2-phenylacetamide: ^{1}H NMR (400MHz, d6-DMSO): 8.8 (d, 2H), 8.40 (s, 1H), 8.05 (d, 2H), 7.80 (d,1H),7.60-7.2 (m, 10H), 7.1-6.90 (m, 5H), 3.80-3.60 (m, 4H), 3.7 (s, 2H)3.20-3.25 (m, 4H); MS (EI) for $C_{34}H_{31}N_7O_2$: 570 (MH^+).

[01607] 3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(diphenylmethyl)benzamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.22 (s, 1H), 9.78 (s, 1H), 9.24 (d, 1H), 8.52 (d, 1H), 8.39 (s br, 1H), 8.16 (d, 2H), 7.95 (d, 1H), 7.75 (d, 2H), 7.53 (d t, 1H), 7.39-7.43 (m, 3H), 7.38 (d, 3H), 7.32-7.36 (m, 4H), 7.24-7.28 (m, 2H), 6.43 (d, 1H), 2.10 (s, 3H). MS (EI) for $C_{32}H_{27}N_5O_2$: 514.3 (MH+).

[01608] N-[4-(2-{[4-(4-methylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.24 (s, 1H), 9.35 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.65 (d, 2H), 7.26 (d, 1H), 6.93 (d, 2H), 3.07 (m, 4H), 2.45 (m, 4H), 2.22 (s, 3H), 2.09 (s, 3H). MS (EI) for $C_{23}H_{26}N_6O$: 403.4(MH+).

[01609] N-{4-[2-({4-[4-(phenylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR (400MHz,d6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.45 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.73-7.79 (m, 5H), 7.28 (d, 1H), 6.98 (d, 2H), 3.78 (m, 2H), 3.48 (m, 2H), 3.15 (m, 2H), 3.07 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{28}N_6O_2$: 493.4 (MH+).

[01610] N-{4-[2-({4-[4-(2-cyclopentylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR (400MHz,d6-DMSO): 10.22 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.68 (d, 2H), 7.27 (s, 1H), 6.96 (d, 2H), 3.60 (m, 4H), 3.04 (m, 4H), 2.37 (d, 2H), 2.15 (m, 1H), 2.09 (s, 3H), 1.61-1.78 (m, 2H), 1.53-1.59 (m, 2H), 1.46-1.52 (m, 2H), 1.09-1.77 (m, 2H). MS (EI) for $C_{29}H_{34}N_6O_2$: 499.3 (MH+).

[01611] N-{4-[2-({4-[4-(cyclohexylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.22 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.68 (d, 2H), 7.27 (d, 1H), 6.96 (d, 2H), 3.61 (m, 4H), 3.04 (m, 4H), 2.09 (s, 3H), 1.62-1.70 (m, 6H), 1.26-1.38 (m, 5H). MS (EI)for $C_{29}H_{34}N_6O$: 499.2 (MH+).

[01612] N-(4-{2-[(4-{4-[(2-chlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz,d6-DMSO): 10.21 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.10 (d, 2H), 7.74 (d, 2H), 7.69 (d. 2H), 7.56 (d, 1H), 7.41-7.49 (m, 3H), 7.27 (d, 1H), 6.96 (d, 2H), 3.81 (m, 2H), 3.28 (m, 2H), 3.16 (m, 2H), 3.05 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{27}ClN_6O_2$: 527.8 (MH+).

[01613] N-(4-{2-[(4-{4-[(3-fluorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.21 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.53 (m, 1H), 7.27-7.35 (m, 4H), 6.97 (d, 2H), 3.77 (m, 2H), 3.46 (m, 2H), 3.16 (m, 2H), 3.07 (m, 2H), 2.09 (s, 3H).MS(EI) for $C_{29}H_{27}FN_6O_2$: 511.5 (MH+).

[01614] N-(4-{2-[(4-{4-[(3-fluoro-4-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.21 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.38 (m, 1H), 7.28 (d, 1H), 7.25 (d, 1H), 7.18 (d, 1H), 6.56 (d, 2H), 3.75 (m, 2H), 3.49 (m, 2H), 3.14 (m, 2H), 3.07 (m, 2H), 2.28 (d, 3H), 2.09 (s, 3H). MS(EI) for $C_{30}H_{29}FN_6O_2$: 525.7 (MH+).

[01615] N-(4-{2-[(4-{4-[(3,4-dichlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.45 (s, 1H), 8.11 (d, 2H), 7.75 (m, 3H), 7.69 (d, 2H), 7.45 (dd, 1H), 7.28 (d, 1H), 6.97 (d, 2H), 3.77 (m, 2H), 3.47 (m, 2H), 3.16 (m, 2H), 3.07 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{26}Cl_2N_6O_2$: 562.3(MH+).

[01616] N-(4-{2-[(4-{4-[(3,5-dichlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.21 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.75 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.54 (d, 2H), 7.28 (d, 1H), 6.97 (d, 2H), 3.77 (m, 2H), 3.45 (m, 2H), 3.17 (m, 2H), 3.08 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{26}Cl_2N_6O_2$: 562.6(MH+).

[01617] N-[4-(2-{[4-(4-{[3-(methyloxy)phenyl]carbonyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.21 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.38 (t, 1H), 7.28 (d, 1H), 7.04 (dd, 1H), 6.95-6.99 (m, 4H), 3.79 (s, 3H), 3.77 (m, 2H), 3.47 (m, 2H), 3.15 (m, 2H), 3.06 (m, 2H), 2.09 (s, 3H). MS(EI) for $C_{30}H_{30}N_6O_3$: 523.5(MH+).

[01618] N-(4-{2-[(4-{4-[(4-chlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.53 (d, 2H), 7.49 (d, 2H), 7.27 (d, 1H), 6.97 (d, 2H), 3.77 (m, 2H), 3.47 (m, 2H), 3.15 (m, 2H), 3.06 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{27}ClN_6O_2$: 527.8(MH+).

[01619] N-(4-{2-[(4-{4-[(4-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.44)d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.34 (d,

2H), 7.27 (m, 3H), 6.97 (d, 2H), 3.75 (m, 2H), 3.51 (m, 2H), 3.10 (m, 4H), 2.36 (s, 3H), 2.09 (s, 3H). MS (EI) for $C_{30}H_{30}N_6O_2$: 507.3 (MH+).

[01620] N-(4-{2-[(4-{4-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.21 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.27 (d, 1H), 6.98 (d, 2H), 6.92 (t, 1H), 6.37 (dd, 1H), 6.05 (dd, 1H), 3.76 (m, 4H), 3.69 (s, 3H), 3.11 (m, 4H), 2.09 (s, 3H), MS (EI) for $C_{28}H_{29}N_7O_2$: 496.4(MH+).

[01621] N-{4-[2-({4-[4-(furan-2-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO):10.22 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.87 (d, 1H), 7.74 (d, 2H), 7.69 (d, 2H), 7.28 (d, 1H), 7.04 (d, 1H), 6.98 (d, 2H), 6.66 (dd, 1H), 3.82 (m, 4H), 3.14 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{27}H_{26}N_6O_3$: 483.3 (MH+).

[01622] N-[4-(2-{[4-(4-{2-[(4-fluorophenyl)oxy]acetyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.22 (s, 1H), 9.41 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.27 (d, 1H), 7.12 (m, 2H), 6.94-6.99 (m, 4H), 4.87 (s, 2H), 3.61 (m, 4H), 3.13 (m, 2H), 3.06 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{30}H_{29}FN_6O_3$:541.4(MH+).

[01623] N-(4-{2-[(4-{4-[(3-methylphenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: MS (EI) for $C_{29}H_{30}N_6O_3S$: 543.5 (MH+).

[01624] N-{4-[2-({4-[4-(phenylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.21 (s, 1H), 9.39 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.80 (m, 1H), 7.78 (d, 1H), 7.74-7.77 (m, 2H), 7.70-7.73 (m, 2H), 7.67-7.69 (m, 1H), 7.65 (d, 2H), 7.27 (d, 1H), 6.90 (d, 2H), 3.15 (m, 4H), 3.02 (m, 4H), 2.09 (s,3H). MS (EI) for $C_{26}H_{26}N_6O_3S_2$: 529.4(MH+).

[01625] N-{4-[2-({4-[4-(2-thienylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO):10.21 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.10 (m, 3H), 7.74 (d, 2H), 7.70 (dd, 1H), 7.66 (d, 2H), 7.33 (dd, 1H), 7.27 (d, 1H), 6.93 (d, 2H), 3.19 (m, 4H), 3.07 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{26}H_{26}N_6O_3S_2$: 535.6(MH+).

[01626] N-(4-{2-[(4-{4-[(4-fluorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR(400MHz,d6-DMSO):10.21 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.10 (d, 2H), 7.87 (m, 2H), 7.74 (d, 2H), 7.66 (d, 2H), 7.53 (m, 2H), 7.27 (d, 1H), 6.91 (d, 2H), 3.15 (m, 4H), 3.04 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{28}H_{27}FN_6O_3S$: 547.4 (MH+).

[01627] N-[4-(2-{[4-(4-{[4-(methyloxy)phenyl]sulfonyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR(400MHz,d6-DMSO): MS (EI) for $C_{29}H_{30}N_6O_4S$: 559.9 (MH+).

[01628] N-(4-{2-[(4-{4-[(4-chlorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR(400MHz,d6-DMSO):10.21 (s, 1H), 9.40 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.72-7.82 (d, 6H), 7.66 (d, 2H), 7.27 (d, 1H), 6.91 (d, 2H), 3.15 (m, 4H), 3.05 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{28}H_{27}ClN_6O_3S$: 563.9 (MH+).

[01629] N-(4-{2-[(4-{4-[(3-chlorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR(400MHz,d6-DMSO):10.21 (s, 1H), 9.40 (s, 1H), 8.43 (d, 1H), 8.10 (d, 2H), 7.85 (m, 1H), 7.76-7.81 (m, 2H), 7.73 (d, 3H), 7.66 (d, 2H), 7.27 (d, 1H), 6.91 (d, 2H), 3.14 (m, 4H), 3.09 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{28}H_{27}ClN_6O_3S$: 5640 (MH+).

[01630] N-{4-[2-({4-[4-(biphenyl-4-ylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO):10.21(s, 1H), 9.39 (s, 1H), 8.43 (d, 1H), 8.08 (d, 2H), 7.96 (d, 2H), 7.86 (d, 2H), 7.77 (d, 2H), 7.73 (d, 2H), 7.66 (d, 2H), 7.51-7.55 (m, 2H), 7.46 (m, 1H), 7.26 (d, 1H), 6.91 (d, 2H), 3.18 (m, 4H), 3.08 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{34}H_{32}N_6O_3S$: 605.8 (MH+).

[01631] N-{4-[2-({4-[4-(naphthalen-1-ylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.21 (s, 1H), 9.38 (s, 1H), 8.72 (d, 1H), 8.42 (d, 1H), 8.33 (d, 1H), 8.20 (dd, 1H), 8.14 (d, 1H), 8.09 (d, 2H), 7.74-7.79 (m, 1H), 7.73 (d, 2H), 7.62-7.70 (m, 2H), 7.64 (d, 2H), 7.26 (d, 1H), 6.88 (d, 2H), 3.21 (m, 4H), 3.09 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{32}H_{30}N_6O_3S$: 579.6 (MH+).

[01632] N-(4-{2-[(3-{4-[(2-chlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.21 (s, 1H), 9.46 (s, 1H), 8.49 (d, 1H), 8.14 (d, 2H), 7.74 (d, 2H), 7.64 (s br, 1H), 7.36 (dd, 1H), 7.33 (d, 1H), 7.20-7.27 (m, 2H), 7.13 (t, 1H), 6.92-7.00 (m, 2H), 6.55 (d, 1H), 3.54 (s, 2H), 3.16 (m, 4H), 2.57 (m, 4H), 2.09 (s,3H). MS (EI) for $C_{29}H_{29}ClN_6O$: 513.8 (MH+).

[01633] N-[4-(2-{[3-(4-{[3-(methyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR(400MHz,d6-DMSO):10.21 (s, 1H), 9.46 (s, 1H), 8.48 (d, 1H), 8.13 (d, 2H), 7.74 (d, 2H), 7.62 (s, 1H), 7.33 (d, 1H), 7.22-7.27 (m, 2H), 7.13 (t, 1H), 6.19 (m, 2H), 6.83 (d, 1H), 6.55 (d, 1H), 3.74 (s, 3H), 3.52 (s, 2H), 3.16 (m, 4H), 2.55 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{30}H_{32}N_6O_2$: 509.8(MH+).

[01634] N-{4-[2-({3-[4-(3-methylbutyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.22 (s, 1H), 9.47 (s, 1H), 8.49 (d, 1H), 8.14 (d, 2H), 7.75 (d, 2H), 7.68 (s, 1H), 7.33 (d, 1H), 7.19 (d, 1H), 7.13 (t, 1H), 6.55 (d, 1H), 3.15 (m, 4H), 2.54 (m, 4H), 2.34 (t, 2H), 2.09 (s, 3H), 1.57-1.62 (m, 1H), 1.34-1.40 (m, 2H), 0.90 (d, 6H). MS (EI) for $C_{27}H_{34}N_6O$: 459.7 (MH+).

[01635] N-{4-[2-({3-[4-(2,3-dihydro-1,4-benzodioxin-6-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO): MS (EI) for $C_{31}H_{32}N_6O_3$: 537.5 (MH+).

[01636] N-{4-[2-({3-[4-(cyclopropylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.22 (s, 1H), 9.47 (s, 1H), 8.49 (d, 1H), 8.14 (d, 2H), 7.75 (d, 2H), 7.69 (s, 1H), 7.33 (d, 1H), 7.19 (d, 1H), 7.13 (t, 1H), 6.56 (d, 1H), 3.17 (m, 4H), 2.60 (m, 4H), 2.24 (d, 2H), 2.09 (s, 3H), 0.88 (m, 1H), 0.47-0.51 (m, 2H), 0.11-0.13 (m, 2H). MS (EI) for $C_{26}H_{30}N_6O$: 443.8 (MH+).

[01637] N-(4-{2-[(3-{4-[3-(methylthio)propyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR(400MHz,d6-DMSO):10.22 (s, 1H), 9.47 (s, 1H), 8.49 (d, 1H), 8.14 (d, 2H), 7.75 (d, 2H), 7.68 (s, 1H), 7.33 (d, 1H), 7.20 (d, 1H), 7.14 (t, 1H), 6.56 (d, 1H), 3.15 (m, 4H), 2.56 (m, 4H), 2.41 (t, 4H), 2.09 (s, 3H), 2.06 (s, 3H), 1.71-1.78 (m, 2H). MS (EI) for $C_{26}H_{32}N_6OS$: 477.5(MH+).

[01638] N-(4-{2-[(3-{4-[(4-{[3-(dimethylamino)propyl]oxy}phenyl)methyl]piperazin-1-yl}-phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR(400MHz,d6-DMSO):10.22 (s, 1H), 9.46 (s, 1H), 8.48 (d, 1H), 8.13 (d, 2H), 7.74 (d, 2H), 7.62 (s, 1H), 7.33 (d, 1H), 7.23 (m 3H), 7.13 (t, 1H), 6.88 (d, 2H), 6.55 (d, 1H), 3.97 (t, 2H), 3.46 (s, 2H), 3.14 (m, 4H), 2.55 (m, 4H), 2.34 (t, 2H), 2.14 (s, 6H), 2.10 (s, 3H), 1.80-1.85 (m, 2H). MS (EI) for $C_{34}H_{41}N_7O_2$: 580.5(MH+).

[01639] N-{4-[2-({3-[4-({3-[(trifluoromethyl)oxy]phenyl}methyl)piperazin-1-yl]phenyl}-amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO):10.21 (s, 1H), 9.47 (s, 1H), 8.49 (d, 1H), 8.13 (d, 2H), 7.74 (d, 2H), 7.63 (s, 1H), 7.47 (t, 1H), 7.41 (d, 1H), 7.33 (d, 2H), 7.22-7.28 (m, 2H), 7.13 (t, 1H), 6.56 (dd, 1H), 3.62 (s, 2H), 3.16 (m ,4H), 2.56 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{30}H_{29}F_3N_6O_2$: 563.7(MH+).

[01640] 4-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-N-phenylpiperazine-1-carboxamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.63 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.75 (d, 2H), 7.70 (d, 2H), 7.48 (d, 2H), 7.21-7.28 (m, 3H), 7.00 (d, 2H), 6.94 (t, 1H), 3.61 (m, 4H), 3.11 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{29}N_7O_2$: 508.6 (MH+).

[01641] N-[4-(2-{[3-(4-propanoylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.24 (s, 1H), 9.51 (s, 1H), 8.50 (d, 1H), 8.14 (d, 2H), 7.76 (d, 2H), 7.68 (s, 1H), 7.34 (d, 1H), 7.26 (d, 1H), 7.16 (t, 1H), 6.59 (dd, 1H), 3.62 (m, 4H), 3.13 (m, 4H), 2.35-2.39 (m, 2H), 2.09 (s, 3H), 1.02 (t, 3H). MS (EI) for $C_{25}H_{28}N_6O_2$: 445.4 (MH+).

[01642] N-{4-[2-({3-[4-(phenylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.21 (s, 1H), 9.48 (s, 1H), 8.47 (d, 1H), 8.11 (d, 2H), 7.72 (d, 2H), 7.63 (s, 1H), 7.41-7.47 (m, 5H), 7.31 (d, 1H), 7.26 (d, 1H), 7.14 (t, 1H), 6.56 (dd, 1H), 3.78 (m, 2H), 3.48 (m, 2H), 3.27 (m, 2H), 3.12 (m, 2H), 2.08 (s, 3H). MS (EI) for $C_{29}H_{28}N_6O_2$: 493.7 (MH+).

[01643] N-{4-[2-({3-[4-(2-phenylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.25 (s, 1H), 9.50 (s, 1H), 8.49 (d, 1H), 8.13 (d, 2H), 7.76 (d, 2H), 7.63 (s, 1H), 7.33 (d, 1H), 7.30 (d, 2H), 7.26 (m, 3H), 7.22 (m, 1H), 7.15 (t, 1H), 6.56 (dd, 1H), 3.79 (s, 2H), 3.66 (m, 4H), 3.11 (m, 2H), 3.05 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{30}H_{30}N_6O_2$: 507.7 (MH+).

[01644] N-{4-[2-({3-[4-(cyclopentylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.24 (s, 1H), 9.52 (s, 1H), 8.49 (d, 1H), 8.14 (d, 2H), 7.76 (d, 2H), 7.71 (s, 1H), 7.34 (d, 1H), 7.24 (d, 1H), 7.16 (t, 1H), 6.59 (dd, 1H), 3.66 (m, 4H), 3.13 (m, 4H), 3.00-3.07 (m, 1H), 2.09 (s, 3H), 1.80 (m, 2H), 1.51-1.71 (m, 6H). MS (EI) for $C_{28}H_{32}N_6O_2$: 485.7 (MH+).

[01645] N-{4-[2-({3-[4-(2-pyridin-3-ylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.24 (s, 1H), 9.51 (s, 1H), 8.50 (d, 1H), 8.43-8.46 (m, 2H), 8.14 (d, 2H), 7.76 (d, 2H), 7.63-7.67 (m, 2H), 7.32-7.35 (m, 2H), 7.26 (d, 1H), 7.16 (t, 1H), 6.59 (dd, 1H), 3.84 (s, 2H), 3.73 (m, 2H), 3.66 (m, 2H), 3.15 (m, 4H), 2.08 (s, 3H). MS (EI) for $C_{29}H_{29}N_7O_2$: 508.4 (MH+).

[01646] N-{4-[2-({3-[4-(2-cyclopentylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO):10.24 (s, 1H), 9.51 (s, 1H), 8.50 (d, 1H), 8.14 (d, 2H), 7.76 (d, 2H), 7.70 (s, 1H), 7.34 (d, 1H), 7.25 (d, 1H), 7.16 (t, 1H), 6.59 (dd, 1H), 3.61 (m, 4H), 3.12 (m, 4H), 2.39 (d, 2H), 2.11-2.19 (m, 1H), 2.09 (s, 3H), 1.72-7.78 (m, 2H), 1.52-1.59 (m, 2H), 1.47-1.52 (m, 2H), 1.09-1.18 (m, 2H). MS (EI) for $C_{29}H_{34}N_6O_2$: 499.4 (MH+).

[01647] N-(4-{2-[(3-{4-[(2-chlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.24 (s, 1H), 9.50 (s, 1H), 8.49 (d, 1H), 8.13 (d, 2H), 7.74 (d, 2H), 7.63 (s, 1H), 7.56 (d, 1H), 7.42-

7.50 (m, 3H), 7.33 (d, 1H), 7.29 (d, 1H), 7.16 (t, 1H), 6.59 (dd, 1H), 3.79 (m, 2H), 3.50 (m, 2H), 3.24 (m, 2H), 3.15 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{27}ClN_6O_2$: 527.9 (MH+).

[01648] N-(4-{2-[(3-{4-[(4-chlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.23 (s, 1H), 9.51 (s, 1H), 8.49 (d, 1H), 8.14 (d, 2H), 7.74 (d, 2H), 7.66 (s, 1H), 7.53 (d, 2H), 7.49 (d, 2H), 7.34 (d, 1H), 7.27 (d, 1H), 7.17 (t, 1H), 6.59 (dd, 1H), 3.79 (m, 2H), 3.50 (m, 2H), 3.24 (m, 2H), 3.15 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{27}ClN_6O_2$: 528.1 (MH+).

[01649] N-(4-{2-[(3-{4-[(3,4-dichlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.23 (s, 1H), 9.51 (s, 1H), 8.49 (d, 1H), 8.13 (d, 2H), 7.74 (m, 4H), 7.60 (s, 1H), 7.46 (dd, 1H), 7.34 (d, 1H), 7.27 (d, 1H), 7.17 (t, 1H), 6.59 (dd, 1H), 3.79 (m, 2H), 3.50 (m, 2H), 3.24 (m, 2H), 3.15 (m, 2H), 2.09 (s, 3H). MS (EI) for $C_{29}H_{26}Cl_2N_6O_2$: 562.7 (MH+).

[01650] N-(4-{2-[(3-{4-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.23 (s, 1H), 9.51 (s, 1H), 8.50 (d, 1H), 8.14 (d, 2H), 7.75 (d, 2H), 7.67 (s, 1H), 7.34 (d, 1H), 7.28 (d, 1H), 7.17 (t, 1H), 6.92 (m, 1H), 6.59 (dd, 1H), 6.37 (dd, 1H), 6.05 (m, 1H), 3.80 (m, 4H), 3.69 (s, 3H), 3.19 (m, 4H), 2.09 (s, 3H). MS (EI) for $C_{28}H_{29}N_7O_2$: 450.7 (MH+).

[01651] N^2,N^2-dimethyl-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]glycinamide: ^{1}H-NMR(400MHz,d6-DMSO):10.0 (s, 1H), 9.48 (s, 1H), 8.48 (d, 1H), 8.15 (d, 2H), 7.84 (d, 2H), 7.65 (s, 1H), 7.29-7.33 (m, 2H), 6.86 (d, 1H), 3.81 (s, 3H), 3.72 (m, 4H), 3.11 (s, 2H), 2.92 (m, 4H), 2.29 (s, 6H). MS (EI) for$C_{25}H_{30}N_6O_3$: 463.8 (MH+).

[01652] 3-(methyloxy)-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]propanamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.21 (s, 1H), 9.46 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.74 (d, 2H), 7.64 (s, 1H), 7.26-7.30 (m, 2H), 6.84 (d, 1H), 3.79 (s, 3H), 3.70 (m, 4H), 3.61 (t, 2H), 3.23 (s, 3H), 2.89 (m, 4H), 2.57 (t, 2H). MS (EI) for $C_{25}H_{29}N_5O_4$: 464.8 (MH+).

[01653] N-(4-{2-[(4-{4-[(2-chlorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.19 (s, 1H), 9.38 (s, 1H), 8.42 (d, 1H), 8.08 (d, 2H), 8.00 (dd, 1H), 7.68-7.74 (m, 4H), 7.65 (d, 2H), 7.58 (m, 1H), 7.25 (d, 1H), 6.91 (d, 2H), 3.15 (m, 4H), 3.02 (m, 4H), 2.07 (s, 3H). MS (EI) for $C_{28}H_{27}ClN_6O_3S$: 563.9 (MH+).

[01654] N-{4-[2-({3-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.24 (s, 1H), 9.52 (s, 1H), 8.50 (d,

1H), 8.14 (d, 2H), 7.76 (d, 2H), 7.71 (s, 1H), 7.34 (d, 1H), 7.25 (d, 1H), 7.17 (t, 1H), 6.60 (dd, 1H), 3.56 (m, 2H), 3.65 (m, 2H), 3.20 (m, 2H), 3.13 (m, 2H), 2.09 (s, 3H), 2.04 (m, 1H), 0.77-0.49 (m, 4H). MS (EI) for $C_{26}H_{28}N_6O_2$: 457.5(MH+).

[01655] N-{4-[2-({3-[4-(2-cyclopropylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.24 (s, 1H), 9.51 (s, 1H), 8.50 (d, 1H), 8.14 (d, 2H), 7.76 (d, 2H), 7.70 (s, 1H), 7.34 (d, 1H), 7.25 (d, 1H), 7.16 (t, 1H), 6.58 (dd, 1H), 3.62 (m, 4H), 3.13 (m, 4H), 2.32 (d, 2H), 2.09 (s, 3H), 0.99 (m, 1H), 0.45 (m, 2H), 0.14 (m, 2H). MS (EI) for $C_{27}H_{30}N_6O_2$: 477.5(MH+).

[01656] N-[4-(2-{[3-(4-{[3-(methyloxy)phenyl]carbonyl}piperazin-1-yl)phenyl]amino}-pyrimidin-4-yl)phenyl]acetamide: ^{1}H-NMR(400MHz,d6-DMSO): 10.22 (s, 1H), 9.48 (s, 1H), 8.47 (d, 1H), 9.11 (d, 2H), 7.72 (d, 2H), 7.62 (s, 1H), 7.35 (t, 1H), 7.31 (d, 1H), 7.26 (d, 1H), 7.14 (t, 1H), 7.01 (m, 1H), 6.97 (m, 2H), 6.56 (dd, 1H), 3.76 (s, 3H), 3.73 (m, 2H), 3.47 (m, 2H), 3.14 (m, 4H), 2.07 (s, 3H). MS (EI) for $C_{30}H_{30}N_6O_3$: 523.7 (MH+).

[01657] N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H-NMR (400MHz, d6-DMSO): 10.21 (s, 1H), 9.40 (s, 1H), 8.44 (d, 1H), 8.11 (d, 2H), 7.74 (d, 2H), 7.69 (d, 2H), 7.27 (d, 1H), 6.96 (d, 2H), 3.70 (m, 4H), 3.05 (m, 4H), 2.09 (s, 3H), 1.23 (s, 9H), MS(EI) for $C_{27}H_{32}N_6O_2$: 473.4(MH+).

[01658] 2,6-dichloro-N-(3-(4-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)pyrimidin-2-ylamino)propyl)benzamide: (400 MHz, CDCl3): 8.16 (br, 1H), 8.0 – 8.8 (m, 2H), 7.26 (m, 4H), 6.82 (d, 1H), 6.75 (br, 1H), 5.4 (t, 1H), 4.29 (m, 4H), 3.68 (m, 2H), 3.56 (m, 2H), 1.92 (m, 2H). MS (EI): 459 (MH+).

[01659] 1-(4-(4-(4-acetamidophenyl)pyrimidin-2-ylamino)phenyl)piperidine-3-carboxylic acid: MS (EI) for $C_{24}H_{25}N_5O_3$: 432 (MH+).

[01660] tert-butyl methyl(2-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenylamino)-2-oxoethyl)carbamate: MS (EI) for $C_{28}H_{34}N_6O_4$: 519 (MH+).

[01661] tert-butyl 4-(2-(4-(4-ethylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenylcarbamate: MS (EI) for $C_{27}H_{34}N_6O_2$: 475 (MH+).

[01662] 2-(dimethylamino)-N-(4-(2-(4-(4-ethylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide: NMR (400 MHz, d6-DMSO): 10.0 (s, 1H), 9.37 (s, 1H), 8.41 (d, 1H), 8.11 (d, 1H), 7.85 (d, 2H), 7.63 (f, 2H), 7.46 (d, 1H), 7.25 (d, 1H), 6.83 – 6.92 (m, 2H), 3.11 (m, 4H), 2.51 (m, 4H), 2.37 (q, 2H), 2.36 (s, 6H), 2.26 (s, 2H), 1.05 (t, 3H). MS (EI): 460 (MH+).

[01663] 4-(4-aminophenyl)-N-(4-(4-ethylpiperazin-1-yl)phenyl)pyrimidin-2-amine: MS (EI) for $C_{22}H_{26}N_6$: 375 (MH+).

[01664] (S)-tert-butyl 1-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenylamino)-1-oxo-3-phenylpropan-2-ylcarbamate: MS (EI) for $C_{34}H_{38}N_6O_4$: 595 (MH+).

[01665] (R)-tert-butyl 1-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenylamino)-1-oxo-3-phenylpropan-2-ylcarbamate: MS (EI) for $C_{34}H_{38}N_6O_4$: 595 (MH+).

[01666] (R)-2-amino-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-3-phenylpropanamide: NMR (400 MHz, d6-DMSO): 11.40 (s, 1H), 10.20 (s, 1H), 8.43 – 8.62 (m, 3H), 8.17 (d, 2H), 7.91 (d, 2H), 7.89 (d, 2H), 7.84 (m, 2H), 7.20 – 7.38 (m, 4H), 4.10 (m, 4H), 3.63 (m, 2H), 3.40 – 3.57 (m, 6H), 3.20 (m, 1H), MS (EI): 495 (MH+).

[01667] (S)-2-amino-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-3-phenylpropanamide: NMR (400 MHz, d6-DMSO): 11.40 (s, 1H), 10.20 (s, 1H), 8.43 – 8.62 (m, 3H), 8.17 (d, 2H), 7.91 (d, 2H), 7.89 (d, 2H), 7.84 (m, 2H), 7.20 – 7.38 (m, 4H), 4.10 (m, 4H), 3.63 (m, 2H), 3.40 – 3.57 (m, 6H), 3.20 (m, 1H), MS (EI): 495 (MH+).

[01668] (S)-2-amino-N-(4-(2-(4-(4-ethylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-methylbutanamide: MS (EI) for $C_{27}H_{35}N_7O$: 474 (MH+).

[01669] (R)-2-amino-N-(4-(2-(4-(4-ethylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-methylbutanamide: MS (EI) for $C_{27}H_{35}N_7O$: 474 (MH+).

[01670] 1-ethyl-3-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)urea: NMR (400 MHz, d6-DMSO): 9.41 (s, 1H), 8.75 (s, 1H), 8.42 (d, 1H), 8.10 (d, 2H), 7.64 (s, 1H), 7.54 (d, 2H), 7.26 (m, 2H), 6.85 (d, 1H), 6.21 (br, 1H), 3.79 (s, 3H), 3.70 (m, 4H), 3.11 (q, 2H), 2.89 (m, 4H), 1.06 (t, 3H). MS (EI): 449 (MH+).

[01671] (R)-N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)piperidine-2-carboxamide: NMR (400 MHz, d6-DMSO): 11.36 (s, 1H), 10.0 (s, 1H), 9.4 (d, 1H), 8.84 (m, 1H), 8.57 (d, 1H), 8.2 (d, 2H), 7.82 (m, 4H), 7.6 (br, 1H), 7.4 (d, 1H), 4.0 (m, 4H), 3.82 (m, 1H), 3.42 (m, 4H), 3.23 (m, 1H), 2.94 (m, 1H), 2.3 (m, 1H), 1.82 (m, 1H), 1.54 – 1.92 (m, 4H). MS (EI): 458 (MH+).

[01672] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-methylpyrimidin-4-yl)phenyl]-acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.1 (s,1H), 9.23 (s, 1H), 8.31 (s, 1H), 7.6-7.7 (m, 6H), 6.87 (d, 2H), 3.04 (m, 4H), 2.48 (m, 4H), 3.05 (m, 4H), 2.36 (q, 2H), 2.2 (s, 3H), 2.08 (s, 3H), 1.03 (s, 3H). MS (EI): 431(MH+).

[01673] 4-{4-[(4-{4-[(N,N-dimethylglycyl)amino]phenyl}pyrimidin-2-yl)amino]phenyl}-N-ethylpiperazine-1-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.0 (s,1H), 9.4 (s, 1H), 8.43 (d, 1H), 8.12 (d, 2H), 7.82 (d, 2H), 7.68 (d, 2H), 7.27 (d, 1H), 6.97 (d, 2H), 3.42 (m, 4H), 3.12 (s, 2H), 3.06 (q, 2H), 3.02 (m, 4H), 2.3 (s, 6H), 1.11 (t, 3H). MS (EI): 503 (MH+).

[01674] N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-N^2, N^2-dimethylglycinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.0 (s,1H), 9.4 (s, 1H), 8.44 (d, 1H), 8.11(d, 2H), 7.83 (d, 2H), 7.69 (d, 2H), 7.29 (d, 1H), 6.96 (d, 2H), 3.7 (m, 4H), 3.16 (s, 2H), 3.05 (m, 4H), 2.31 (s, 6H), 1.2 (s, 9H). MS (EI): 516(MH+).

[01675] N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-N^2,N^2-dimethylglycinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.0 (s,1H), 9.4 (s, 1H), 8.45 (d, 1H), 8.12(d, 2H), 7.84 (d, 2H), 7.67 (d, 2H), 7.30 (d, 1H), 6.95 (d, 2H), 3.56-3.62 (m, 4H), 3.1 (s, 2H), 2.99-3.05 (m, 4H), 2.31 (s, 6H), 1.8-2.25 (m, 7H). MS (EI): 514(MH+).

[01676] N^2,N^2-dimethyl-N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)-pyrimidin-4-yl]phenyl}glycinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.0 (s,1H), 9.4 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.84 (d, 2H), 7.68 (d, 2H), 7.29 (d, 1H), 6.95 (d, 2H), 3.58-3.67 (m, 4H), 3.11 (s, 2H), 2.99-3.10 (m, 4H), 2.92 (m, 1H), 2.29 (s, 6H), 1.02 (d, 6H). MS (EI): 502(MH+).

[01677] N-{4-[2-({4-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-N^2,N^2-dimethylglycinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.0 (s,1H), 9.4 (s, 1H), 8.43 (d, 1H), 8.14 (d, 2H), 7.68 (d, 2H), 7.26 (d, 1H), 6.97 (d, 2H), 3.8 (m, 2H), 3.6 (m, 2H),3.18 (m, 4H),3.07 (m, 2H), 2.28 (s, 6H), 2.02 (m, 1H), 0.78 (m, 4H). MS (EI): 501(MH+).

[01678] N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-N^2,N^2-dimethylglycinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.0 (s,1H), 9.4 (s, 1H), 8.55 (d, 1H), 8.23 (d, 2H), 7.84 (d, 2H), 7.71 (d, 2H), 7.28 (d, 1H), 6.97 (d, 2H), 3.8 (m, 2H), 3.84 (q, 1H), 3.62 (m, 4H), 3.12 (s, 2H),3.05 (m, 4H), 2.31 (s, 6H), 1.12 (d, 3H). MS (EI): 504(MH+).

[01679] N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-N^2,N^2-dimethylglycinamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.0 (s,1H), 9.4 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.84 (d, 2H), 7.69 (d, 2H), 7.28 (d, 1H), 6.97 (d, 2H), 3.8 (m, 2H), 3.84

(q, 1H), 3.62 (m, 4H), 3.12 (s, 2H),3.05 (m, 4H), 2.31 (s, 6H), 1.12 (d, 3H). MS (EI): 504(MH+).

[01680] 2,6-dichloro-N-(3-{[4-(4-fluorophenyl)pyrimidin-2-yl]amino}propyl)benzamide: ^{1}H NMR (400 MHz, DMSO): 8.705 (t, 1H), 8.354(d, 1H), 7.136 (br s, 2H), 7.515 (d, 2H), 7.5 (d, 2H), 7.425 (m, 1H), 7.34 (t, 2H), 7.26 (t, 1H), 7.14 (d, 1H), 3.456 (br s, 2H), 3.355 (m, 2H), 1.827 (t, 2H). MS (EI): 420.1 (MH^+).

[01681] N-(4-{2-[({1-[(2,6-dichlorophenyl)carbonyl]azetidin-3-yl}methyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, DMSO): 11.031 (s, 1H), 8.344 (d, 1H), 8.137 (d, 2H), 7.839 (d, 2H), 7.621 (d, 2H), 7.531 (m, 1H), 7.45 (t, 1H), 7.146 (d, 1H), 4.157 (m, 1H), 3.867 (t, 2H), 3.626-3.556 (m, 3H), 2.842 (br s, 1H), 1.725 (s, 3H). MS (EI) for $C_{23}H_{21}Cl_2N_5O_2$: 470.2 (MH^+).

[01682] N-(4-{2-[(3-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, DMSO): 10.22 (s, 1H), 9.511 (s, 1H), 8.504 (d, 1H), 8.154 (d, 2H), 7.76 (d, 3H), 7.343 (d, 1H), 7.215-7.153 (m, 2H), 6.584 (d, 1H), 3.775 (t, 4H), 3.14 (t, 4H), 2.094 (s, 3H). MS (EI) for $C_{22}H_{23}N_5O_2$: 390.1 (MH^+).

[01683] N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)cyclohexyl]-2,6-dichloro-benzamide: ^{1}H NMR (400 MHz, MeOD): 8.25 (d, 1H), 8.08 (d, 2H), 7.7 (d, 2H), 7.45-7.35 (m, 3H), 7.05 (d, 1H), 4.05 (m, 2H), 2.5 (m, 1H), 2.1 (m, 3H), 2.05 (s, 3H), 1.5 (m, 1H), 1.3 (m, 3H). MS (EI) for $C_{25}H_{25}Cl_2N_5O_2$: 498.3 (MH^+).

[01684] N-{4-[2-({[4-(4-methylpiperazin-1-yl)phenyl]methyl}amino)pyrimidin-4-yl]phenyl}-acetamide: ^{1}H NMR (400 MHz, DMSO): 10.192 (s, 1H), 8.294 (d, 1H), 8.062 (d, 2H), 7.713 (d, 2H), 7.653 (t, 1H), 7.285 (br d, 2H), 7.09 (d, 1H), 6.953 (d, 2H), 4.485 (d, 2H), 3.3 (br s, 8H), 2.827 (s, 3H), 2.079 (s, 3H). MS (EI) for $C_{24}H_{28}N_6O$: 417.4 (MH^+).

[01685] N-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dichloro-benzamide ^{1}H NMR (400 MHz, DMSO): 10.66 (s, 1H), 10.324 (s, 1H), 9.638 (s, 1H), 8.501 (d, 1H), 8.144 (d, 2H), 7.782 (m, 4H), 7.65 (d, 2H), 7.597 (d, 2H), 7.498 (m, 1H), 7.349 (d, 1H), 2.11 (s, 3H). MS (EI) for $C_{25}H_{19}Cl_2N_5O_2$: 492 (MH^+).

[01686] N-{4-[2-(piperidin-4-ylamino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, DMSO): 10.184 (s, 1H), 8.288 (d, 1H), 8.044 (d, 2H), 7.71 (d, 2H), 7.049 (t, 2H), 3.8 (br s, 1H), 2.962 (d, 2H), 2.077 (s, 3H), 1.838 (br d, 2H), 1.372-1.334 (m, 2H). MS (EI) for $C_{17}H_{21}N_5O$: 312.3 (MH^+).

[01687] N-{4-[2-({1-[(2,6-dichlorophenyl)carbonyl]piperidin-4-yl}amino)pyrimidin-4-yl]-phenyl}acetamide: ^{1}H NMR (400 MHz, DMSO): 10.171 (s, 1H), 8.312 (d, 1H), 8.067 (d, 2H), 7.71 9d, 2H), 7.584-7.546 (m, 2H), 7.461 (t, 1H), 7.246 (d, 1H), 7.093 (d, 1H), 4.468

(m, 1H), 4.1 (br s, 1H), 3.25-3.05 (m, 2H), 2.077 (s, 3H), 2.05 (m, 1H), 1.915 (br s, 1H0, 1.58-1.532 (m, 2H). MS (EI) for $C_{24}H_{23}Cl_2N_5O_2$: 485.3 (MH^+).

[01688] N-{4-[2-({4-[(2-hydroxyethyl)oxy]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, DMSO): 10.211 (s, 1H), 9.43 (s, 1H), 8.455 (d, 1H), 8.12 (d, 2H), 7.754-7.69 (m, 4H), 7.292 (d, 1H), 6.93 (m, 2H), 4.865 (t, 1H), 3.97 (t, 2H), 3.715 (q, 2H), 2.09 (s, 3H). MS (EI) for $C_{20}H_{20}N_4O_3$: 365.1 (MH^+).

[01689] 1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-phenylurea: ^{1}H NMR (400 MHz, DMSO): 9.371 (s, 1H), 8.986 (s, 1H), 8.795 9s, 1H), 8.436 (d, 1H), 8.121 (d, 2H), 7.697 (d, 2H), 7.633 (d, 2H), 7.49 (d, 2H), 7.321-7.265 (m, 3H), 7.014-6.928 (t d, 3H), 3.758 (t, 4H), 3.063 (t, 4H). MS (EI) for $C_{27}H_{26}N_6O_2$: 467.3 (MH^+).

[01690] N-[5-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-2-(4-ethylpiperazin-1-yl)phenyl]-2,6-dichlorobenzamide: ^{1}H NMR (400 MHz, DMSO): 10.224 (s, 1H), 9.623 (d, 2H), 8.6 (br s, 1H), 8.48 (d, 1H), 8.237 (d, 2H), 7.735 (d, 2H). 7.598 (d, 2H), 7.521 (m, 2H), 7.35 (d, 1H), 7.181 (d, 1H), 3.36 (br s, 4H), 2.877 (t, 4H), 2.344 (q, 2H), 2.071 (s, 3H), 1.005 (t, 3H). MS (EI) for $C_{31}H_{31}Cl_2N_7O_2$: 604.3 (MH^+).

[01691] 1-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-3-(phenylmethyl)urea: ^{1}H NMR (400 MHz, MeOD): 8.082 (t, 3H), 7.53 (d, 2H), 7.422 (m, 3H), 7.236 (m, 4H), 7.159 (m, 1H), 7.037 (d, 2H), 4.32 (s, 2H), 3.971 (d, 2H), 3.608 (d, 2H), 3.195 (t, 2H), 3.126 (d, 2H), 3.045 (t, 2H), 1.3 (t, 3H). MS (EI) for $C_{30}H_{33}N_7O$: 508.4 (MH^+).

[01692] N^2,N^2-dimethyl-N-{4-[2-({4-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}glycinamide: ^{1}H NMR (400 MHz, DMSO): 9.994 (s, 1H), 9.418 (s, 1H), 8.667 (m, 2H), 8.454 (d, 1H), 8.127 (d, 2H), 7.907-7.827 (m d, 3H), 7.7 (d, 2H), 7.513 (m, 1H), 7.298 (d, 1H), 6.98 (d, 2H), 3.799 (br s, 2H), 3.489 (br s, 2H), 3.179 (br s, 2H), 3.113 (br s, 4H), 2.289 (s, 6H). MS (EI) for $C_{30}H_{32}N_8O_2$: 537.4 (MH^+).

[01693] N-(3-fluoro-4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-cyclopropanecarboxamide: ^{1}H NMR (400 MHz, DMSO): 10.671 (s, 1H), 9.452 (s, 1H), 8.47 (d, 1H), 8.045 (t, 1H), 7.758 (d, 1H), 7.656 (d, 2H), 7.46 (d, 1H), 7.12 (q, 1H), 6.932 (d, 2H), 3.749 (t, 4H), 3.052 (t, 4H), 1.813 (m, 1H), 0.847 (d, 4H). MS (EI) for $C_{24}H_{24}FN_5O_2$: 434.3(MH^+).

[01694] N-(4-{2-[(4-{4-[(1-methyl-1H-imidazol-2-yl)methyl]piperazin-1-yl}phenyl)amino]-pyrimidin-4-yl}phenyl)cyclopropanecarboxamide: ^{1}H NMR (400 MHz, DMSO): 7.851 (d, 1H), 7.67 (d, 2H), 7.452 (br d, 2H), 7.285 (d, 2H), 7.091 (d, 1H),

7.763 (d, 1H), 6.688 (d, 2H), 6.291 (br s, 1H), 3.668 (s, 3H), 3.561 (s, 2H), 2.946 (br s, 4H), 2.5 (br s, 4H), 1.413 (m, 1H), 0.541 (m, 2H), 0.3 (m, 2H). MS (EI) for $C_{29}H_{32}N_8O$: 509.4(MH^+).

[01695] N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H NMR (400 MHz, DMSO): 10.212 (s, 1H), 9.407 (s, 1H), 8.449 (d, 1H), 8.121 (d, 2H), 7.732 (d, 2H), 7.698 (d, 2H), 7.282 (d, 1H), 6.978 (d, 2H), 3.804 (q, 1H), 3.621 (m, 4H), 3.037 (br m, 4H), 2.091 (s, 3H), 1.864 (br s, 2H), 1.10 (d, 3H). MS (EI) for $C_{25}H_{29}N_7O_2$: 460.4(MH^+).

[01696] N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H NMR (400 MHz, DMSO): 10.234 (s, 1H), 9.409 (s, 1H), 8.449 (d, 1H), 8.121 (d, 2H), 7.757 (d, 2H), 7.699 (d, 2H), 7.282 (d, 1H), 6.979 (d, 2H), 3.849 (m, 1H), 3.619 (m, 4H), 2.992 (m, 6H), 2.625 (m, 1H), 2.092 (s, 3H), 1.986 (m, 1H), 1.685-1.536 (m, 3H). MS (EI) for $C_{27}H_{31}N_7O_2$: 486.2(MH^+).

[01697] N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl-acetamide: ^{1}H NMR (400 MHz, DMSO): 10.22 (s, 1H), 9.406 (s, 1H), 8.449 (d, 1H), 8.12 (d, 2H), 7.755 (d, 2H), 7.697 (d, 2H), 7.282 (d, 1H), 6.978 (d, 2H), 3.791 (q, 1H), 3.621 (br s, 4H), 3.081 (br d, 4H), 2.091 (s, 3H), 1.709 (br s, 2H), 1.096 (d, 3H). MS (EI) for $C_{25}H_{29}N_7O_2$: 460.4(MH^+).

[01698] N-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-acetamide: ^{1}H NMR (400 MHz, DMSO): 10.211 (s, 1H), 9.407 (s, 1H), 8.449 (d, 1H), 8.121 (d, 2H), 7.754 (d, 2H), 7.698 (d, 2H), 7.282 (d, 1H), 6.979 (d, 2H), 3.872 (t, 1H), 3.621 (m, 4H), 3.082-2.979 (m, 6H), 2.656 (m, 1H), 2.091 (s, 3H), 2.013 (m, 2H), 1.676-1.522 (m, 3H). MS (EI) for $C_{27}H_{31}N_7O_2$: 486.4(MH^+).

[01699] N-{4-[2-({4-[4-(2-piperazin-1-ylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide: ^{1}H NMR (400 MHz, DMSO): 10.219 (s, 1H), 9.401 (s, 1H), 8.448 (d, 1H), 8.121 (d, 2H), 7.754 (d, 2H), 7.694 (d, 2H), 7.281 (d, 1H), 6.977 (d, 2H), 3.707 (t, 2H), 3.59 (t, 2H), 3.319 (s, 2H), 3.1 (t, 2H), 3.018 (t, 2H), 2.702 (s, 4H), 2.336 (br s, 4H), 2.090 (s, 3H). MS (EI) for $C_{28}H_{34}N_8O_2$: 515.2(MH^+).

[01700] N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, DMSO): 9.938 (s, 1H), 9.417 (s, 1H), 8.457 (d, 1H), 8.135 (d, 2H), 7.885 (d, 2H), 7.693 (d, 2H), 7.305 (d, 1H), 6.976 (d, 2H), 4.436 (q, 1H), 3.991 (q, 1H), 3.878-3.761 (q q, 4H), 3.622 (br s, 4H), 3.083 (br d, 4H), 2.222 (m, 1H), 2.019 (m, 1H), 1.913 (m, 2H), 1.843 (br s, 2H). MS (EI) for $C_{28}H_{33}N_7O_3$: 516.3(MH^+).

[01701] N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, DMSO): 9.945 (s, 1H), 9.419 (s, 1H), 8.458 (d, 1H), 8.135 (d, 2H), 7.887 (d, 2H), 7.696 (d, 2H), 7.306 (d, 1H), 6.978 (d, 2H), 4.452 (q, 1H), 4.011 (q, 1H), 3.861 (q, 2H), 3.633 (m, 4H), 3.084-2.968 (m, 6H), 2.62 (m, 1H), 2.191 (m, 1H), 2.002 (m, 2H), 1.897 (m, 2H), 1.691-1.544 (m, 3H). MS (EI) for $C_{30}H_{35}N_7O_3$: 542.3(MH^+).

[01702] N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, DMSO): 9.945 (s, 1H), 9.418 9s, 1H), 8.457 (d, 1H), 8.135 (d, 2H), 7.887 (d, 2H), 7.694 (d, 2H), 7.305 (d, 1H), 6.976 (d, 2H), 4.452 (q, 1H), 4.028 (q, 1H), 3.878-3.768 (m, 2H), 3.633 (m, 4H), 3.083 (br d, 4H), 2.209 (m, 1H), 2.002 (m, 1H), 1.862 (m, 3H), 1.1 (d, 3H). MS (EI) for $C_{28}H_{33}N_7O_3$: 516.3(MH^+).

[01703] N-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-tetrahydrofuran-2-carboxamide: ^{1}H NMR (400 MHz, DMSO). 9.954 (s, 1H), 9.421 (s, 1H), 8.458 (d, 1H), 8.136 (d, 2H), 7.889 (d, 2H), 7.697 (d, 2H), 7.306 (d, 1H), 6.978 (d, 2H), 4.454 (q, 1H), 4.028 (q, 1H), 3.889 (m, 2H), 3.645 (m, 4H), 3.083-2.985 (m, 6H), 2.669 (m, 1H), 2.209 (m, 1H), 2.002 (m, 2H), 1.879 (m, 2H), 1.681-1.548 (m, 3H), MS (EI) for $C_{30}H_{35}N_7O_3$: 542.3(MH^+).

[01704] (2,6-dichlorophenyl)(4-(4-(4-methylthiophen-2-yl)pyrimidin-2-ylamino)piperidin-1-yl)methanone: ^{1}H-NMR (400MHz, d6-DMSO): 8.28 (d, 1H), 7.72 (m, 1H), 7.57 (m, 2H), 7.47 (m, 1H), 7.32 (s, 1H), 7.27 (m, 1H), 7.01 (m, 1H), 4.45 (m, 1H), 4.03 (m, 1H), 3.28-3.05 (m, 3H), 2.45 (s, 3H), 2.03-1.80 (m, 2H), 1.59-1.48 (m, 2H); MS (EI): 447 (MH+).

[01705] (2,6-dichlorophenyl)(4-(4-(pyridin-3-yl)pyrimidin-2-ylamino)piperidin-1-yl)-methanone: ^{1}H-NMR (400MHz, d6-DMSO): 9.28 (br. s, 1H), 8.69 (m, 1H), 8.41 (m, 2H), 7.59-7.52 (m, 2H), 7.46 (m, 2H), 7.25 (d, 1H), 4.46 (m, 1H), 4.14 (m, 1H), 3.32-3.10 (m, 3H), 2.06-1.89 (m, 2H), 1.63-1.54 (m, 3H); MS (EI): 428 (MH+).

[01706] (2,6-dichlorophenyl)(4-(4-(5-methylthiophen-2-yl)pyrimidin-2-ylamino)piperidin-1-yl)methanone: ^{1}H-NMR (400MHz, d6-DMSO): 8.24 (d, 1H), 7.70 (m, 1H), 7.57 (m, 2H), 7.47 (m, 1H), 7.24 (m, 1H), 7.00 (m, 1H), 6.88 (m, 1H), 4.45 (m, 1H), 4.02 (m, 1H), 3.28-3.05 (m, 3H), 2.47 (s, 3H), 2.03-1.80 (m, 2H), 1.57-1.50 (m, 2H); MS (EI): 447 (MH+).

[01707] 1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1H-pyrrole-2-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 9.99 (s, 1H), 9.39 (s, 1H), 8.45 (d, 1H), 8.13 (d, 2H), 7.90 (d, 2H), 7.68 (d, 2H), 7.30 (d, 1H), 7.09-7.08 (m, 1H), 7.05

(t, 1H), 6.97 (d, 2H), 6.13-6.11 (m, 1H), 3.90 (s, 3H), 3.74 (t, 4H), 3.05 (t, 4H). MS (EI) for $C_{26}H_{26}N_6O_2$: 455 (MH+).

[01708] 3-fluoro-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-4-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.96 (s, 1H), 9.43 (s, 1H), 8.79 (s, 1H), 8.62 (d, 1H), 8.47 (d, 1H), 8.20 (d, 2H), 7.88 (d, 2H), 7.76-7.67 (m, 2H), 7.32 (d, 1H), 6.94 (d, 2H), 6.56 (s, 1H), 3.74 (t, 4H), 3.05 (t, 4H). MS (EI) for $C_{26}H_{23}FN_6O_2$: 471 (MH+).

[01709] 6-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.61 (s, 1H), 9.41 (s, 1H), 9.03 (d, 1H), 8.47 (d, 1H), 8.23 (dd, 1H), 8.19 (d, 2H), 7.95 (d, 2H), 7.68 (d, 2H), 7.45 (d, 1H), 7.31 (d, 1H), 6.94 (d, 2H), 3.74 (t, 4H), 3.05 (t, 4H), 2.57 (s, 3H). MS (EI) for $C_{27}H_{26}N_6O_2$: 467 (MH+).

[01710] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridazine-4-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.98 (s, 1H), 9.67 (s, 1H), 9.52 (d, 1H), 9.42 (s, 1H), 8.47 (d, 1H), 8.21 (d, 2H), 8.16-8.14 (m, 1H), 7.96 (d, 2H), 7.68 (d, 2H), 7.33 (d, 2H), 7.33 (d, 1H), 6.95 (d, 2H), 3.74 (t, 4H), 3.05 (t, 4H). MS (EI) for $C_{25}H_{23}N_7O_2$: 454 (MH+).

[01711] 2-cyclopropyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.09 (s, 1H), 9.45 (s, 1H), 8.45 (d, 1H), 8.12 (d, 2H), 7.78 (d, 2H), 7.69 (d, 2H), 7.30 (d, 1H), 7.00 (s, 2H), 3.76 (s, 4H), 3.09 (s, 4H), 2.25 (d, 2H), 1.12-1.02 (m, 1H), 0.50-0.48 (m, 2H), 0.22-0.20 (m, 2H). MS (EI) for $C_{25}H_{27}N_5O_2$: 430 (MH+).

[01712] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)isoxazole-5-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.99 (s, 1H), 9.42 (s, 1H), 8.47 (d, 1H), 8.19 (d, 2H), 7.95 (d, 2H), 7.68 (d, 2H), 7.33-7.31 (m, 2H), 6.95 (d, 2H), 6.55 (s, 1H), 3.74 (t, 4H), 3.05 (t, 4H). MS (EI) for $C_{24}H_{22}N_6O_3$: 443 (MH+).

[01713] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.69 (s, 1H), 9.41 (s, 1H), 9.14 (s, 1H), 8.79 (d, 1H), 8.47 (d, 1H), 8.34-8.31 (m, 1H), 8.20 (d, 2H), 7.97 (d, 2H), 7.70 (d, 2H), 7.67-7.58 (m, 1H), 7.33 (d, 1H), 6.95 (d, 2H), 3.78 (t, 4H), 3.05 (t, 4H). MS (EI) for $C_{26}H_{24}N_6O_2$: 453 (MH+).

[01714] 4-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-benzamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.42 (s, 1H), 9.53 (s, 1H), 8.47 (s, 1H), 8.17

(d, 2H), 7.98 (d, 2H), 7.91 (d, 2H), 7.72 (s, 2H), 7.37 (d, 3H), 7.05 (s, 2H), 3.78 (s, 4H), 3.14 (s, 4H), 2.40 (s, 3H). MS (EI) for $C_{28}H_{27}N_5O_2$: 466 (MH+).

[01715] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide: ^{1}H NMR (400 MHz, d6-DMSO): 11.55 (s, 1H), 11.15 (s, 1H), 10.16 (s, 2H), 8.74 (s, 1H), 8.52 (s, 1H), 8.23 (d, 2H), 7.89 (d, 2H), 7.67 (d, 2H), 7.48 (s, 1H), 7.11 (d, 2H), 4.50 (s, br, 1H), 3.81 (d, 2H), 3.57 (d, 2H), 3.28-3.11 (m, 8H), 2.05-1.92 (m, 3H), 1.30 (t, 3H). MS (EI) for $C_{27}H_{33}N_7O$: 472 (MH+).

[01716] N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-butanamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.25 (s, 1H), 9.37 (s, 1H), 8.43 (s, 1H), 8.12 (d, 2H), 7.77 (d, 2H), 7.68 (d, 2H), 7.29 (s, 1H), 6.93 (d, 2H), 3.08 (s, 4H), 2.42-2.30 (m, 4H), 1.68-1.58 (m, 2H), 1.05 (t, 3H), 0.93 (t, 3H). MS (EI) for $C_{26}H_{32}N_6O$: 445 (MH+).

[01717] 1-ethyl-3-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]urea: ^{1}H NMR (400 MHz, d6-DMSO): 9.32 (s, 1H), 8.85 (s, 1H), 8.40 (d, 1H), 8.05 (d, 2H), 7.68 (d, 2H), 7.54 (d, 2H), 7.23 (d, 1H), 6.92 (d, 2H), 6.36 (t, 1H), 3.18-3.05 (m, 6H), 2.54 (t, 4H), 2.46-2.38 (m, 2H), 1.09-1.02 (m, 6H). MS (EI) for $C_{25}H_{31}N_7O$: 446 (MH+).

[01718] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)furan-3-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.17 (s, 1H), 9.46 (s, 1H), 8.47-8.43 (m, 2H), 8.18 (d, 2H), 7.91 (d, 2H), 7.83 (d, 1H), 7.70 (s, 2H), 7.32 (s, 1H), 7.03-6.95 (m, 3H), 3.76 (s, 4H), 3.09 (s, 4H). MS (EI) for $C_{25}H_{23}N_5O_3$: 442 (MH+).

[01719] N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1,3-thiazole-4-carboxamide: ^{1}H NMR (400 MHz, d6-DMSO): 10.61 (s, 1H), 9.40 (s, 1H), 9.30 (d, 1H), 8.56 (d, 1H), 8.46 (d, 1H), 8.16 (d, 2H), 8.06 (d, 2H), 7.69 (d, 2H), 7.32 (d, 1H), 6.96 (d, 2H), 6.56 (s, 1H), 3.74 (t, 4H), 3.05 (t, 4H). MS (EI) for $C_{24}H_{22}N_6O_2S$: 459 (MH+).

[01720] Based on the synthetic examples described hereinabove, the skilled artisan would be able to make the remainder of the JAK compounds intended to be within the scope of the invention described in the appended claims.

ASSAYS FOR JAK-2 COMPOUNDS

Assay Example 1

Measurement of JAK-2 Kinase Activity by ATP Hydrolysis

[01721] JAK-2 kinase activity was measured by monitoring peptide substrate dependent hydrolysis of ATP via quantitation of remaining ATP with luciferase based chemiluminescence. For compound evaluation, 0.5 µl of the compound dissolved in DMSO

was added to 10 µl of JAK-2 dissolved in assay buffer (20 mM HEPES pH 7.5, 10 mM $MgCl_2$, 0.03% Triton and 1mM DTT). After preincubation for 30 minutes at room temperature, the reaction was initiated by addition of 10 µl of ATP and the substrate peptide poly-Glu-Tyr in assay buffer. Final enzyme, ATP, and peptide concentrations were 3 nM, 1 µM , and 2 µM, respectively. After incubation for 60 minutes at room temperature, reaction progress was quantitated by addition of 10 µl Kinase-Glo (Promega) and measurement of chemiluminescence in a Victor reader (Perkin Elmer). A reaction in which compound was omitted was used to determine maximum reaction progress. Omission of compound and enzyme from the reaction was used to determine zero reaction progress.

Assay Example 2

Measurement of JAK-3 Kinase Activity by ATP Hydrolysis

[01722] JAK-3 was assayed similarly as JAK-2 (see Assay Example 1) except that the enzyme reaction was carried out for 180 minutes and enzyme, ATP, and peptide concentrations were 30 nM, 2 µM, and 4 µM, respectively.

Biological Activity

[01723] JAK compounds in Table 2 were determined to have inhibitory activity for JAK-2 of less than 10 µM. Other more preferred JAK compounds have inhibitory activity for JAK-2 of less than 100 nm. One of ordinary skill in the art can use the disclosures herein as well as what is known in the art to test the inhibitory activity of a particular compound.

Pharmaceutical Composition Examples

[01724] The following are representative pharmaceutical formulations containing a compound of Formula I(J).

Tablet Formulation

[01725] The following ingredients are mixed intimately and pressed into single scored tablets.

Ingredient	Quantity per tablet, mg
compound of formula I(J)	400
Cornstarch	50
croscarmellose sodium	25
Lactose	120
magnesium stearate	5

Capsule Formulation

[01726] The following ingredients are mixed intimately and loaded into a hard-shell gelatin capsule.

Ingredient	Quantity per tablet, mg
compound of I(J)	200
lactose, spray-dried	148
magnesium stearate	2

Suspension Formulation

[01727] The following ingredients are mixed to form a suspension for oral administration.

Ingredient	Amount
compound of formula I(J)	1.0 g
fumaric acid	0.5 g
Sodium chloride	2.0 g
methyl paraben	0.15 g
propyl paraben	0.05 g
granulated sugar	25.5 g
sorbitol (70% solution)	12.85 g
Veegum K (Vanderbilt Co.)	1.0 g
Flavoring	0.035 mL
Colorings	0.5 mg
distilled water	q.s. to 100 mL

Injectable Formulation

[01728] The following ingredients are mixed to form an injectable formulation.

Ingredient	Amount
compound of formula I(J)	1.2 g
Sodium acetate buffer solution	0.4 M 2.0 mL
HCl (1 N) or NaOH (1 M)	q.s. to suitable pH
water (distilled, sterile)	q.s.to 20 mL

[01729] All of the above ingredients, except water, are combined and heated to 60-70 °C. with stirring. A sufficient quantity of water at 60°C. is then added with vigorous stirring to emulsify the ingredients, and water then added q.s. to 100 g.

Suppository Formulation

[01730] A suppository of total weight 2.5 g is prepared by mixing the JAK compound with Witepsol® H-15 (triglycerides of saturated vegetable fatty acid; Riches-Nelson, Inc., New York), and has the following composition:

Ingredient	Quantity per tablet, mg
JAK compound	500
Witepsol® H-15	Balance

General Administration

[01731] The combinations of JAK-2 and MEK compounds described herein can be used to to treat diseases in mammals such as cancer as defined herein, hyperproliferative disorders, myeloproliferative disorders, wherein the human is in need of the treatment. In another embodiment, combinations of JAK-2 and MEK compounds described herein can be used to to treat cancer in mammals, such as a cancer prostate cancer, breast cancer, multiple myeloma, leukemia, lymphoma, lung cancer, colorectal cancer, renal cancer, melanoma, hepatocellular, gastric, GIST, pancreatic carcinoma, and papillary thyroid cancer.

[01732] In one aspect, the MEK and JAK-2 compounds described herein can be in the form of pharmaceutical compositions comprising an inhibitor of MEK according to Formula I(M) as described above and an inhibitor of JAK-2 according to Formula I(J) as desribed herein, each with a pharmaceutically acceptable carrier. The pharmaceutical formulations can also include one or more excipients and/or one or more diluents. The MEK and JAK-2 compounds described herein can be administered together in one pharmaceutical composition, or separately as two separate pharmaceutical compositions.

[01733] When the pharmaceutical compositions includes both of the JAK-2 and MEK compounds, the weight percentage JAK-2 compounds can range from about 0.01% by weight to about 0.99% by weight, or from about 0.05% by weight to about 0.95% by weight, or from about 0.1% by weight to about 0.90% by weight, or from about 0.20% by weight to about 0.80% by weight, or from about 0.30% by weight to about 0.70% by weight, or from about 0.40% by weight to about 0.60% by weight, or from about 0.1% by weight to about 0.2% by weight, or from about 0.20% by weight to about 0.30% by weight, or from about 0.30% by weight to about 0.40% by weight, or from about 0.40% by weight to about 0.50% by weight, or from about 0.50% by weight to about 0.60% by weight, or from about 0.60% by weight to about 0.70% by weight, or from about 0.70% by weight to about 0.80% by weight, or from about 0.80% by weight to about 0.90% by weight.

[01734] In another embodiment, the pharmaceutical compositions includes both of the JAK-2 and MEK compounds, and the weight percentage of the MEK compounds range from about 0.01% by weight to about 0.99% by weight, or from about 0.05% by weight to about

0.95% by weight, or from about 0.1% by weight to about 0.90% by weight, or from about 0.20% by weight to about 0.80% by weight, or from about 0.30% by weight to about 0.70% by weight, or from about 0.40% by weight to about 0.60% by weight, or from about 0.1% by weight to about 0.2% by weight, or from about 0.20% by weight to about 0.30% by weight, or from about 0.30% by weight to about 0.40% by weight, or from about 0.40% by weight to about 0.50% by weight, or from about 0.50% by weight to about 0.60% by weight, or from about 0.60% by weight to about 0.70% by weight, or from about 0.70% by weight to about 0.80% by weight, or from about 0.80% by weight to about 0.90% by weight.

[01735] In another embodiment, the pharmaceutical compositions includes both of the JAK-2 and MEK compounds, and the weight ratio of JAK-2:MEK compounds is about 0.01:100, 0.05:50, 0.1:50, 0.2:30, 0.4:25, 0.5:20, 0.6:15, 0.8:10, 1:5, 1:2, or 1:1.

[01736] In another embodiment, the pharmaceutical compositions includes both of the JAK-2 and MEK compounds, and the weight ratio of MEK:JAK-2 compounds is about 0.01:100, 0.05:50, 0.1:50, 0.2:30, 0.4:25, 0.5:20, 0.6:15, 0.8:10, 1:5, 1:2, or 1:1.

[01737] In certain other embodiments, administration can be by the oral route. Administration of the combination compounds JAK-2 and MEK compounds described herein, or their pharmaceutically acceptable salts, in pure form or in an appropriate pharmaceutical composition, can be carried out via any of the accepted modes of administration or agents for serving similar utilities. Thus, administration can be, for example, orally, nasally, parenterally (intravenous, intramuscular, or subcutaneous), topically, transdermally, intravaginally, intravesically, intracistemally, or rectally, in the form of solid, semi-solid, lyophilized powder, or liquid dosage forms, such as for example, tablets, suppositories, pills, soft elastic and hard gelatin capsules, powders, solutions, suspensions, or aerosols, or the like, preferably in unit dosage forms suitable for simple administration of precise dosages.

[01738] The compositions will include a conventional pharmaceutical carrier or excipient and a JAK-2 and/or MEK compound described herein as the active agent(s), and, in addition, may include carriers and adjuvants, etc.

[01739] Adjuvants include preserving, wetting, suspending, sweetening, flavoring, perfuming, emulsifying, and dispensing agents. Prevention of the action of microorganisms can be ensured by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, and the like. It may also be desirable to include isotonic agents, for example sugars, sodium chloride, and the like. Prolonged absorption of the

injectable pharmaceutical form can be brought about by the use of agents delaying absorption, for example, aluminum monostearate and gelatin.

[01740] If desired, a pharmaceutical composition described herein may also contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, antioxidants, and the like, such as, for example, citric acid, sorbitan monolaurate, triethanolamine oleate, butylalted hydroxytoluene, etc.

[01741] The choice of formulation depends on various factors such as the mode of drug administration (e.g., for oral administration, formulations in the form of tablets, pills or capsules are preferred) and the bioavailability of the drug substance. Recently, pharmaceutical formulations have been developed especially for drugs that show poor bioavailability based upon the principle that bioavailability can be increased by increasing the surface area i.e., decreasing particle size. For example, U.S. Pat. No. 4,107,288 describes a pharmaceutical formulation having particles in the size range from 10 to 1,000 nm in which the active material is supported on a crosslinked matrix of macromolecules. U.S. Pat. No. 5,145,684 describes the production of a pharmaceutical formulation in which the drug substance is pulverized to nanoparticles (average particle size of 400 nm) in the presence of a surface modifier and then dispersed in a liquid medium to give a pharmaceutical formulation that exhibits remarkably high bioavailability.

[01742] Compositions suitable for parenteral injection may comprise physiologically acceptable sterile aqueous or nonaqueous solutions, dispersions, suspensions or emulsions, and sterile powders for reconstitution into sterile injectable solutions or dispersions. Examples of suitable aqueous and nonaqueous carriers, diluents, solvents or vehicles include water, ethanol, polyols (propyleneglycol, polyethyleneglycol, glycerol, and the like), suitable mixtures thereof, vegetable oils (such as olive oil) and injectable organic esters such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersions and by the use of surfactants.

[01743] One specific route of administration is oral, using a convenient daily dosage regimen that can be adjusted according to the degree of severity of the disease-state to be treated.

[01744] Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound is admixed with at least one inert customary excipient (or carrier) such as sodium citrate or dicalcium phosphate or (a) fillers or extenders, as for example, starches, lactose, sucrose, glucose, mannitol, and silicic

acid, (b) binders, as for example, cellulose derivatives, starch, alignates, gelatin, polyvinylpyrrolidone, sucrose, and gum acacia, (c) humectants, as for example, glycerol, (d) disintegrating agents, as for example, agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, croscarmellose sodium, complex silicates, and sodium carbonate, (e) solution retarders, as for example paraffin, (f) absorption accelerators, as for example, quaternary ammonium compounds, (g) wetting agents, as for example, cetyl alcohol, and glycerol monostearate, magnesium stearate and the like (h) adsorbents, as for example, kaolin and bentonite, and (i) lubricants, as for example, talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, or mixtures thereof. In the case of capsules, tablets, and pills, the dosage forms may also comprise buffering agents.

[01745] Solid dosage forms as described above can be prepared with coatings and shells, such as enteric coatings and others well known in the art. They may contain pacifying agents, and can also be of such composition that they release the active compound or compounds in a certain part of the intestinal tract in a delayed manner. Examples of embedded compositions that can be used are polymeric substances and waxes. The active MEK or JAK-2 compounds described herein can also be in microencapsulated form, if appropriate, with one or more of the above-mentioned excipients.

[01746] Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and elixirs. Such dosage forms are prepared, for example, by dissolving, dispersing, etc., a MEK or JAK-2 compound(s) described herein, or a pharmaceutically acceptable salt thereof, and optional pharmaceutical adjuvants in a carrier, such as, for example, water, saline, aqueous dextrose, glycerol, ethanol and the like; solubilizing agents and emulsifiers, as for example, ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propyleneglycol, 1,3-butyleneglycol, dimethylformamide; oils, in particular, cottonseed oil, groundnut oil, corn germ oil, olive oil, castor oil and sesame oil, glycerol, tetrahydrofurfuryl alcohol, polyethyleneglycols and fatty acid esters of sorbitan; or mixtures of these substances, and the like, to thereby form a solution or suspension.

[01747] Suspensions, in addition to the active MEK or JAK-2 compounds, may contain suspending agents, as for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth, or mixtures of these substances, and the like.

[01748] Compositions for rectal administrations are, for example, suppositories that can be prepared by mixing the MEK or JAK-2 compounds described herein with, for example,

suitable non-irritating excipients or carriers such as cocoa butter, polyethylene-glycol or a suppository wax, which are solid at ordinary temperatures but liquid at body temperature and therefore, melt while in a suitable body cavity and release the active component therein.

[01749] Dosage forms for topical administration of a MEK or JAK-2 compound described herein include ointments, powders, sprays, and inhalants. The active component is admixed under sterile conditions with a physiologically acceptable carrier and any preservatives, buffers, or propellants as may be required. Ophthalmic formulations, eye ointments, powders, and solutions are also contemplated as being within the scope of this invention.

[01750] Compressed gases may be used to disperse a MEK or JAK-2 compound described herein in aerosol form. Inert gases suitable for this purpose are nitrogen, carbon dioxide, etc.

[01751] Generally, depending on the intended mode of administration, the pharmaceutically acceptable compositions will contain about 1% to about 99% by weight of a MEK or JAK-2 compound(s) described herein, or a pharmaceutically acceptable salt thereof, and 99% to 1% by weight of a suitable pharmaceutical excipient. In one example, the composition will be between about 5% and about 75% by weight of a MEK or JAK-2 compound(s) described herein, or a pharmaceutically acceptable salt thereof, with the rest being suitable pharmaceutical excipients.

[01752] Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see Remington's Pharmaceutical Sciences, 18th Ed., (Mack Publishing Company, Easton, Pa., 1990). The composition or compositions to be administered will, in any event, contain a therapeutically effective amount of a JAK-2 compound and a MEK compound described herein, or a pharmaceutically acceptable salt thereof, for treatment of a disease-state in accordance with the teachings of this invention.

[01753] The MEK or JAK-2 compounds described herein, or their pharmaceutically acceptable salts or hydrates, are administered in a therapeutically effective amount which will vary depending upon a variety of factors including the activity of the specific compounds employed, the metabolic stability and length of action of the compound, the age, body weight, general health, sex, diet, mode and time of administration, rate of excretion, drug combination, the severity of the particular disease-states, and the host undergoing therapy. The JAK-2 and MEK compounds described herein can be administered to a patient at dosage levels in the range of about 0.1 to about 1,000 mg per day. For a normal human adult having a body weight of about 70 kilograms, a dosage in the range of about 0.01 to about 100 mg per kilogram of body weight per day is an example. The specific dosage used, however, can vary. For example, the dosage can depend on a number of factors including the

requirements of the patient, the severity of the condition being treated, and the pharmacological activity of the compound being used. The determination of optimum dosages for a particular patient is well known to one of ordinary skill in the art.

[01754] If formulated as a fixed dose, such combination products employ the MEK and JAK-2 compounds described herein within the dosage range described above and the other pharmaceutically active agent(s) within its approved dosage range. The MEK and JAK-2 compounds described herein may alternatively be used sequentially with known pharmaceutically acceptable agent(s) when combined with other chemotherapeutic, or otherwise active agents.

[01755] Representative pharmaceutical formulations containing a MEK and/or JAK-2, either by themselves or in combination, are described hereinabove.

ADDITIONAL COMBINATIONS

[01756] In another embodiment, the method of using the combination of MEK and JAK-2 compounds described herein can be in combination with one or more additional treatment(s).

[01757] In another embodiment, the method of combining JAK-2 and MEK compounds further comprises one or more additional treatments selected from one or more chemotherapeutic agents, one or more antibodies, radiation therapy, surgery, hormone therapy, and hypothermia therapy, wherein the chemotherapeutic agent is selected from one or more taxanes, one or more platin(s), one or more topoisomerase inhibitor(s), one or more alkylating agent(s), one or more antimetabolite(s), one or more antimicrotubule agent(s), one or more bcr-abl inhibitor(s), rapamycin, carboplatin, cisplatin, oxaliplatin, gemcitabine, dacarbazine, topotecan, irinotecan, one or more AKT inhibitors, one or more c-Met inhibitors, one or more EGFR inhibitors, one or more ErbB2 inhibitors, one or more HSP90 inhibitors, one or more IGF1R inhibitors, and one or more Raf inhibitors.

[01758] In another embodiment, the one or more treatments can be chemotherapeutic agent(s).

[01759] In another embodiment, the one or more of the chemotherapeutic agent(s) is selected from a taxane(s), a platin(s), a topoisomerase inhibitor(s), an alkylating agent(s), an antimetabolite(s), an antimicrotubule agent(s), and a bcr-abl inhibitor(s). Non-limiting examples of chemotherapeutic agent(s) include an antimicrotubule agent(s) selected from Vincristine,Vinblastine, Vinorelbine, and Vindesine.

[01760] In another embodiment, one or more of the chemotherapeutic agent(s) is selected from rapamycin, carboplatin, cisplatin, oxaliplatin, gemcitabine, dacarbazine, topotecan, and irinotecan.

[01761] In another embodiment, one or more of the chemotherapeutic agent(s) is an AKT inhibitor or c-Met inhibitor.

[01762] In another embodiment, the one or more of the chemotherapeutic agent(s) is an EGFR inhibitor. Non-limiting examples of EGFR inhibitors include Lapatinib (Tykerb®), gefitinib (Iressa®), erlotinib (Tarceva®), Zactima (ZD6474), AEE778, HKI-272, EKB-569 and CI1033.

[01763] In another embodiment, one or more of the chemotherapeutic agent(s) is an ErbB2 inhibitor. Non-limiting examples of ErbB2 inhibitors include lapatinib, EXB-569, HKI272, and CI1033.

[01764] In another embodiment, one or more of the chemotherapeutic agent(s) is an HSP90 inhibitor. Non-limiting examples of the HSP90 inhibitor include 17-AAG, 17-DMAG, Geldanamycin, CNF2024, and SNX-2112.

[01765] In another embodiment, one or more of the chemotherapeutic agent(s) is an IGF1R inhibitor.

[01766] In another embodiment, one or more of the chemotherapeutic agent(s) is a Raf inhibitor such as, for example, sorafenib.

[01767] In another embodiment, one or more of the chemotherapeutic agent(s) is a VEGFR or VEGF inhibitor.

[01768] In another embodiment, one or more of the chemotherapeutic agent(s) is selected from rapamycin, a rapamycin analogue, PI103, PI504, and SF1126. Non-limiting examples of the chemotherapeutic agent(s) include rapamycin, CCI-779, AP23573, RAD001, TAFA93, PI103, PI504, and SF1126. In another embodiment, the chemotherapeutic agent is rapamycin.

[01769] In another embodiment, one or more of the treatment(s) is selected from radiation and hypothermia therapy. In another embodiment, the treatment is radiation.

[01770] In another embodiment, one or more of the treatment(s) is one or more antibody(s). Non-limiting examples include one or more of the antibody(s) selected from an IGF1R antibody (including, for example, αIGF-1R A12 MoAb, 19D12, h7C10 and CP-751871), Alemtuzumab, Bevacizumab (Avastin®), Cetuximab (Erbitux®), Gemtuzumab, Gemtuzumab ozogamicin, Ibritumomab tiuxetan, Panitumumab, Rituximab, Tositumomab, and Trastuzumab (Herceptin®).

[01771] In another embodiment, one or more of the treatment(s) is surgery.

[01772] In another embodiment, one or more of the treatment(s) is one or more hormone therapy(s). Non-limiting examples of hormone treatments include tamoxifen and an aromatase inhibitor.

[01773] In another embodiment, one or more of the chemotherapeutic agent(s) is gemcitabine.

[01774] In another embodiment, one or more of the chemotherapeutic agent(s) is Imatinib (i.e. Gleevec®).

[01775] In another embodiment, the cancer is primary or relapsed CML and/or acute myelogenous leukemia (AML) and one or more of the treatment(s) is selected from one or more of the chemotherapeutic agent(s) and one or more antibody(s). Non-limiting examples of the chemotherapeutic agent(s) in this embodiment include Imatinib (i.e. Gleevec®) and PKC412. In another embodiment, the one or more of the chemotherapeutic agent(s) is Imatinib (i.e. Gleevec®). Non-limiting examples of the one or more antibody(s) in this embodiment include $^{\alpha}$IGF-1R A12 MoAb and trastuzumab.

[01776] In another embodiment, the cancer is prostate cancer and one or more of the treatment(s) is selected from one or more antibody(s). Non-limiting examples of the one or more of the antibody(s) in this embodiment include $^{\alpha}$IGF-1R A12 MoAb.

[01777] In another embodiment, the cancer is malignant melanoma and one or more of the treatment(s) is selected from surgery and one or more chemotherapeutic agent(s). Non-limiting examples of chemotherapeutic agent(s) in this embodiment include an alkylating agent(s), a taxane(s), a platin(s), and a Raf inhibitor(s). In another embodiment, the one or more chemotherapeutic agent(s) is selected from sorafenib, Paclitaxel (Taxol®), Docetaxel (Taxotere®), dacarbazine, rapamycin, imatinib mesylate (Gleevec®), sorafenib, and carboplatin.

[01778] In another embodiment, the cancer is colon or rectal cancer and one or more of the treatment(s) is selected from surgery, radiation, one or more chemotherapeutic agent(s), and one or more antibody(s). Non-limiting examples of the chemotherapeutic agent(s) include cisplatin, oxaliplatin, carboplatin, 5-fluorouracil, Capecitabine (Xeloda), Irinotecan (Camptosar), FOLFOX (Folinic acid, 5-FU, Oxaliplatin), and leucovorin. Non-limiting examples of the one or more of the antibody(s) include bevacizumab and cetuximab.

[01779] In another embodiment, the cancer is pancreatic cancer and one or more of the treatment(s) include surgery, radiation, and one or more chemotherapeutic agent(s). Non-limiting examples of the one or more of the chemotherapeutic agent(s) include erlotinib

(Tarceva®), gemcitabine, 5-fluorouracil, leucovorin, cisplatin, oxaliplatin, carboplatin, gemcitabine, irinotecan, paclitaxel, capecitabine, and streptozocin.

[01780] In another embodiment, the cancer is breast cancer and one or more of the treatment(s) is selected from surgery, radiation, one or more chemotherapeutic agent(s), one or more hormone therapy(s), and one or more antibody(s). Non-limiting examples of the chemotherapeutic agent(s) in this embodiment include lapatinib (Tykerb®), Paclitaxel (Taxol®), docetaxel, capecitabine, Cyclophosphamide (Cytoxan), methotrexate, fluorouracil, doxorubicin, epirubicin, gemcitabine, carboplatin (Paraplatin), cisplatin (Platinol), vinorelbine (Navelbine), capecitabine (Xeloda), pegylated liposomal doxorubicin (Doxil), and albumin-bound paclitaxel (Abraxane). Specifically one or more of the antibody(s) is selected from αIGF-1R A12 MoAb, bevacizumab (Avastin), and trastuzumab. Non-limiting examples of the hormone therapy(s) in this embodiment include tamoxifen, Toremifene (Fareston), Fulvestrant (Faslodex), Megestrol acetate (Megace), ovarian ablation, and an aromatase inhibitor(s). Non-limiting examples of the aromatase inhibitor(s) include selected from etrozole (Femara), anastrozole (Arimidex), and exemestane (Aromasin).

[01781] In another embodiment, the cancer is non-small cell lung cancer and one or more of the treatment(s) is selected from surgery, radiation, one or more antibody(s), and one or more chemotherapeutic agent(s). Non-limiting examples of the chemotherapeutic agent(s) in this embodiment include cisplatin, oxaliplatin, carboplatin, Zactima (ZD6474), Paclitaxel, Docetaxel (Taxotere®), Gemcitabine (Gemzar®), Vinorelbine, Irinotecan, Etoposide, Vinblastine, Erlotinib (Tarceva®), and Pemetrexed. Non-limiting examples of the antibody(s) include Bevacizumab.

[01782] In another embodiment, the cancer is small cell lung cancer and one or more of the treatment(s) is selected from surgery, radiation, and one or more chemotherapy agent(s). Non-limiting examples of the chemotherapy agent(s) in this embodiment include cisplatin, oxaliplatin, carboplatin, etoposide, irinotecan, fosfamide, paclitaxel, docetaxel, gemcitabine, Topotecan, cyclophosphamide/doxorubicin/vincristine (CAV), methotrexate, and vinorelbine.

[01783] In another embodiment, the cancer is papillary or anaplastic thyroid cancer, and one or more of the treatment(s) is selected from surgery, radiation, radioactive iodine therapy, one or more hormone therapy(s), and one or more chemotherapeutic agent(s). Non-limiting example of the chemotherapeutic agent(s) in this embodiment include thyroid hormone pills, Doxorubucin and a platin(s).

[01784] In another embodiment, the cancer is endometrial cancer and one or more of the treatment(s) is selected from surgery, radiation, hormone therapy, and one or more chemotherapeutic agent(s). Non-limiting examples of the one or more of the chemotherapeutic agent(s) in this embodiment include paclitaxel, doxorubicin, and cisplatin. Nonlimiting examples of the one or more of the hormone therapies in this embodiment include medroxyprogesterone acetate, megestrol acetate, and Tamoxifen.

[01785] In another embodiment, the cancer is ovarian cancer and one or more of the treatment(s) is selected from surgery, radiation, and one or more chemotherapeutic agent(s). Non-limiting examples of chemotherapeutic agent(s) in this embodiment include a platin(s) compound (such as cisplatin, oxaliplatin and carboplatin), a taxane (such as paclitaxel or docetaxel), topotecan, anthracyclines (such as doxorubicin (Adriamycin) and liposomal doxorubicin (Doxil)), gemcitabine, cyclophosphamide, vinorelbine (Navelbine), hexamethylmelamine, ifosfamide, and etoposide.

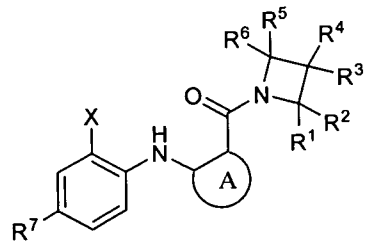
[01786] In another embodiment, one or more of the treatment(s) is selected from one or more chemotherapeutic agent(s), radiation, hypothermia therapy, one or more antibody(s), and surgery. Specifically, one or more of the chemotherapeutic agent(s) is selected from an EGFR inhibitor, isotretinoin, a platin (e.g., cisplatin, oxaliplatin, and carboplatin), epirubicin, bleomycin, doxorubicin, cyclophosphamide, a taxane (e.g. docetaxel (Taxotere®)), and fluorouracil [5-FU]. Non-limiting examples of the one or more chemotherapeutic agent(s) in this embodiment include cisplatin, carboplatin, and docetaxel. In another embodiment, the one or more antibody(s) is cetuximab (Erbitux®).

[01787] In another embodiment one or more of the treatment(s) is selected from radiation and surgery.

[01788] In another embodiment of the invention, one or more of the treatments is selected from rapamycin, CCI-779, AP23573, RAD001, TAFA93, carboplatin, cisplatin, oxaliplatin, gemcitabine, dacarbazine, topotecan, irinotecan, sorafenib, paclitaxel, docetaxel, Lapatinib (Tykerb®), gefitinib (Iressa®), erlotinib (Tarceva®), Zactima (ZD6474), 5-fluorouracil, Capecitabine (Xeloda), FOLFOX (Folinic acid, 5-FU, Oxaliplatin), streptozocin, Cyclophosphamide (Cytoxan), methotrexate, doxorubicin, epirubicin, vinorelbine (Navelbine), pegylated liposomal doxorubicin (Doxil), albumin-bound paclitaxel (Abraxane), Etoposide, Vinblastine, Pemetrexed, leucovorin, fosfamide, cyclophosphamide/doxorubicin/vincristine (CAV), thyroid hormone pills, hexamethylmelamine, ifosfamide, Imatinib (i.e. Gleevec®), $^{\alpha}$IGF-1R A12 MoAb, IGF-1R 19D12, IGF-1R h7C10, IGF-1R CP-751871, Alemtuzumab, Bevacizumab (Avastin®),

Cetuximab (Erbitux®), Gemtuzumab, Gemtuzumab ozogamicin, Ibritumomab tiuxetan, Panitumumab, Rituximab, Tositumomab, Trastuzumab (Herceptin®), tamoxifen, Toremifene (Fareston), Fulvestrant (Faslodex), Megestrol acetate (Megace), ovarian ablation, medroxyprogesterone acetate, megestrol acetate, and an aromatase inhibitor.

[01789] Another aspect of the invention relates to a method of treating a disease in a mammal, comprising administering to the mammal a therapeutically effective amount of a MEK compound of Formula I(M), or a pharmaceutical composition comprising a therapeutically effective amount of the MEK compound of Formula I(M) and a pharmaceutically acceptable carrier, in combination with a therapeutically effective amount of a JAK-2 compound of Formula I(J), or a pharmaceutical composition comprising a therapeutically effective amount of the JAK-2 compound of Formula I(J) and a pharmaceutically acceptable carrier, wherein the MEK compound of Formula I(M) is defined as follows:



I(M)

or a pharmaceutically acceptable salt or solvate thereof, wherein A, X, R^1, R^2, R^3, R^4, R^5, R^6, and R^7 are as defined in Group A, Group B, Group C, or Group D:

Group A

A is phenylene optionally substituted with one or two groups selected from R^{10}, R^{12}, R^{14}, and R^{16} wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen or halo;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen, halo, hydroxy, alkoxy, or amino;

R^4 is hydrogen, $-NR^8R^{8'}$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, cycloalkyl, heterocycloalkyl, or heteroaryl; wherein the alkyl is optionally substituted with one, two, or three groups independently selected from $-OR^8$, halo, nitro, $-S(O)_mR^9$, optionally substituted heterocycloalkyl, $-NR^8R^{8'}$, $-NR^8C(O)R^{8'}$,

$-NR^8S(O)_2R^9$, $-NR^8C(O)OR^{8'}$, and aryl; wherein the cycloalkyl is optionally substituted with one or two groups selected from $-OR^8$ and $-NR^8R^{8'}$; wherein the heterocycloalkyl is optionally substituted with one or two groups independently selected from alkyl and $-C(O)OR^8$; and wherein the heteroaryl is optionally substituted with $-NR^8R^{8'}$; or

R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH);

m is 0;

R^7 is halo;

R^8 and $R^{8'}$ are independently selected from hydrogen, hydroxy, alkyl, alkenyl, alkynyl, aryl, heterocycloalkyl, heteroaryl, and cycloalkyl;

wherein the R^8 and $R^{8'}$ alkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, $-NR^{30}R^{30'}$ (wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), optionally substituted heteroaryl, optionally substituted cycloalkyl), optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, $-C(O)NR^{33}R^{33a}$ (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), optionally substituted aryloxy, $-S(O)_nR^{31}$ (wherein n is 0 and R^{31} is alkyl), carboxy, alkoxycarbonyl, and $-NR^{32}C(O)R^{32a}$ (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl); or wherein the alkyl is optionally substituted with one, two, three, four, or five halo;

wherein the R^8 and $R^{8'}$ heteroaryl are independently optionally substituted with one or two groups indendently selected from amino and alkyl;

wherein the R^8 and $R^{8'}$ heterocycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from alkyl, alkoxycarbonyl, optionally substituted arylalkyl, hydroxy, alkoxy, and hydroxyalkyl;

wherein the R^8 and $R^{8'}$ aryl are independently optionally substituted with one or two groups indendently selected from hydroxy, alkoxy, halo, $-NR^{32}C(O)R^{32a}$ (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl), and $-NR^{34}SO_2R^{34a}$ (wherein R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl); and

wherein the R^8 and $R^{8'}$ cycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, hydroxyalkyl, alkoxy, carboxy,

-C(O)NR^{33}R^{33a} (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), and optionally substituted cycloalkyl; and

R^9 is alkyl or aryl;

Group B

A is thien-3,4-diyl, benzo[*d*]isoxazol-5,6-diyl, 1*H*-indazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), benzo[*d*]oxazol-5,6-diyl, 1*H*-benzo[d]imidazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), 1*H*-benzo[*d*][1,2,3]triazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), imidazo[1,2-*a*]pyridin-6,7-diyl, cinnolin-6,7-diyl, quinolin-6,7-diyl, pyridin-3,4-diyl, 1-oxido-pyridin-3,4-diyl, [1,2,4]triazolo[4,3-a]pyridin-6,7-diyl, or 2,3-dihydroimidazo[1,2-a]pyridin-6,7-diyl; wherein A is optionally substituted with one, two, or three groups independently selected from R^{10}, R^{12}, R^{14}, R^{16} and R^{19} wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen, alkyl, halo, or amino; and R^{19} is hydrogen or alkyl;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

R^4 is -NR^{8}R$^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; wherein the alkyl is optionally substituted with -NR^{8}R$^{8'}$ and wherein the heteroaryl is optionaly substituted with alkyl;

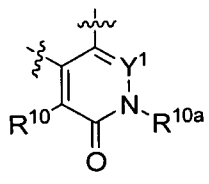
R^7 is halo;

R^8 is hydrogen or alkyl; and

R$^{8'}$ is hydrogen, alkyl, or cycloalkyl; wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl;

Group C

A is



(a)

R^{10} is hydrogen or halo;

R^{10a} is hydrogen or alkyl;

Y^1 is =CH- or =N-;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

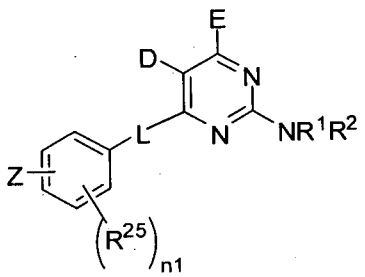
R^4 is $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ and wherein the heteroaryl is optionaly substituted with alkyl;

R^7 is halo;

R^8 is hydrogen or alkyl; and

$R^{8'}$ is hydrogen, alkyl, or cycloalkyl; wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl;

and wherein the JAK-2 compound is defined as follows:



I(J)

or a pharmaceutically acceptable salt or solvate thereof, wherein

D is hydrogen, halo, $-CF_3$, heterocycloalkyl or alkyl;

E is hydrogen, halo, $-CF_3$, heterocycloalkyl or alkyl; or

D and E, together with the carbon atoms to which they are attached, form a 5-7 membered heteroaryl or a 5-7 membered heterocycloalkyl, wherein the 5-7 membered heteroaryl or 5-7 membered heterocycloalkyl are each fused to the pyrimidinyl moiety to which D and E are attached;

L is a bond, -O- or -N(H)-;

Z is selected from alkoxy, cycloalkyl, heteroaryl optionally substituted with alkyl, halo, $-C(O)OR^{26}$, -C(=N-OH)alkyl, $-C(O)R^8$, $-C(O)NR^{30}R^{30a}$, $-CH_2R^2$, $-(CH_2)_{n5}NR^{26}R^{26a}$, $-CF_3$, -CN, $-SO_2R^{12}$, $-S-R^{12a}$, $-OR^{32a}$, $-NHC(O)R^{32}$, aryl, and heterocycloalkyl optionally substituted with 1 or 2 oxo, or

Z and R^{25}, together with the carbon atoms to which they are attached, join to form a 5 or 6 membered heterocycloalkyl, a 5 or 6 membered heteroaryl, or a 5 or 6 membered cycloalkyl ring, wherein the 5 or 6 membered heterocycloalkyl, 5 or 6 membered

heteroaryl, or 5 or 6 membered cycloalkyl ring are fused to the phenyl moiety to which Z and R^{25} are attached, and wherein the 5 or 6 membered heterocycloalkyl, 5 or 6 membered heteroaryl, or 5 or 6 membered cycloalkyl ring are each optionally substituted with 1, 2, or 3 groups independently selected from oxo, alkyl, alkoxy and halo;

n1 is 0, 1, 2, 3, or 4, and each n1 is independently selected when more than one n1 is present;

n2 is 0, 1, 2, 3, or 4, and each n2 is independently selected when more than one n2 is present;

n3 is 0, 1, 2, or 3, and each n3 is independently selected when more than one n3 is present;

n4 is 0, 1, 2, 3 or 4, and each n4 is independently selected when more than one n4 is present;

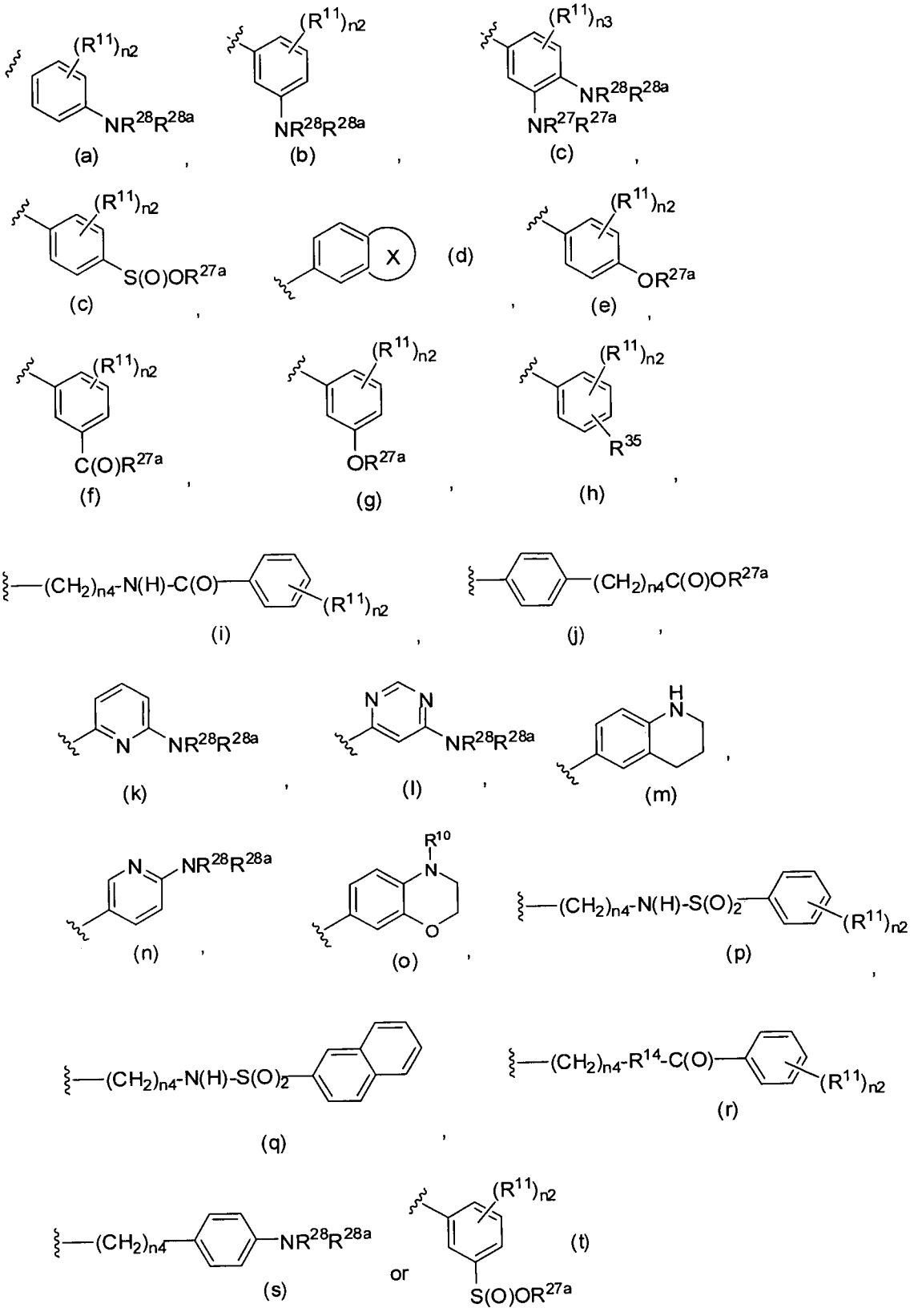
n5 is 0, 1, 2, 3 or 4, and each n5 is independently selected when more than one n5 is present;

p is 0-3;

r is 1-3;

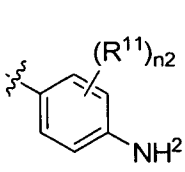
R^1 is hydrogen;

R^2 is selected from one of the following groups:

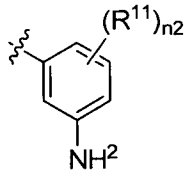


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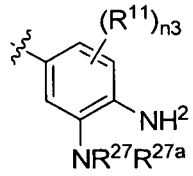
or R^2 is selected from one of the following groups:



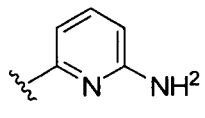
(u) ,



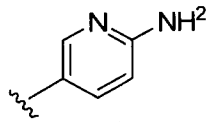
(v) ,



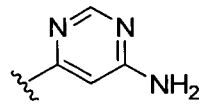
(w) ,



(x) ,



(y) , or



(z) ;

ring X in formula (d) of R^2 is a 5 or 6 membered unsaturated heterocyclic ring fused to the two carbon atoms of the phenyl moiety to which ring X is attached, wherein ring X contains 1 or 2 nitrogen atoms;

R^7, $R^{7'}$, R^9, R^{10}, R^{12} and R^{15} are each independently hydrogen, alkyl, alkoxy, or alkoxyalkyl;

R^8 is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, hydroxyalkyl, alkoxyalkyl, dihydroxyalkyl, alkylamino, dialkylamino, aminoalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, alkylaminoalkyl, dialkylaminoalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl;

each R^{11}, when R^{11} is present, is independently selected from alkyl, alkenyl, lower alkynyl, $-CF_3$, alkoxy, halo, haloalkoxy, haloalkyl, aminoalkyl, aminoalkoxy, alkylaminoalkyl, alkylaminoalkoxy, dialkylaminoalkyl, dialkylaminoalkoxy, oxo, thioalkyl, alkylthioalkyl, $-(CH_2)_p-OR^{17}$, -CN, $-O-CH_2-C(O)-R^{17}$, $-C(O)R^{16}$, $-(CH_2)_p-C(O)OR^{17}$, $-S(O)_2R^{17}$, $-S(O)_2NR^{15}R^{17}$, aryl, heteroaryl, cycloalkyl, arylalkyl, arylalkoxy, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at any ring position with 1, 2, 3 or 4 R^{21};

R^{12} is hydrogen or alkyl;

R^{12a} is hydrogen or alkyl;

R^{13} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with 1, 2, 3, 4 or 5 groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl are independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

R^{14} is a bond, heterocycloalkyl or cycloalkyl;

R^{16} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, dialkylaminoalkyl, $-(CH_2)_r-C(O)OR^7$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl is optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

R^{17} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl,

aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, dialkylaminoalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl is optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

each R^{21}, when R^{21} is present, is independently selected from alkyl, alkenyl, lower alkynyl, cyano, halo, haloalkoxy, haloalkyl, hydroxyalkyl, amino, alkylamino, dialkylamino, dialkylaminoalkyl, dialkylaminoalkyloxy, haloalkyl, oxo, $-OR^{13}$, $-NHS(O)_2R^{17}$, $-S(O)_2R^{17}$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-C(O)NR^{15}R^{17}$, $-NR^{15}C(O)R^{17}$, aryl, arylalkyl, heteroarylalkyl, aryloxy, and heteroaryl; wherein each of the aryl, arylalkyl, heteroarylalkyl, aryloxy, and heteroaryl within R^{21} are optionally substituted at any ring position with 1, 2, or 3 groups selected from alkyl, lower alkoxy halo, phenyl, heteroaryl and alkylheteroalkyl;

R^{25} is selected from alkyl, alkenyl, lower alkyl, halo, haloalkyl, haloalkoxy, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, $-OR^{12}$, cyano, $-CH_2NHC(O)OR^7$, $-CH_2NHC(O)R^7$, $-SR^7$, $-S(O)_2R^7$, $-S(O)_2NR^7R^8$, $-C(O)OR^8$, $-C(O)NR^7R^8$, cycloalkyl, heterocycloalkyl, aryl and heteroaryl; wherein the cycloalkyl, heterocycloalkyl, aryl and heteroaryl are each optionally substituted with one, two or three groups independently selected from alkyl, alkenyl, halo, haloalkoxy, haloalkyl, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, $-OR^8$, $-NHS(O)_2R^8$, cyano, $-C(O)R^8$, $-CH_2NHC(O)OR^7$, $-CH_2NHC(O)R^7$, $-SR^7$, $-S(O)_2R^7$, $-S(O)_2NR^7R^8$, $-C(O)OR^8$, $-C(O)NR^7R^8$, $-NR^{7'}C(O)-CHR^3-OR^8$, $-NR^{7'}C(O)-CHR^3-NR^7-R^8$, and $-NR^7C(O)R^8$;

R^{26} is hydrogen, -C(O)-phenyl or alkyl, wherein the -C(O)-phenyl is optionally substituted at any ring position with 1, 2 or 3 halo;

R^{26a} is hydrogen, alkyl, heteroaryl, $-C(O)R^{32}$, $-C(O)NHR^{32a}$, $-S(O)_2R^9$, $-SR^9$, $-C(O)OR^{32}$, or $-C(O)NR^{32a}R^{32}$;

R^{27} and R^{28} are each independently selected from alkyl, alkenyl, hydroxy, alkoxy, and alkoxyalkyl;

R^{27a} and R^{28a} are independently selected from hydrogen, alkyl, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, dialkylaminoalkyl, arylcarbonylalkyl, aryloxyalkyl, dialkylaminoalkyl, alkyl-O-C(O)heterocylcoalkyl, $-(CH_2)_{n4}$heterocycloalkyl, heterocycloalkylalkyl, heteroaryl, heteroarylalkyl, $-(CH_2)_{n4}-C(O)R^{29}$, $-(CH_2)_{n4}NR^{28}R^{28a}$, $-(CH_2)_{n4}NHR^{28a}$, $-CH(phenyl)_2$, $-S(O)_2R^{29}$, $-C(O)R^{29}$, $-C(O)OR^{29}$, and $-C(O)NR^{29a}R^{29}$, wherein the aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{27a} and R^{28a} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkylcarbonyl, phenyl, phenoxy, arylcarbonyl, $-CF_3$, oxo, $-OCF_3$, alkoxyphenyl, and heteroaryl optionally substituted with alkyl or halo;

or R^{27} and R^{27a}, together with the nitrogen to which they are attached, form heterocycloalkylamino, heterocycloalkyl or heteroaryl, wherein the heterocycloalkylamino and heteroaryl are each independently optionally substituted with 1, 2, 3, 4, or 5 R^{31};

or R^{28} and R^{28a} together with the nitrogen to which they are attached form heterocycloalkyl or heteroaryl, wherein the heterocycloalkyl and heteroaryl are each optionally substituted with 1, 2, 3, 4, or 5 R^{31};

R^{29a} is hydrogen or alkyl;

R^{29} is selected from alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{29} are each optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkylcarbonyl, phenyl, phenoxy, arylcarbonyl, $-CF_3$, oxo, $-OCF_3$, alkoxyphenyl, and heteroaryl optionally substituted with alkyl or halo;

R^{30a} is hydrogen or alkyl;

R^{30} is selected from hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkoxycarbonylalkyl, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, aryl, arylalkyl, phenoxyalkyl, cycloalkyl, cycloalkylalkyl,

heteroaryl, heteroarylalkyl, arylheteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, arylalkyl, phenoxyalkyl, cycloalkyl, arylheteroarylalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{30} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkoxyalkyl, $-C(O)OCH_3$, $-CF_3$, $-OCF_3$, alkylcarbonyl, phenyl, phenoxy, alkylphenoxy, dialkylaminoalkoxy and heteroaryl;

R^{31} is selected from alkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkylthioalkyl, $-C(O)R^{30}$, $-C(O)NR^{30}R^{30a}$, $-C(O)OR^{30}$, $-S(O)_2R^{30}$, amino, dihydroxyalkyl, arylcarbonyl, alkylcarbonylamino, alkoxyphenyl, phenylalkoxyalkyl, arylheteroarylalkyl, alkylamino, -O-dialkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, dialkylaminoalkoxy, oxo, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, spirocyclic cycloalkyl, spirocyclic heterocycloalkyl, and heterocycloalkylalkyl, wherein the aryl, arylalkyl, cycloalkyl, arylheteroarylalkyl, arylalkoxyalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{31} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, $-CF_3$, $-OCF_3$, cyano, alkoxy, alkoxyalkyl, $-C(O)OCH_3$, alkylcarbonyl, phenyl optionally substituted at any ring position with halo, phenoxy, alkylphenoxy, arylalkoxyalkyl, dialkylaminoalkoxy and heteroaryl;

R^{32a} is hydrogen, $-OCF_3$, $-CF_3$, or alkyl;

R^{32} is selected from aryl, arylalkyl, arylalkoxy, arylcycloalkyl, alkoxycarbonylalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkylhydroxyalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl, wherein the aryl, arylalkyl, cycloalkyl, arylcycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from hydroxy, oxo, alkyl, alkoxy, amino, hydroxyalkyl, alkylcarbonyl, alkoxycarbonyl, halo, $-CF_3$, $-OCF_3$, aminoalkyl, alkylaminoalkyl, aryl and dialkylaminoalkyl, and wherein the alkyl portion of the heteroarylalkyl can be substituted with amino;

or R^{32} is alkyl optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from hydroxy, alkoxycarbonyl, alkoxy, $-CF_3$, halo, aminocarbonyl, alkylaminocarbonyl, alkoxycarbonylalkylamino, dialkylaminocarbonyl, $-NR^{34}R^{34a}$ and phenyl optionally substituted with 1, 2, or 3 halo;

or R^{32} is alkylamino or arylalkylamino;

R^{34} is hydrogen or alkyl;

R^{34a} is selected from hydrogen, alkyl, heteroaryl, aryl, aminoalkyl, aminocarbonylalkyl, heteroarylalkyl, arylalkoxy and arylalkyloxycarbonylalkyl; wherein the heteroaryl, aryl, heteroarylalkyl, arylalkoxy or arylalkyloxycarbonylalkyl are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from hydroxy, oxo, alkyl, amino, hydroxyalkyl, alkylcarbonyl, alkoxycarbonyl, halo, aminoalkyl, alkylaminoalkyl, and dialkylaminoalkyl; and

R^{35} is selected from halo, $-(CH_2)_pC(O)OR_{17}$, cycloalkyl, heterocycloalkyl, and heterocycloalklylalkyl; wherein the heterocycloalkyl and heterocycloalklylalkyl are each optionally substituted with 1, 2, 3, 4, or 5 groups each independently selected from alkyl, alkoxy, and halo,

wherein the mammal is in need of the treatment.

[01790] In another embodiment of the above method(s), the MEK compound of Formula I(M) is selected from Group A wherein A is phenylene; R^3 is alkoxy; and R^4 is alkyl or heterocycloalkyl wherein the alkyl is substituted with $-NR^8R^{8'}$.

[01791] In another embodiment of the above method(s), the MEK compound of Formula I(M) is selected from Group A wherein A is phenylene; R^3 is hydroxy; and R^4 is hydrogen, $-C(O)NR^8R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, heterocycloalkyl, cycloalkyl, heterocycloalkyl, or heteroaryl; wherein the alkyl is optionally substituted with one, two, or three groups selected from $-OR^8$, halo, nitro, $-S(O)_mR^9$, optionally substituted heterocycloalkyl, $-NR^8R^{8'}$, $-NR^8C(O)R^{8'}$, optionally substituted heteroaryl, $-NR^8S(O)_2R^9$, $-NR^8C(O)OR^{8'}$, and aryl; wherein the cycloalkyl is optionally substituted with one or two groups indeopendently selected from $-NR^8R^{8'}$ and $-C(O)NR^{33}R^{33a}$; wherein the heterocycloalkyl is optionally substituted with one, two or three groups independently selected from alkyl and $-C(O)OR^8$; and wherein the heteroaryl is optionally substituted with $-NR^8R^{8'}$.

[01792] In another embodiment of the above method(s), R^{10} is 3-fluoro and R^{12}, R^{14}, and R^{16} are hydrogen or halo; R^{10} is 3-fluoro, R^{12} is 4-fluoro, and R^{14} and R^{16} are hydrogen; R^{10} is 4-fluoro, R^{12} is 5-fluoro, and R^{14} and R^{16} are hydrogen; R^{10} is 4-fluoro, R^{12} is 6-fluoro, and R^{14} and R^{16} are hydrogen; or R^{12} is 4-fluoro and R^{10}, R^{14}, and R^{16} are hydrogen.

[01793] In another embodiment of the above method(s), R^4 is $-C(O)NR^8R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, cycloalkyl, heterocycloalkyl, or heteroaryl; wherein the alkyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, or four groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or wherein the alkyl is optionally substituted with one, two, three, four, five, six or seven halo.

[01794] In another embodiment of the above method(s), the MEK compound of Formula I(M) is selected from Group A where A is phenylene; R^7 is iodo or bromo; X is fluoro or chloro; R^1, R^2, R^5, and R^6 are hydrogen; and R^{10}, R^{12}, R^{14}, and R^{16} are defined as follows:

(i) R^{10} is 3-fluoro and R^{12}, R^{14}, and R^{16} are hydrogen or halo, or

(ii) R^{10} is 3-fluoro, R^{12} is 4-fluoro, and R^{14} and R^{16} are hydrogen;

(iii) R^{10} is 4-fluoro, R^{12} is 5-fluoro, and R^{14} and R^{16} are hydrogen; or

(iv) R^{10} is 4-fluoro, R^{12} is 6-fluoro, and R^{14} and R^{16} are hydrogen; or

(v) R^{12} is 4-fluoro and R^{10}, R^{14}, and R^{16} are hydrogen.

[01795] In another embodiment of the above method(s), the MEK compound of Formula I(M) is selected from Group A where A is phenylene; R^3 is hydroxyl, and R^4 is $-C(O)NR^8R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, cycloalkyl, heterocycloalkyl, or heteroaryl; where the alkyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, or four groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, -CN, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or where the alkyl is optionally substituted with one, two, three, four, five, six or seven halo.

[01796] In another embodiment of the above method(s), R^4 of the MEK compound of Formula I(M) is alkyl, heterocycloalkyl, or heteroaryl; where the alkyl is optionally

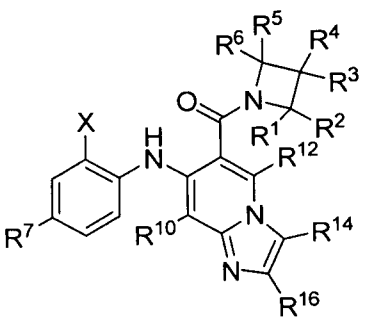
substituted with -$NR^8R^{8'}$; where the heterocycloalkyl is optionally substituted with alkyl or -$C(O)OR^8$; and where the heteroaryl is optionally substituted with alkyl.

[01797] In another embodiment of the above method(s), R^4 of the MEK compound of Formula I(M)is selected from Group B where A is thien-3,4-diyl, benzo[*d*]isoxazol-5,6-diyl, 1*H*-indazol-5,6-diyl (optionally substituted at the N1 position with R^{19} where R^{19} is alkyl or alkenyl), benzo[*d*]oxazol-5,6-diyl, 1*H*-benzo[d]imidazol-5,6-diyl (optionally substituted at the N1 position with R^{19} where R^{19} is alkyl or alkenyl), 1*H*-benzo[*d*][1,2,3]triazol-5,6-diyl (optionally substituted at the N1 position with R^{19} where R^{19} is alkyl or alkenyl), imidazo[1,2-*a*]pyridin-6,7-diyl, cinnolin-6,7-diyl, quinolin-6,7-diyl, pyridin-3,4-diyl, 1-oxido-pyridin-3,4-diyl, [1,2,4]triazolo[4,3-a]pyridin-6,7-diyl, or 2,3-dihydroimidazo[1,2-a]pyridin-6,7-diyl.

[01798] In another embodiment of the above method(s), A of the MEK compound of Formula I(M) is thien-3,4-diyl; X and R^7 are halo; R^1, R^2, R^5, R^6, R^{10}, and R^{12} are hydrogen, R^3 is hydrogen or hydroxy; and R^4 is -$NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl, where the alkyl is optionally substituted with -$NR^8R^{8'}$.

[01799] In another embodiment of the above method(s), A of the MEK compound of Formula I(M) is selected from Group B, wherein A is benzo[*d*]isoxazol-5,6-diyl; R^{10}, R^{12}, and R^{14} are independently hydrogen, halo, or alkyl; R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with -$NR^8R^{8'}$ and where the heteroaryl is optionally substituted with alkyl.

[01800] In another embodiment of the above method(s), A of the MEK compound of Formula I(M) is according to Formula I(q):

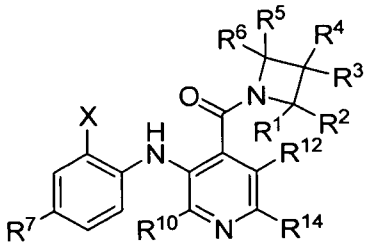


I(q)

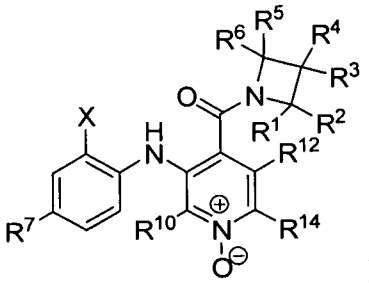
wherein R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^{10}, R^{12}, R^{14}, and R^{16} are independently hydrogen or halo; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or

heteroaryl, where the alkyl is optionally substituted with -$NR^8R^{8'}$ and where the heteroaryl is optionally substituted with alkyl.

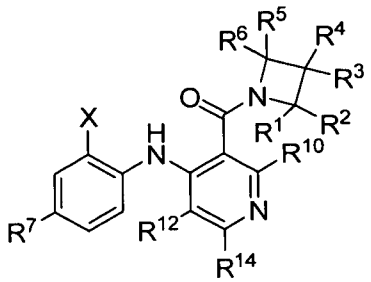
[01801] In another embodiment of the above method(s), the MEK compound of Formula I(M) is according to Formula I(u), I(v), I(w), or I(x):



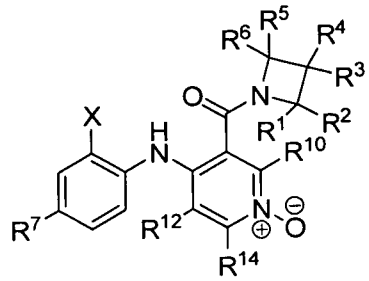
I(u);



I(v);



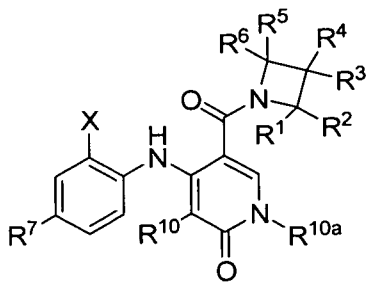
I(w);



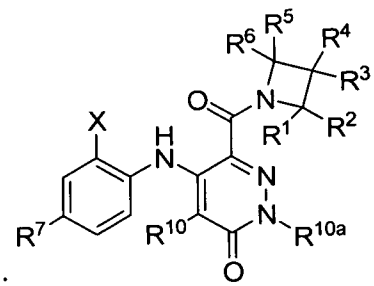
I(x);

wherein R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^{10}, R^{12}, and R^{14} are independently hydrogen, halo, or alkyl; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with -$NR^8R^{8'}$ and where the heteroaryl is optionally substituted with alkyl.

[01802] In another embodiment of the above method(s), the MEK compound of Formula I(M) is selected from Group C and according to Formula I(y) or I(z):



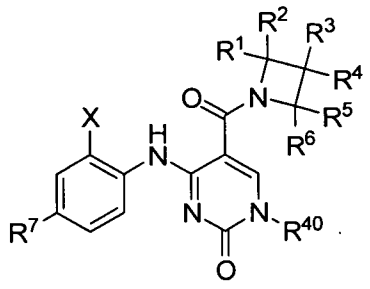
I(y);

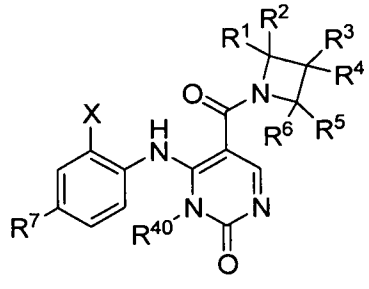


I(z)

wherein R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^{10} is hydrogen, halo, or alkyl; R^{10a} is alkyl; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with -$NR^8R^{8'}$, and wherein the heteroaryl is optionally substituted with alkyl.

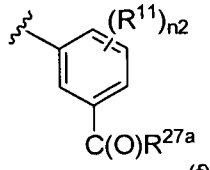
[01803] In another embodiment of the above method(s), the MEK compound of Formula I(M) is selected from Group D and according to Formula I(aa) or I(bb):



I(aa) or  **I(bb)**

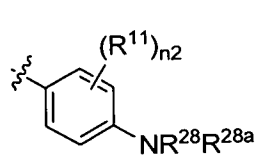
wherein R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ and wherein the heteroaryl is optionally substituted with alkyl.

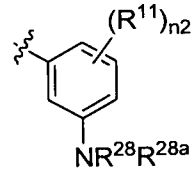
[01804] In another embodiment of the above method(s), R^2 of Formula I(J) is



(f)

[01805] In another embodiment of the above method(s), R^2 of Formula I(J) is

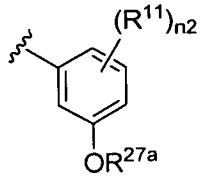


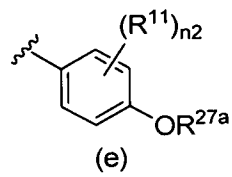
(a) or 

(b),

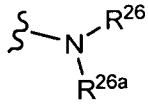
wherein R^{28a} is selected from lower alkyl, dialkylaminoalkyl, alkoxyalkyl, arylalkyl, heteroarylalkyl, and hetercycloalkylalkyl.

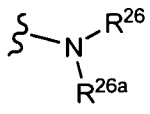
[01806] In another embodiment of the above method(s), R^2 of Formula I(J) is

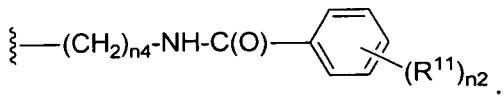


(g) or 

(e).

[01807] In another embodiment of the above method(s), L of Formula I(J) is a bond, Z is  , R^{25} is hydrogen and E and D are hydrogen.

[01808] In another embodiment of the above method(s), Z of Formula I(J) is  , R^{26a} is $-C(O)R^{32}$, R^{26} is hydrogen, and R^{32} is selected from tetrahydrofuran, pyrrolidinyl or pryimidinyl, wherein R^{32} is optionally substituted with 1, 2, 3, 4 or 5 groups selected from hydroxyl, oxo, alkyl, alkoxy, amino, hydroxyalkyl and halo.

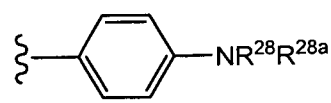
[01809] In another embodiment of the above method(s), R^2 of Formula I(J) is  .

[01810] In another embodiment of the above method(s), R^{32} of Formula I(J) is U or $-CH_2-U$, wherein U is selected from pyrolidinyl, thiazolidinyl, morpholinyl, azetidinyl, cyclobutyl, cyclopropyl, tetrahydofuranyl, pyrazinyl, imidazolyl, piperazinyl, thienyl, thienylmethyl, furanyl, phenyl, prolinamidyl, pyridinyl, tetrahydronaphthalene, tetrazolyl, isoindolinyl, pyranyl, cyclopentyl, and octahydro-1H-indolyl.

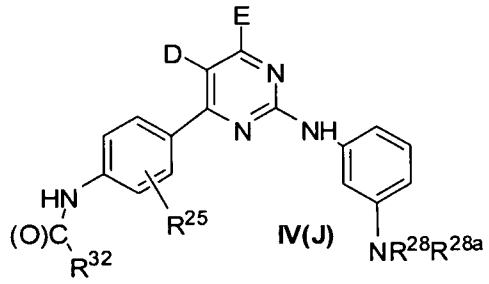
[01811] In another embodiment of the above method(s), R^{11} of Formula I(J), when present, is halo or lower alkyl.

[01812] In another embodiment of the above method(s), R^{35} of Formula I(J) is heterocycloalkylalkyl, wherein the heterocyloalkyl is selected from piperazinyl, piperidinyl, morpholinyl and dioxanyl.

[01813] In another embodiment of the above method(s), n2 of Formula I(J) is 0.

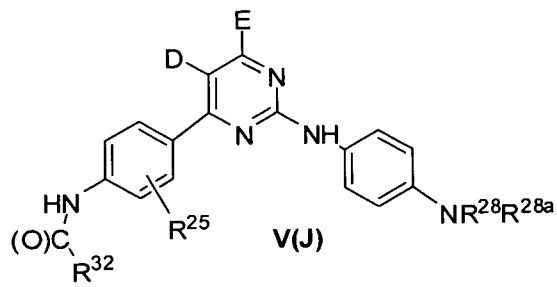
In another embodiment of the above method(s), R^2 of Formula I(J) is  , and wherein R^{28} and R^{28a}, together with the nitrogen atom to which they are attached, form a heterocycloalkyl.

[01814] In another embodiment of the above method(s), the JAK-2 compound has Formula IV(J):



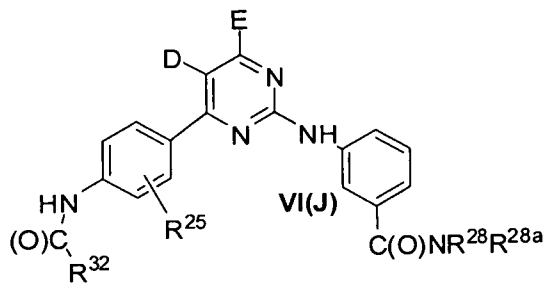
wherein and R^{28} and R^{28a}, together with the nitrogen atom to which they are attached, form a heterocycloalkyl, wherein the heterocycloalkyl is optionally substituted with one or two R^{31}.

[01815] In another embodiment of the above method(s), the JAK-2 compound has Formula V(J):



wherein R^{28} and R^{28a}, together with the nitrogen atom to which they are attached, form a heterocycloalkyl, wherein the heterocycloalkyl is optionally substituted with one or two R^{31}.

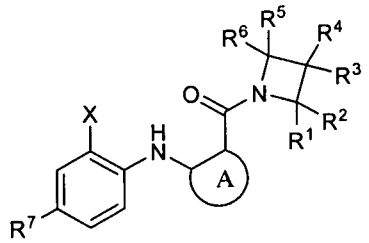
[01816] In another embodiment of the above method(s), the JAK-2 compound has Formula VI(J):



wherein R^{28} and R^{28a}, together with the nitrogen atom to which they are attached, form a heterocycloalkyl, wherein the heterocycloalkyl is optionally substituted with one or two R^{31}.

[01817] Another aspect of the invention relates to a method of treating a disease in a mammal, comprising administering to the mammal a therapeutically effective amount of a

MEK compound of Formula I(M), or a pharmaceutical composition comprising a therapeutically effective amount of the MEK compound of Formula I(M) and a pharmaceutically acceptable carrier, in combination with a therapeutically effective amount of a JAK-2 inhibitor, or a pharmaceutical composition comprising a therapeutically effective amount of a JAK-2 inhibitor and a pharmaceutically acceptable carrier, wherein the MEK compound of Formula I(M) is defined as follows:



I(M)

or a pharmaceutically acceptable salt or solvate thereof, wherein A, X, R^1, R^2, R^3, R^4, R^5, R^6, and R^7 are as defined in Group A, Group B, Group C, or Group D:

Group A

A is phenylene optionally substituted with one or two groups selected from R^{10}, R^{12}, R^{14}, and R^{16} wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen or halo;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen, halo, hydroxy, alkoxy, or amino;

R^4 is hydrogen, $-NR^8R^{8'}$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, cycloalkyl, heterocycloalkyl, or heteroaryl; wherein the alkyl is optionally substituted with one, two, or three groups independently selected from $-OR^8$, halo, nitro, $-S(O)_mR^9$, optionally substituted heterocycloalkyl, $-NR^8R^{8'}$, $-NR^8C(O)R^{8'}$, $-NR^8S(O)_2R^9$, $-NR^8C(O)OR^{8'}$, and aryl; wherein the cycloalkyl is optionally substituted with one or two groups selected from $-OR^8$ and $-NR^8R^{8'}$; wherein the heterocycloalkyl is optionally substituted with one or two groups independently selected from alkyl and $-C(O)OR^8$; and wherein the heteroaryl is optionally substituted with $-NR^8R^{8'}$; or

R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH);

m is 0;

R^7 is halo;

R^8 and $R^{8'}$ are independently selected from hydrogen, hydroxy, alkyl, alkenyl, alkynyl, aryl, heterocycloalkyl, heteroaryl, and cycloalkyl;

wherein the R^8 and $R^{8'}$ alkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, $-NR^{30}R^{30'}$ (wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), optionally substituted heteroaryl, optionally substituted cycloalkyl), optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, $-C(O)NR^{33}R^{33a}$ (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), optionally substituted aryloxy, $-S(O)_nR^{31}$ (wherein n is 0 and R^{31} is alkyl), carboxy, alkoxycarbonyl, and $-NR^{32}C(O)R^{32a}$ (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl); or wherein the alkyl is optionally substituted with one, two, three, four, or five halo;

wherein the R^8 and $R^{8'}$ heteroaryl are independently optionally substituted with one or two groups indendently selected from amino and alkyl;

wherein the R^8 and $R^{8'}$ heterocycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from alkyl, alkoxycarbonyl, optionally substituted arylalkyl, hydroxy, alkoxy, and hydroxyalkyl;

wherein the R^8 and $R^{8'}$ aryl are independently optionally substituted with one or two groups indendently selected from hydroxy, alkoxy, halo, $-NR^{32}C(O)R^{32a}$ (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl), and $-NR^{34}SO_2R^{34a}$ (wherein R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl); and

wherein the R^8 and $R^{8'}$ cycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, hydroxyalkyl, alkoxy, carboxy, $-C(O)NR^{33}R^{33a}$ (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), and optionally substituted cycloalkyl; and

R^9 is alkyl or aryl;

Group B

A is thien-3,4-diyl, benzo[*d*]isoxazol-5,6-diyl, 1*H*-indazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), benzo[*d*]oxazol-5,6-diyl, 1*H*-benzo[d]imidazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), 1*H*-benzo[*d*][1,2,3]triazol-5,6-diyl (optionally

substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), imidazo[1,2-*a*]pyridin-6,7-diyl, cinnolin-6,7-diyl, quinolin-6,7-diyl, pyridin-3,4-diyl, 1-oxido-pyridin-3,4-diyl, [1,2,4]triazolo[4,3-a]pyridin-6,7-diyl, or 2,3-dihydroimidazo[1,2-a]pyridin-6,7-diyl; wherein A is optionally substituted with one, two, or three groups independently selected from R^{10}, R^{12}, R^{14}, R^{16} and R^{19} wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen, alkyl, halo, or amino; and R^{19} is hydrogen or alkyl;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

R^4 is $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ and wherein the heteroaryl is optionaly substituted with alkyl;

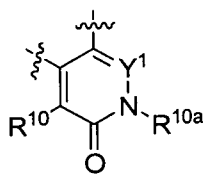
R^7 is halo;

R^8 is hydrogen or alkyl; and

$R^{8'}$ is hydrogen, alkyl, or cycloalkyl; wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl;

Group C

A is



(a)

R^{10} is hydrogen or halo;

R^{10a} is hydrogen or alkyl;

Y^1 is =CH- or =N-;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

R^4 is $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ and wherein the heteroaryl is optionaly substituted with alkyl;

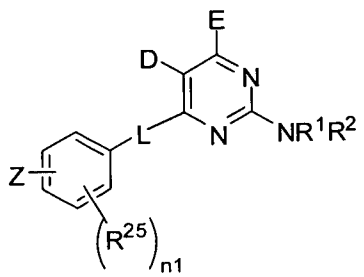
R^7 is halo;

R^8 is hydrogen or alkyl; and

$R^{8'}$ is hydrogen, alkyl, or cycloalkyl; wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl;

wherein the mammal is in need of the treatment.

[01818] Another aspect of the invention relates to a method of treating a disease in a mammal, comprising administering to the mammal a therapeutically effective amount of a MEK inhibitor, or a pharmaceutical composition comprising a therapeutically effective amount of the MEK inhibitor and a pharmaceutically acceptable carrier, in combination with a therapeutically effective amount of a JAK-2 compound of Formula I(J), or a pharmaceutical composition comprising a therapeutically effective amount of the JAK-2 compound of Formula I(J) and a pharmaceutically acceptable carrier, wherein the JAK-2 compound of Formula I(J) is defined as follows:



I(J)

or a pharmaceutically acceptable salt or solvate thereof, wherein

D is hydrogen, halo, $-CF_3$, heterocycloalkyl or alkyl;

E is hydrogen, halo, $-CF_3$, heterocycloalkyl or alkyl; or

D and E, together with the carbon atoms to which they are attached, form a 5-7 membered heteroaryl or a 5-7 membered heterocycloalkyl, wherein the 5-7 membered heteroaryl or 5-7 membered heterocycloalkyl are each fused to the pyrimidinyl moiety to which D and E are attached;

L is a bond, -O- or -N(H)-;

Z is selected from alkoxy, cycloalkyl, heteroaryl optionally substituted with alkyl, halo, $-C(O)OR^{26}$, -C(=N-OH)alkyl, $-C(O)R^8$, $-C(O)NR^{30}R^{30a}$, $-CH_2R^2$, $-(CH_2)_{n5}NR^{26}R^{26a}$, $-CF_3$, -CN, $-SO_2R^{12}$, $-S-R^{12a}$, $-OR^{32a}$, $-NHC(O)R^{32}$, aryl, and heterocycloalkyl optionally substituted with 1 or 2 oxo, or

Z and R^{25}, together with the carbon atoms to which they are attached, join to form a 5 or 6 membered heterocycloalkyl, a 5 or 6 membered heteroaryl, or a 5 or 6 membered cycloalkyl ring, wherein the 5 or 6 membered heterocycloalkyl, 5 or 6 membered

heteroaryl, or 5 or 6 membered cycloalkyl ring are fused to the phenyl moiety to which Z and R^{25} are attached, and wherein the 5 or 6 membered heterocycloalkyl, 5 or 6 membered heteroaryl, or 5 or 6 membered cycloalkyl ring are each optionally substituted with 1, 2, or 3 groups independently selected from oxo, alkyl, alkoxy and halo;

n1 is 0, 1, 2, 3, or 4, and each n1 is independently selected when more than one n1 is present;

n2 is 0, 1, 2, 3, or 4, and each n2 is independently selected when more than one n2 is present;

n3 is 0, 1, 2, or 3, and each n3 is independently selected when more than one n3 is present;

n4 is 0, 1, 2, 3 or 4, and each n4 is independently selected when more than one n4 is present;

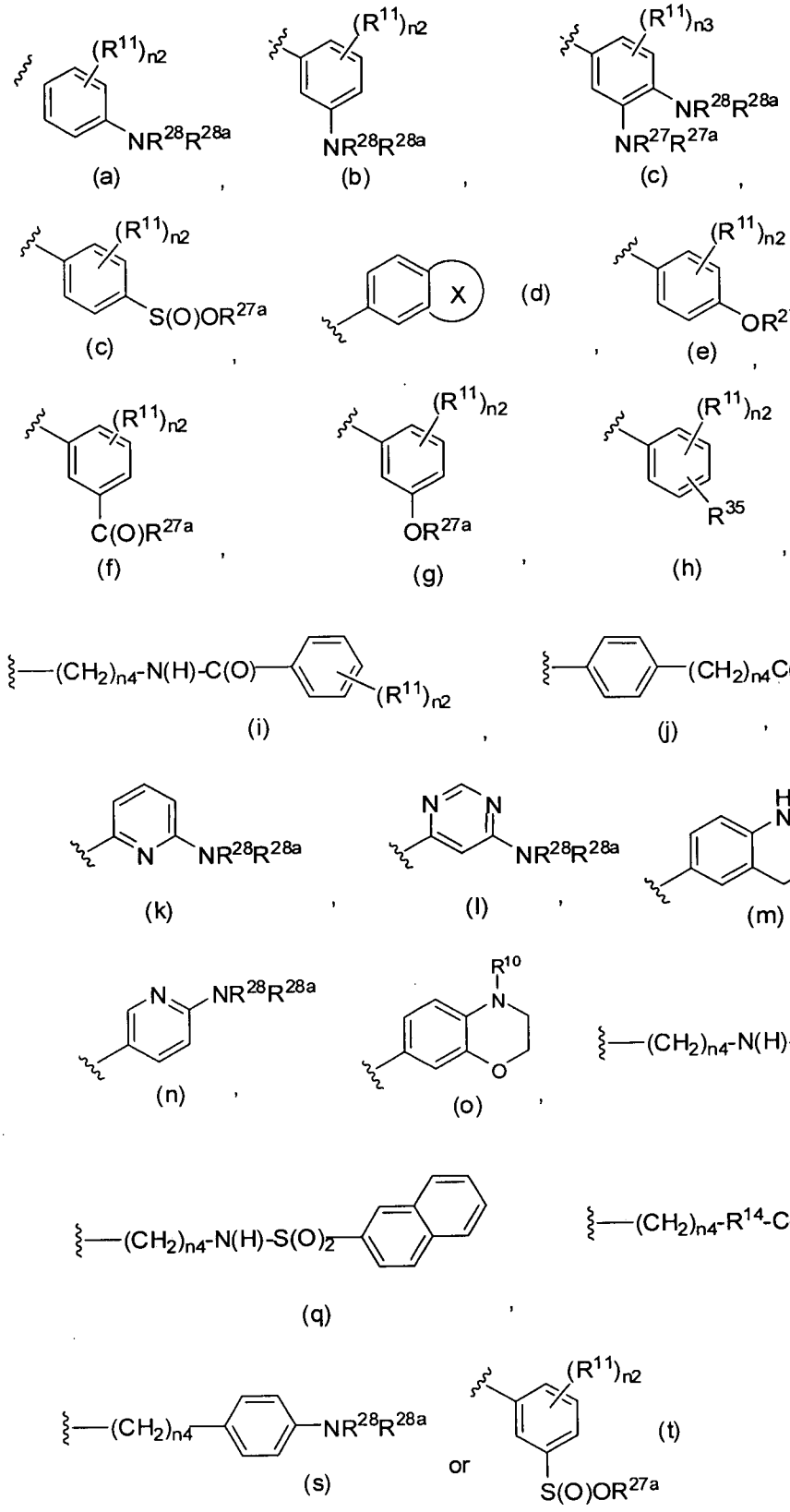
n5 is 0, 1, 2, 3 or 4, and each n5 is independently selected when more than one n5 is present;

p is 0-3;

r is 1-3;

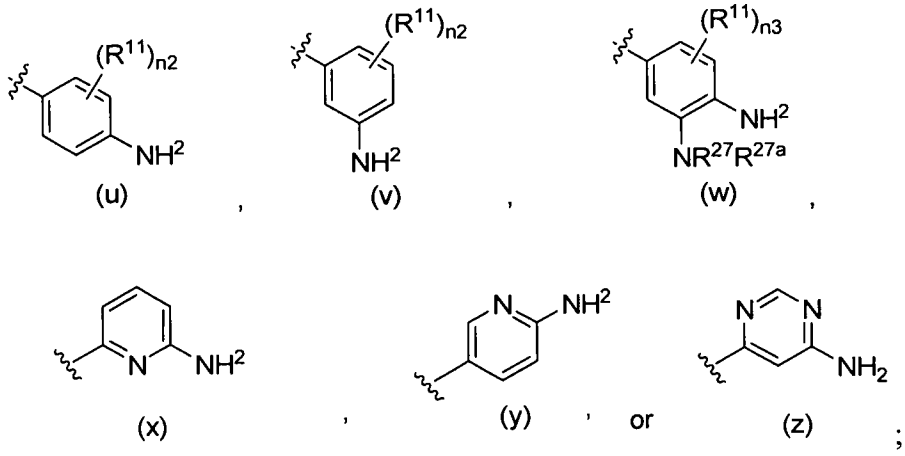
R^1 is hydrogen;

R^2 is selected from one of the following groups:



;

or R^2 is selected from one of the following groups:



;

ring X in formula (d) of R^2 is a 5 or 6 membered unsaturated heterocyclic ring fused to the two carbon atoms of the phenyl moiety to which ring X is attached, wherein ring X contains 1 or 2 nitrogen atoms;

R^7, $R^{7'}$, R^9, R^{10}, R^{12} and R^{15} are each independently hydrogen, alkyl, alkoxy, or alkoxyalkyl;

R^8 is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, hydroxyalkyl, alkoxyalkyl, dihydroxyalkyl, alkylamino, dialkylamino, aminoalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, alkylaminoalkyl, dialkylaminoalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl;

each R^{11}, when R^{11} is present, is independently selected from alkyl, alkenyl, lower alkynyl, $-CF_3$, alkoxy, halo, haloalkoxy, haloalkyl, aminoalkyl, aminoalkoxy, alkylaminoalkyl, alkylaminoalkoxy, dialkylaminoalkyl, dialkylaminoalkoxy, oxo, thioalkyl, alkylthioalkyl, $-(CH_2)_p-OR^{17}$, -CN, $-O-CH_2-C(O)-R^{17}$, $-C(O)R^{16}$, $-(CH_2)_p-C(O)OR^{17}$, $-S(O)_2R^{17}$, $-S(O)_2NR^{15}R^{17}$, aryl, heteroaryl, cycloalkyl, arylalkyl, arylalkoxy, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at any ring position with 1, 2, 3 or 4 R^{21};

R^{12} is hydrogen or alkyl;

R^{12a} is hydrogen or alkyl;

R^{13} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with 1, 2, 3, 4 or 5 groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl are independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

R^{14} is a bond, heterocycloalkyl or cycloalkyl;

R^{16} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, dialkylaminoalkyl, $-(CH_2)_r-C(O)OR^7$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl is optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

R^{17} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl,

aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, dialkylaminoalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl is optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

each R^{21}, when R^{21} is present, is independently selected from alkyl, alkenyl, lower alkynyl, cyano, halo, haloalkoxy, haloalkyl, hydroxyalkyl, amino, alkylamino, dialkylamino, dialkylaminoalkyl, dialkylaminoalkyloxy, haloalkyl, oxo, $-OR^{13}$, $-NHS(O)_2R^{17}$, $-S(O)_2R^{17}$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-C(O)NR^{15}R^{17}$, $-NR^{15}C(O)R^{17}$, aryl, arylalkyl, heteroarylalkyl, aryloxy, and heteroaryl; wherein each of the aryl, arylalkyl, heteroarylalkyl, aryloxy, and heteroaryl within R^{21} are optionally substituted at any ring position with 1, 2, or 3 groups selected from alkyl, lower alkoxy halo, phenyl, heteroaryl and alkylheteroalkyl;

R^{25} is selected from alkyl, alkenyl, lower alkyl, halo, haloalkyl, haloalkoxy, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, $-OR^{12}$, cyano, $-CH_2NHC(O)OR^7$, $-CH_2NHC(O)R^7$, $-SR^7$, $-S(O)_2R^7$, $-S(O)_2NR^7R^8$, $-C(O)OR^8$, $-C(O)NR^7R^8$, cycloalkyl, heterocycloalkyl, aryl and heteroaryl; wherein the cycloalkyl, heterocycloalkyl, aryl and heteroaryl are each optionally substituted with one, two or three groups independently selected from alkyl, alkenyl, halo, haloalkoxy, haloalkyl, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, $-OR^8$, $-NHS(O)_2R^8$, cyano, $-C(O)R^8$, $-CH_2NHC(O)OR^7$, $-CH_2NHC(O)R^7$, $-SR^7$, $-S(O)_2R^7$, $-S(O)_2NR^7R^8$, $-C(O)OR^8$, $-C(O)NR^7R^8$, $-NR^{7'}C(O)-CHR^3-OR^8$, $-NR^{7'}C(O)-CHR^3-NR^7-R^8$, and $-NR^7C(O)R^8$;

R^{26} is hydrogen, -C(O)-phenyl or alkyl, wherein the -C(O)-phenyl is optionally substituted at any ring position with 1, 2 or 3 halo;

R^{26a} is hydrogen, alkyl, heteroaryl, $-C(O)R^{32}$, $-C(O)NHR^{32a}$, $-S(O)_2R^9$, $-SR^9$, $-C(O)OR^{32}$, or $-C(O)NR^{32a}R^{32}$;

R^{27} and R^{28} are each independently selected from alkyl, alkenyl, hydroxy, alkoxy, and alkoxyalkyl;

R^{27a} and R^{28a} are independently selected from hydrogen, alkyl, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, dialkylaminoalkyl, arylcarbonylalkyl, aryloxyalkyl, dialkylaminoalkyl, alkyl-O-C(O)heterocylcoalkyl, $-(CH_2)_{n4}$heterocycloalkyl, heterocycloalkylalkyl, heteroaryl, heteroarylalkyl, $-(CH_2)_{n4}-C(O)R^{29}$, $-(CH_2)_{n4}NR^{28}R^{28a}$, $-(CH_2)_{n4}NHR^{28a}$, $-CH(phenyl)_2$, $-S(O)_2R^{29}$, $-C(O)R^{29}$, $-C(O)OR^{29}$, and $-C(O)NR^{29a}R^{29}$, wherein the aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{27a} and R^{28a} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkylcarbonyl, phenyl, phenoxy, arylcarbonyl, $-CF_3$, oxo, $-OCF_3$, alkoxyphenyl, and heteroaryl optionally substituted with alkyl or halo;

or R^{27} and R^{27a}, together with the nitrogen to which they are attached, form heterocycloalkylamino, heterocycloalkyl or heteroaryl, wherein the heterocycloalkylamino and heteroaryl are each independently optionally substituted with 1, 2, 3, 4, or 5 R^{31};

or R^{28} and R^{28a} together with the nitrogen to which they are attached form heterocycloalkyl or heteroaryl, wherein the heterocycloalkyl and heteroaryl are each optionally substituted with 1, 2, 3, 4, or 5 R^{31};

R^{29a} is hydrogen or alkyl;

R^{29} is selected from alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{29} are each optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkylcarbonyl, phenyl, phenoxy, arylcarbonyl, $-CF_3$, oxo, $-OCF_3$, alkoxyphenyl, and heteroaryl optionally substituted with alkyl or halo;

R^{30a} is hydrogen or alkyl;

R^{30} is selected from hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkoxycarbonylalkyl, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, aryl, arylalkyl, phenoxyalkyl, cycloalkyl, cycloalkylalkyl,

heteroaryl, heteroarylalkyl, arylheteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, arylalkyl, phenoxyalkyl, cycloalkyl, arylheteroarylalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{30} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkoxyalkyl, $-C(O)OCH_3$, $-CF_3$, $-OCF_3$, alkylcarbonyl, phenyl, phenoxy, alkylphenoxy, dialkylaminoalkoxy and heteroaryl;

R^{31} is selected from alkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkylthioalkyl, $-C(O)R^{30}$, $-C(O)NR^{30}R^{30a}$, $-C(O)OR^{30}$, $-S(O)_2R^{30}$, amino, dihydroxyalkyl, arylcarbonyl, alkylcarbonylamino, alkoxyphenyl, phenylalkoxyalkyl, arylheteroarylalkyl, alkylamino, -O-dialkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, dialkylaminoalkoxy, oxo, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, spirocyclic cycloalkyl, spirocyclic heterocycloalkyl, and heterocycloalkylalkyl, wherein the aryl, arylalkyl, cycloalkyl, arylheteroarylalkyl, arylalkoxyalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{31} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, $-CF_3$, $-OCF_3$, cyano, alkoxy, alkoxyalkyl, $-C(O)OCH_3$, alkylcarbonyl, phenyl optionally substituted at any ring position with halo, phenoxy, alkylphenoxy, arylalkoxyalkyl, dialkylaminoalkoxy and heteroaryl;

R^{32a} is hydrogen, $-OCF_3$, $-CF_3$, or alkyl;

R^{32} is selected from aryl, arylalkyl, arylalkoxy, arylcycloalkyl, alkoxycarbonylalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkylhydroxyalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl, wherein the aryl, arylalkyl, cycloalkyl, arylcycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from hydroxy, oxo, alkyl, alkoxy, amino, hydroxyalkyl, alkylcarbonyl, alkoxycarbonyl, halo, $-CF_3$, $-OCF_3$, aminoalkyl, alkylaminoalkyl, aryl and dialkylaminoalkyl, and wherein the alkyl portion of the heteroarylalkyl can be substituted with amino;

or R^{32} is alkyl optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from hydroxy, alkoxycarbonyl, alkoxy, $-CF_3$, halo, aminocarbonyl, alkylaminocarbonyl, alkoxycarbonylalkylamino, dialkylaminocarbonyl, $-NR^{34}R^{34a}$ and phenyl optionally substituted with 1, 2, or 3 halo;

or R^{32} is alkylamino or arylalkylamino;

R^{34} is hydrogen or alkyl;

R^{34a} is selected from hydrogen, alkyl, heteroaryl, aryl, aminoalkyl, aminocarbonylalkyl, heteroarylalkyl, arylalkoxy and arylalkyloxycarbonylalkyl; wherein the heteroaryl, aryl, heteroarylalkyl, arylalkoxy or arylalkyloxycarbonylalkyl are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from hydroxy, oxo, alkyl, amino, hydroxyalkyl, alkylcarbonyl, alkoxycarbonyl, halo, aminoalkyl, alkylaminoalkyl, and dialkylaminoalkyl; and

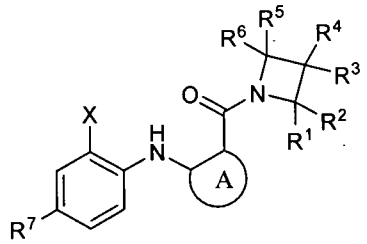
R^{35} is selected from halo, $-(CH_2)_pC(O)OR_{17}$, cycloalkyl, heterocycloalkyl, and heterocycloalklylalkyl; wherein the heterocycloalkyl and heterocycloalklylalkyl are each optionally substituted with 1, 2, 3, 4, or 5 groups each independently selected from alkyl, alkoxy, and halo,

wherein the mammal is in need of the treatment.

[01819] The foregoing invention has been described in some detail by way of illustration and example, for purposes of clarity and understanding. The invention has been described with reference to various specific embodiments and techniques. However, it should be understood that many variations and modifications may be made while remaining within the spirit and scope of the invention. It will be obvious to one of skill in the art that changes and modifications may be practiced within the scope of the appended claims. Therefore, it is to be understood that the above description is intended to be illustrative and not restrictive. All patents, patent applications and publications cited in this application are hereby incorporated by reference in their entirety for all purposes to the same extent as if each individual patent, patent application or publication were so individually denoted.

What is claimed is:

1. A method of treating a disease in a mammal, comprising administering to the mammal a therapeutically effective amount of a MEK compound of Formula I(M), or a pharmaceutical composition comprising a therapeutically effective amount of the MEK compound of Formula I(M) and a pharmaceutically acceptable carrier, in combination with a therapeutically effective amount of a JAK-2 compound of Formula I(J), or a pharmaceutical composition comprising a therapeutically effective amount of the JAK-2 compound of Formula I(J) and a pharmaceutically acceptable carrier, wherein the MEK compound of Formula I(M) is defined as follows:



I(M)

or a pharmaceutically acceptable salt or solvate thereof, wherein A, X, R^1, R^2, R^3, R^4, R^5, R^6, and R^7 are as defined in Group A, Group B, Group C, or Group D:

Group A

A is phenylene optionally substituted with one or two groups selected from R^{10}, R^{12}, R^{14}, and R^{16} wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen or halo;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen, halo, hydroxy, alkoxy, or amino;

R^4 is hydrogen, $-NR^8R^{8'}$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, cycloalkyl, heterocycloalkyl, or heteroaryl; wherein the alkyl is optionally substituted with one, two, or three groups independently selected from $-OR^8$, halo, nitro, $-S(O)_mR^9$, optionally substituted heterocycloalkyl, $-NR^8R^{8'}$, $-NR^8C(O)R^{8'}$, $-NR^8S(O)_2R^9$, $-NR^8C(O)OR^{8'}$, and aryl; wherein the cycloalkyl is optionally substituted with one or two groups selected from $-OR^8$ and

$-NR^8R^{8'}$; wherein the heterocycloalkyl is optionally substituted with one or two groups independently selected from alkyl and $-C(O)OR^8$; and wherein the heteroaryl is optionally substituted with $-NR^8R^{8'}$; or

R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH);

m is 0;

R^7 is halo;

R^8 and $R^{8'}$ are independently selected from hydrogen, hydroxy, alkyl, alkenyl, alkynyl, aryl, heterocycloalkyl, heteroaryl, and cycloalkyl;

wherein the R^8 and $R^{8'}$ alkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, $-NR^{30}R^{30'}$ (wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), optionally substituted heteroaryl, optionally substituted cycloalkyl), optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, $-C(O)NR^{33}R^{33a}$ (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), optionally substituted aryloxy, $-S(O)_nR^{31}$ (wherein n is 0 and R^{31} is alkyl), carboxy, alkoxycarbonyl, and $-NR^{32}C(O)R^{32a}$ (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl); or wherein the alkyl is optionally substituted with one, two, three, four, or five halo;

wherein the R^8 and $R^{8'}$ heteroaryl are independently optionally substituted with one or two groups indendently selected from amino and alkyl;

wherein the R^8 and $R^{8'}$ heterocycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from alkyl, alkoxycarbonyl, optionally substituted arylalkyl, hydroxy, alkoxy, and hydroxyalkyl;

wherein the R^8 and $R^{8'}$ aryl are independently optionally substituted with one or two groups indendently selected from hydroxy, alkoxy, halo, $-NR^{32}C(O)R^{32a}$ (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl), and $-NR^{34}SO_2R^{34a}$ (wherein R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl); and

wherein the R^8 and $R^{8'}$ cycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, hydroxyalkyl, alkoxy, carboxy, $-C(O)NR^{33}R^{33a}$ (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), and optionally substituted cycloalkyl; and

R^9 is alkyl or aryl;

Group B

A is thien-3,4-diyl, benzo[*d*]isoxazol-5,6-diyl, 1*H*-indazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), benzo[*d*]oxazol-5,6-diyl, 1*H*-benzo[d]imidazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), 1*H*-benzo[*d*][1,2,3]triazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), imidazo[1,2-*a*]pyridin-6,7-diyl, cinnolin-6,7-diyl, quinolin-6,7-diyl, pyridin-3,4-diyl, 1-oxido-pyridin-3,4-diyl, [1,2,4]triazolo[4,3-a]pyridin-6,7-diyl, or 2,3-dihydroimidazo[1,2-a]pyridin-6,7-diyl; wherein A is optionally substituted with one, two, or three groups independently selected from R^{10}, R^{12}, R^{14}, R^{16} and R^{19} wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen, alkyl, halo, or amino; and R^{19} is hydrogen or alkyl;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

R^4 is $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ and wherein the heteroaryl is optionaly substituted with alkyl;

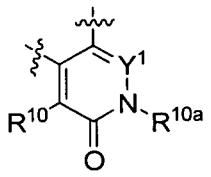
R^7 is halo;

R^8 is hydrogen or alkyl; and

$R^{8'}$ is hydrogen, alkyl, or cycloalkyl; wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl;

Group C

A is



(a)

R^{10} is hydrogen or halo;

R^{10a} is hydrogen or alkyl;

Y^1 is =CH- or =N-;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

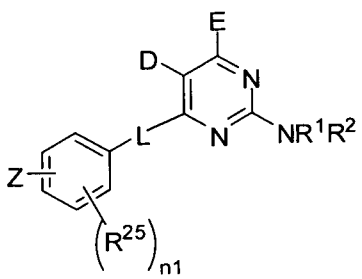
R^4 is $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ and wherein the heteroaryl is optionaly substituted with alkyl;

R^7 is halo;

R^8 is hydrogen or alkyl; and

$R^{8'}$ is hydrogen, alkyl, or cycloalkyl; wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl;

and wherein the JAK-2 compound is defined as follows:



I(J)

or a pharmaceutically acceptable salt or solvate thereof, wherein

D is hydrogen, halo, $-CF_3$, heterocycloalkyl or alkyl;

E is hydrogen, halo, $-CF_3$, heterocycloalkyl or alkyl; or

D and E, together with the carbon atoms to which they are attached, form a 5-7 membered heteroaryl or a 5-7 membered heterocycloalkyl, wherein the 5-7

membered heteroaryl or 5-7 membered heterocycloalkyl are each fused to the pyrimidinyl moiety to which D and E are attached;

L is a bond, -O- or -N(H)-;

Z is selected from alkoxy, cycloalkyl, heteroaryl optionally substituted with alkyl, halo,

$-C(O)OR^{26}$, -C(=N-OH)alkyl, $-C(O)R^{8}$, $-C(O)NR^{30}R^{30a}$, $-CH_2R^{2}$, $-(CH_2)_{n5}NR^{26}R^{26a}$, $-CF_3$, -CN, $-SO_2R^{12}$, $-S-R^{12a}$, $-OR^{32a}$, $-NHC(O)R^{32}$, aryl, and heterocycloalkyl optionally substituted with 1 or 2 oxo, or

Z and R^{25}, together with the carbon atoms to which they are attached, join to form a 5 or 6 membered heterocycloalkyl, a 5 or 6 membered heteroaryl, or a 5 or 6 membered cycloalkyl ring, wherein the 5 or 6 membered heterocycloalkyl, 5 or 6 membered heteroaryl, or 5 or 6 membered cycloalkyl ring are fused to the phenyl moiety to which Z and R^{25} are attached, and wherein the 5 or 6 membered heterocycloalkyl, 5 or 6 membered heteroaryl, or 5 or 6 membered cycloalkyl ring are each optionally substituted with 1, 2, or 3 groups independently selected from oxo, alkyl, alkoxy and halo;

n1 is 0, 1, 2, 3, or 4, and each n1 is independently selected when more than one n1 is present;

n2 is 0, 1, 2, 3, or 4, and each n2 is independently selected when more than one n2 is present;

n3 is 0, 1, 2, or 3, and each n3 is independently selected when more than one n3 is present;

n4 is 0, 1, 2, 3 or 4, and each n4 is independently selected when more than one n4 is present;

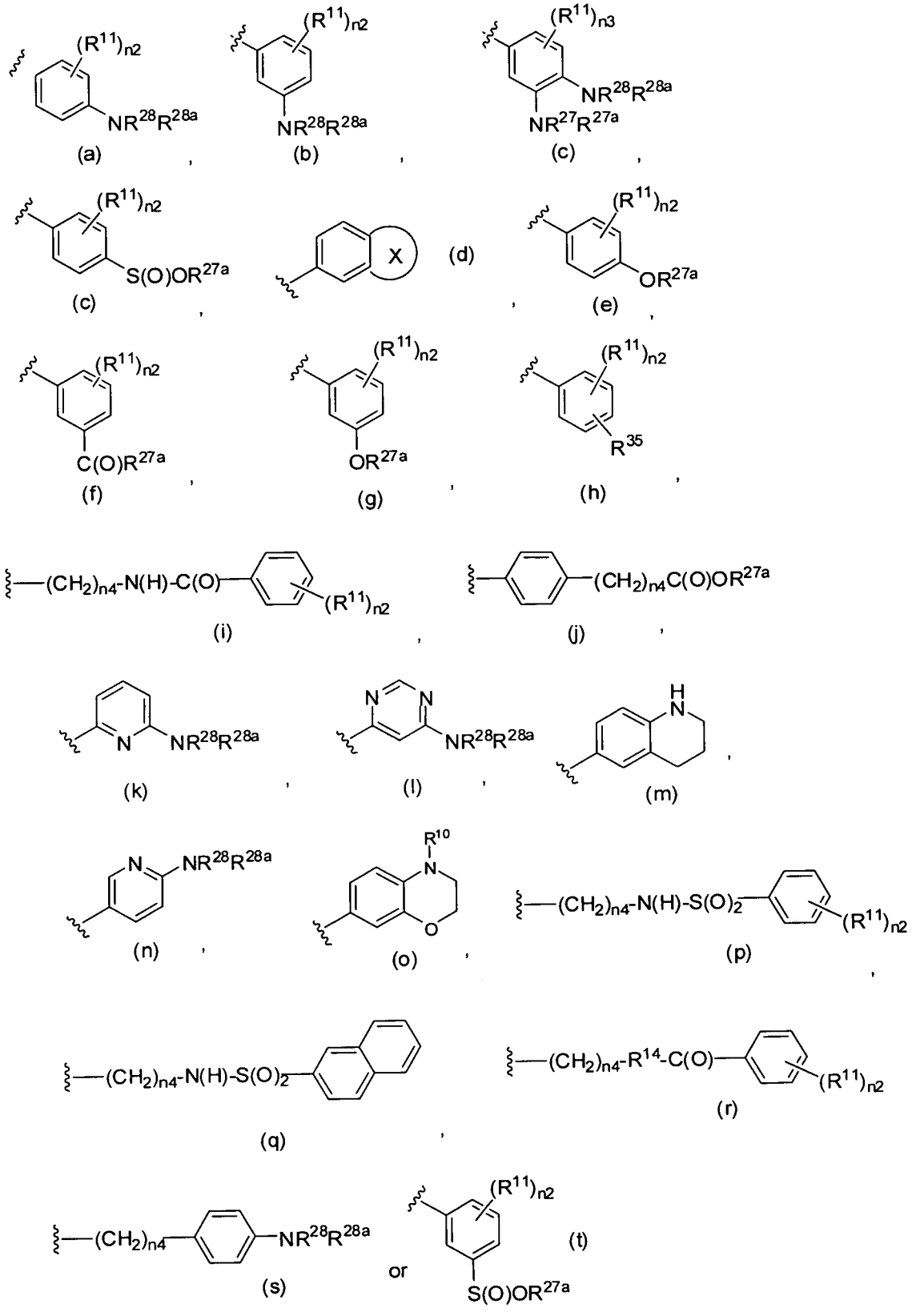
n5 is 0, 1, 2, 3 or 4, and each n5 is independently selected when more than one n5 is present;

p is 0-3;

r is 1-3;

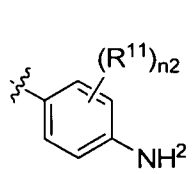
R^1 is hydrogen;

R^2 is selected from one of the following groups:

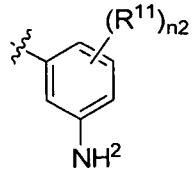


;

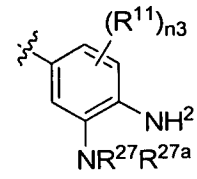
or R^2 is selected from one of the following groups:



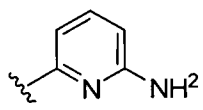
(u) ,



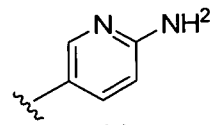
(v) ,



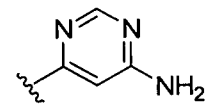
(w) ,



(x) ,



(y) , or



(z) ;

ring X in formula (d) of R^2 is a 5 or 6 membered unsaturated heterocyclic ring fused to the two carbon atoms of the phenyl moiety to which ring X is attached, wherein ring X contains 1 or 2 nitrogen atoms;

R^7, $R^{7'}$, R^9, R^{10}, R^{12} and R^{15} are each independently hydrogen, alkyl, alkoxy, or alkoxyalkyl;

R^8 is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, hydroxyalkyl, alkoxyalkyl, dihydroxyalkyl, alkylamino, dialkylamino, aminoalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, alkylaminoalkyl, dialkylaminoalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl;

each R^{11}, when R^{11} is present, is independently selected from alkyl, alkenyl, lower alkynyl,

$-CF_3$, alkoxy, halo, haloalkoxy, haloalkyl, aminoalkyl, aminoalkoxy, alkylaminoalkyl, alkylaminoalkoxy, dialkylaminoalkyl, dialkylaminoalkoxy, oxo, thioalkyl, alkylthioalkyl, $-(CH_2)_p-OR^{17}$, -CN, $-O-CH_2-C(O)-R^{17}$,

$-C(O)R^{16}$, $-(CH_2)_p-C(O)OR^{17}$, $-S(O)_2R^{17}$, $-S(O)_2NR^{15}R^{17}$, aryl, heteroaryl, cycloalkyl, arylalkyl, arylalkoxy, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at any ring position with 1, 2, 3 or 4 R^{21};

R^{12} is hydrogen or alkyl;

R^{12a} is hydrogen or alkyl;

R^{13} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with 1, 2, 3, 4 or 5 groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl are independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

R^{14} is a bond, heterocycloalkyl or cycloalkyl;

R^{16} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, dialkylaminoalkyl,
$-(CH_2)_r-C(O)OR^7$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and

heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl is optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

R^{17} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, dialkylaminoalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl is optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

each R^{21}, when R^{21} is present, is independently selected from alkyl, alkenyl, lower alkynyl, cyano, halo, haloalkoxy, haloalkyl, hydroxyalkyl, amino, alkylamino, dialkylamino, dialkylaminoalkyl, dialkylaminoalkyloxy, haloalkyl, oxo, $-OR^{13}$, $-NHS(O)_2R^{17}$, $-S(O)_2R^{17}$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-C(O)NR^{15}R^{17}$, $-NR^{15}C(O)R^{17}$, aryl, arylalkyl, heteroarylalkyl, aryloxy, and heteroaryl; wherein each of the aryl, arylalkyl, heteroarylalkyl, aryloxy, and heteroaryl within R^{21} are optionally substituted at any ring position with 1, 2, or 3 groups

selected from alkyl, lower alkoxy halo, phenyl, heteroaryl and alkylheteroalkyl;

R^{25} is selected from alkyl, alkenyl, lower alkyl, halo, haloalkyl, haloalkoxy, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, $-OR^{12}$, cyano, $-CH_2NHC(O)OR^7$, $-CH_2NHC(O)R^7$, $-SR^7$, $-S(O)_2R^7$, $-S(O)_2NR^7R^8$, $-C(O)OR^8$, $-C(O)NR^7R^8$, cycloalkyl, heterocycloalkyl, aryl and heteroaryl; wherein the cycloalkyl, heterocycloalkyl, aryl and heteroaryl are each optionally substituted with one, two or three groups independently selected from alkyl, alkenyl, halo, haloalkoxy, haloalkyl, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, $-OR^8$, $-NHS(O)_2R^8$, cyano, $-C(O)R^8$, $-CH_2NHC(O)OR^7$, $-CH_2NHC(O)R^7$, $-SR^7$, $-S(O)_2R^7$, $-S(O)_2NR^7R^8$, $-C(O)OR^8$, $-C(O)NR^7R^8$, $-NR^{7'}C(O)-CHR^3-OR^8$, $-NR^{7'}C(O)-CHR^3-NR^7-R^8$, and $-NR^7C(O)R^8$;

R^{26} is hydrogen, -C(O)-phenyl or alkyl, wherein the -C(O)-phenyl is optionally substituted at any ring position with 1, 2 or 3 halo;

R^{26a} is hydrogen, alkyl, heteroaryl, $-C(O)R^{32}$, $-C(O)NHR^{32a}$, $-S(O)_2R^9$, $-SR^9$, $-C(O)OR^{32}$, or $-C(O)NR^{32a}R^{32}$;

R^{27} and R^{28} are each independently selected from alkyl, alkenyl, hydroxy, alkoxy, and alkoxyalkyl;

R^{27a} and R^{28a} are independently selected from hydrogen, alkyl, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, dialkylaminoalkyl, arylcarbonylalkyl, aryloxyalkyl, dialkylaminoalkyl, alkyl-O-C(O)heterocylcoalkyl, $-(CH_2)_{n4}$heterocycloalkyl, heterocycloalkylalkyl, heteroaryl, heteroarylalkyl, $-(CH_2)_{n4}-C(O)R^{29}$, $-(CH_2)_{n4}NR^{28}R^{28a}$, $-(CH_2)_{n4}NHR^{28a}$, $-CH(phenyl)_2$, $-S(O)_2R^{29}$, $-C(O)R^{29}$, $-C(O)OR^{29}$, and $-C(O)NR^{29a}R^{29}$, wherein the aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{27a} and R^{28a} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkylcarbonyl, phenyl, phenoxy, arylcarbonyl, $-CF_3$, oxo, $-OCF_3$, alkoxyphenyl, and heteroaryl optionally substituted with alkyl or halo;

or R^{27} and R^{27a}, together with the nitrogen to which they are attached, form heterocycloalkylamino, heterocycloalkyl or heteroaryl, wherein the heterocycloalkylamino and heteroaryl are each independently optionally substituted with 1, 2, 3, 4, or 5 R^{31};

or R^{28} and R^{28a} together with the nitrogen to which they are attached form heterocycloalkyl or heteroaryl, wherein the heterocycloalkyl and heteroaryl are each optionally substituted with 1, 2, 3, 4, or 5 R^{31};

R^{29a} is hydrogen or alkyl;

R^{29} is selected from alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{29} are each optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkylcarbonyl, phenyl, phenoxy, arylcarbonyl, $-CF_3$, oxo, $-OCF_3$, alkoxyphenyl, and heteroaryl optionally substituted with alkyl or halo;

R^{30a} is hydrogen or alkyl;

R^{30} is selected from hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkoxycarbonylalkyl, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, aryl, arylalkyl, phenoxyalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, arylheteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, arylalkyl, phenoxyalkyl, cycloalkyl, arylheteroarylalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{30} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkoxyalkyl, $-C(O)OCH_3$, $-CF_3$, $-OCF_3$, alkylcarbonyl, phenyl, phenoxy, alkylphenoxy, dialkylaminoalkoxy and heteroaryl;

R^{31} is selected from alkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkylthioalkyl, $-C(O)R^{30}$, $-C(O)NR^{30}R^{30a}$, $-C(O)OR^{30}$, $-S(O)_2R^{30}$, amino, dihydroxyalkyl, arylcarbonyl, alkylcarbonylamino, alkoxyphenyl, phenylalkoxyalkyl, arylheteroarylalkyl, alkylamino,

-O-dialkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, dialkylaminoalkoxy, oxo, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, spirocyclic cycloalkyl, spirocyclic heterocycloalkyl, and heterocycloalkylalkyl, wherein the aryl, arylalkyl, cycloalkyl, arylheteroarylalkyl, arylalkoxyalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{31} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, $-CF_3$, $-OCF_3$, cyano, alkoxy, alkoxyalkyl, $-C(O)OCH_3$, alkylcarbonyl, phenyl optionally substituted at any ring position with halo, phenoxy, alkylphenoxy, arylalkoxyalkyl, dialkylaminoalkoxy and heteroaryl;

R^{32a} is hydrogen, $-OCF_3$, $-CF_3$, or alkyl;

R^{32} is selected from aryl, arylalkyl, arylalkoxy, arylcycloalkyl, alkoxycarbonylalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkylhydroxyalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl, wherein the aryl, arylalkyl, cycloalkyl, arylcycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from hydroxy, oxo, alkyl, alkoxy, amino, hydroxyalkyl, alkylcarbonyl, alkoxycarbonyl, halo, $-CF_3$, $-OCF_3$, aminoalkyl, alkylaminoalkyl, aryl and dialkylaminoalkyl, and wherein the alkyl portion of the heteroarylalkyl can be substituted with amino;

or R^{32} is alkyl optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from hydroxy, alkoxycarbonyl, alkoxy, $-CF_3$, halo, aminocarbonyl, alkylaminocarbonyl, alkoxycarbonylalkylamino, dialkylaminocarbonyl, $-NR^{34}R^{34a}$ and phenyl optionally substituted with 1, 2, or 3 halo;

or R^{32} is alkylamino or arylalkylamino;

R^{34} is hydrogen or alkyl;

R^{34a} is selected from hydrogen, alkyl, heteroaryl, aryl, aminoalkyl, aminocarbonylalkyl, heteroarylalkyl, arylalkoxy and arylalkyloxycarbonylalkyl; wherein the heteroaryl, aryl, heteroarylalkyl, arylalkoxy or arylalkyloxycarbonylalkyl are each independently optionally substituted at any

ring position with 1, 2, 3, 4, or 5 groups selected from hydroxy, oxo, alkyl, amino, hydroxyalkyl, alkylcarbonyl, alkoxycarbonyl, halo, aminoalkyl, alkylaminoalkyl, and dialkylaminoalkyl; and

R^{35} is selected from halo, $-(CH_2)_pC(O)OR_{17}$, cycloalkyl, heterocycloalkyl, and heterocycloalklylalkyl; wherein the heterocycloalkyl and heterocycloalklylalkyl are each optionally substituted with 1, 2, 3, 4, or 5 groups each independently selected from alkyl, alkoxy, and halo,

wherein the mammal is in need of the treatment.

2. The method according to Claim 1, wherein the MEK compound of Formula I(M) is selected from Group A wherein A is phenylene; R^3 is hydroxy; and R^4 is hydrogen, $-C(O)NR^8R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, heterocycloalkyl, cycloalkyl, heterocycloalkyl, or heteroaryl; wherein the alkyl is optionally substituted with one, two, or three groups selected from $-OR^8$, halo, nitro, $-S(O)_mR^9$, optionally substituted heterocycloalkyl, $-NR^8R^{8'}$, $-NR^8C(O)R^{8'}$, optionally substituted heteroaryl, $-NR^8S(O)_2R^9$, $-NR^8C(O)OR^{8'}$, and aryl; wherein the cycloalkyl is optionally substituted with one or two groups indeopendently selected from $-NR^8R^{8'}$ and $-C(O)NR^{33}R^{33a}$; wherein the heterocycloalkyl is optionally substituted with one, two or three groups independently selected from alkyl and $-C(O)OR^8$; and wherein the heteroaryl is optionally substituted with $-NR^8R^{8'}$.

3. The method according to Claim 2, wherein R^{10} is 3-fluoro and R^{12}, R^{14}, and R^{16} are hydrogen or halo; R^{10} is 3-fluoro, R^{12} is 4-fluoro, and R^{14} and R^{16} are hydrogen; R^{10} is 4-fluoro, R^{12} is 5-fluoro, and R^{14} and R^{16} are hydrogen; R^{10} is 4-fluoro, R^{12} is 6-fluoro, and R^{14} and R^{16} are hydrogen; or R^{12} is 4-fluoro and R^{10}, R^{14}, and R^{16} are hydrogen.

4. The method according to Claim 1, wherein the MEK compound of Formula I(M) is selected from Group A where A is phenylene; R^7 is iodo or bromo; X is fluoro or chloro; R^1, R^2, R^5, and R^6 are hydrogen; and R^{10}, R^{12}, R^{14}, and R^{16} are defined as follows:

(i) R^{10} is 3-fluoro and R^{12}, R^{14}, and R^{16} are hydrogen or halo, or

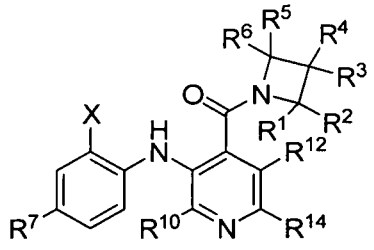
(ii) R^{10} is 3-fluoro, R^{12} is 4-fluoro, and R^{14} and R^{16} are hydrogen;

(iii) R^{10} is 4-fluoro, R^{12} is 5-fluoro, and R^{14} and R^{16} are hydrogen; or

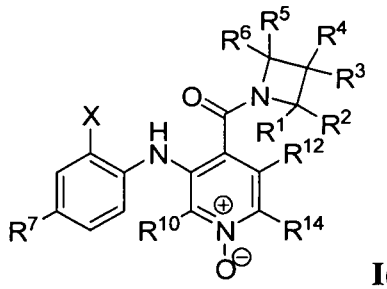
(iv) R^{10} is 4-fluoro, R^{12} is 6-fluoro, and R^{14} and R^{16} are hydrogen; or

(v) R^{12} is 4-fluoro and R^{10}, R^{14}, and R^{16} are hydrogen.

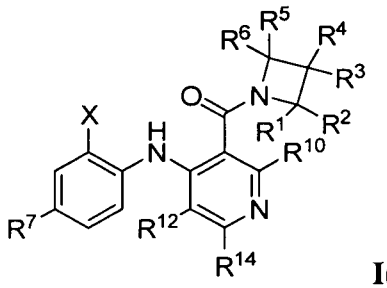
5. The method according to Claim 1, wherein the MEK compound of Formula I(M) is according to Formula I(u), I(v), I(w), or I(x):



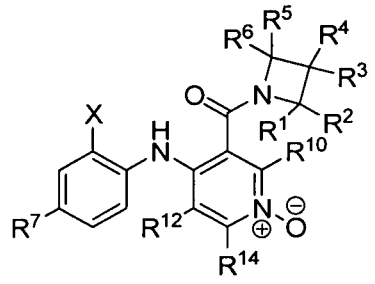
I(u);



I(v);



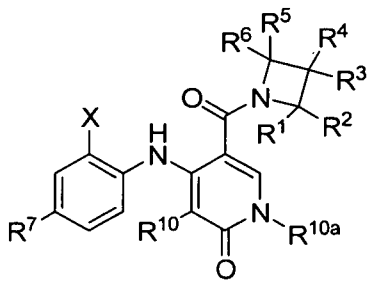
I(w);



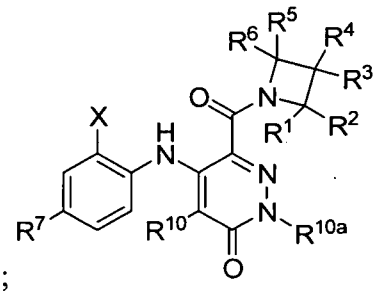
I(x);

wherein R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^{10}, R^{12}, and R^{14} are independently hydrogen, halo, or alkyl; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with $-NR^8R^{8'}$ and where the heteroaryl is optionally substituted with alkyl.

6. The method according to Claim 1, wherein the MEK compound of Formula I(M) is selected from Group C and according to Formula I(y) or I(z):



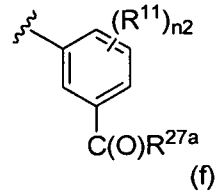
I(y);



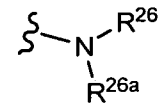
I(z)

wherein R^1, R^2, R^5, and R^6 are hydrogen; X and R^7 are halo; R^{10} is hydrogen, halo, or alkyl; R^{10a} is alkyl; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, wherein the alkyl is optionally substituted with $-NR^8R^{8'}$, and wherein the heteroaryl is optionally substituted with alkyl.

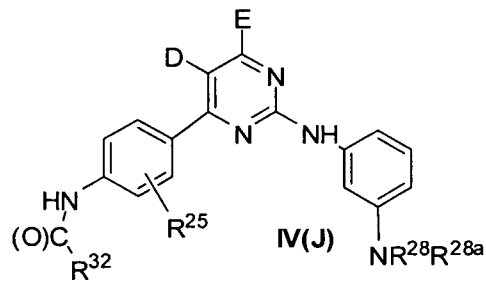
7. The method according to claim 1, wherein R^2 of Formula I(J) is



(f)

8. The method according to claim 1, wherein Z of Formula I(J) is  , R^{26a} is $-C(O)R^{32}$, R^{26} is hydrogen, and R^{32} is selected from tetrahydrofuran, pyrrolidinyl or pryimidinyl, wherein R^{32} is optionally substituted with 1, 2, 3, 4 or 5 groups selected from hydroxyl, oxo, alkyl, alkoxy, amino, hydroxyalkyl and halo.

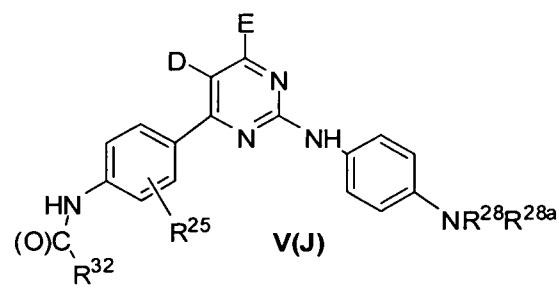
9. The method according to claim 1, wherein the JAK-2 compound has Formula IV(J):



IV(J)

wherein and R^{28} and R^{28a}, together with the nitrogen atom to which they are attached, form a heterocycloalkyl, wherein the heterocycloalkyl is optionally substituted with one or two R^{31}.

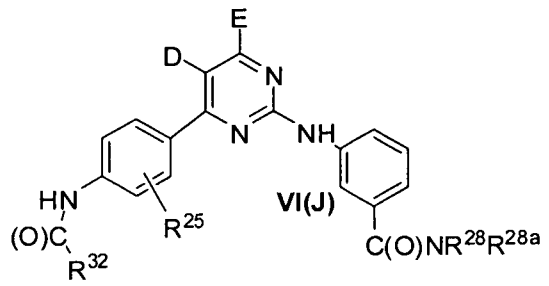
10. The method according to claim 1, wherein the JAK-2 compound has Formula V(J):



V(J)

wherein R^{28} and R^{28a}, together with the nitrogen atom to which they are attached, form a heterocycloalkyl, wherein the heterocycloalkyl is optionally substituted with one or two R^{31}.

11. The method according to claim 1, wherein the JAK-2 compound has Formula VI(J):



wherein R^{28} and R^{28a}, together with the nitrogen atom to which they are attached, form a heterocycloalkyl, wherein the heterocycloalkyl is optionally substituted with one or two R^{31}.

12. The method according to claim 1, wherein the cancers are selected from prostate cancer, breast cancer, multiple myeloma, leukemia, lymphoma, lung cancer, colorectal cancer, renal cancer, melanoma, hepatocellular, gastric, GIST, pancreatic carcinoma, and papillary thyroid cancer.

13. The method according to claim 1, wherein the MEK compound is selected from one or more of the following compounds:

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}-carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one;

6-(azetidin-1-ylcarbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(hydroxymethyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(trifluoromethyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-prop-2-en-1-ylazetidin-3-ol;

3-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]propane-1,2-diol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-ethylazetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-methylazetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-ethenylazetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one oxime;

[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]methanol;

1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethane-1,2-diol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-hydroxyazetidine-3-carboxamide;

1,1-dimethylethyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(pyrrolidin-1-ylmethyl)azetidin-3-ol;

3-[(diethylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(dimethylamino)methyl]azetidin-3-ol;

N-butyl-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-prop-2-en-1-ylazetidine-3-carboxamide;

N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-methylpropanamide;

N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]formamide;

N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-3,4-dihydroxybutanamide;

methyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate;

N-butyl-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine;

1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-amine;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*R*)-piperidin-2-yl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-pyrrolidin-2-ylazetidin-3-ol;

3-(aminomethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-[(1*S*)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-[(1*R*)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

(3-(1-aminopropyl)-3-hydroxyazetidin-1-yl)(3,4-difluoro-2-(2-fluoro-4-iodophenylamino)phenyl)methanone;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-ethylazetidine-3-carboxamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2-hydroxyethyl)azetidine-3-carboxamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2-piperidin-1-ylethyl)azetidine-3-carboxamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-phenylazetidine-3-carboxamide

N-[2-(diethylamino)ethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(morpholin-4-ylmethyl)azetidin-3-ol;

1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}piperidin-4-ol;

3-{[bis(2-hydroxyethyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-(4-methylpiperazin-1-yl)acetamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(4-methylpiperazin-1-yl)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(4-methyl-1,4-diazepan-1-yl)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[methyl(1-methylpyrrolidin-3-yl)amino]methyl}azetidin-3-ol;

3-(1,4'-bipiperidin-1'-ylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N*,*N*-bis(2-hydroxyethyl)glycinamide;

3-({4-[2-(diethylamino)ethyl]piperazin-1-yl}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxyethyl)(methyl)amino]methyl}azetidin-3-ol;

N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-piperidin-1-ylacetamide;

N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N*3-(2-hydroxyethyl)-*N*3-methyl-beta-alaninamide;

N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N*3,*N*3-bis(2-hydroxyethyl)-beta-alaninamide;

N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N*2,*N*2-diethylglycinamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-methylazetidin-3-amine;

1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N*,*N*-dimethylpyrrolidin-3-amine;

2-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]amino}ethanol;

N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]propane-1,3-diamine;

3-[(dimethylamino)methyl]-1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-methyl-*N*-(2-pyridin-2-ylethyl)azetidin-3-amine;

N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-*N*2-methylglycinamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-ethylazetidin-3-amine;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2-methylpropyl)azetidin-3-amine;

N-(cyclopropylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine;

N-(cyclohexylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine;

N-(cyclopentylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine;

3-(azetidin-1-ylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-[(2,3-dihydroxypropyl)oxy]azetidine-3-carboxamide;

2-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-2-yl]methyl}amino)ethanol;

N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-2-yl]methyl}ethane-1,2-diamine;

N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]glycinamide;

6-({3-[(dimethylamino)methyl]azetidin-1-yl}carbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-methylethyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(3,4-dihydroxybutyl)azetidine-3-carboxamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2,3-dihydroxypropyl)azetidine-3-carboxamide;

1-({2,4-difluoro-6-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine;

1-({4,5-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidine-3-carboxamide;

6-{[3-(aminomethyl)-3-(methyloxy)azetidin-1-yl]carbonyl}-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline;

N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}acetamide;

2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)-6-[(3-{[(1-methylethyl)amino]methyl}azetidin-1-yl)carbonyl]aniline;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(ethylamino)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{2-[(1-methylethyl)amino]ethyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(2-hydroxy-1,1-dimethylethyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1,1-dimethyl-2-[(1-methylethyl)amino]ethyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-methylethyl)amino]methyl}azetidin-3-amine;

3-[(cyclopropylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2,2,2-trifluoroethyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-imidazol-1-ylmethyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,1-dimethylethyl)amino]methyl}azetidin-3-ol;

3-[(cyclopentylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxy-*N*-prop-2-en-1-ylazetidine-3-carboxamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-(2,3-dihydroxypropyl)-3-hydroxyazetidine-3-carboxamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-1,2,3-triazol-1-ylmethyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2,2-dimethylpropyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(propylamino)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-methylpropyl)amino]methyl}azetidin-3-ol;

3-{[(cyclopropylmethyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(phenylmethyl)amino]methyl}azetidin-3-ol;

3-{[(cyclohexylmethyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-[(butylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1-ethylpyrrolidin-2-yl)methyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxyethyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(dimethylamino)ethyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxy-1,1-dimethylethyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(4-methylphenyl)ethyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(prop-2-en-1-ylamino)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(1-methylpyrrolidin-2-yl)ethyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2,3-dihydro-1*H*-inden-2-ylamino)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(tetrahydrofuran-2-ylmethyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(tetrahydro-2*H*-pyran-4-yl)ethyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1*S*,2*S*)-2-hydroxycyclopentyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,1-dimethylprop-2-yn-1-yl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-pyrrolidin-1-ylpropyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,2-dimethylpropyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(1*H*-imidazol-4-yl)ethyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-methyl-2-(methyloxy)ethyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(ethyloxy)propyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-ethylpropyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3,3-dimethylbutyl)amino]methyl}azetidin-3-ol;

ethyl 4-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)piperidine-1-carboxylate;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-methylbutyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(ethyloxy)ethyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(dimethylamino)propyl]amino}methyl)azetidin-3-ol;

3-[(cyclobutylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-({[3-(diethylamino)propyl]amino}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(1*H*-imidazol-1-yl)propyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(methylthio)ethyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-(phenylmethyl)piperidin-4-yl]amino}methyl)azetidin-3-ol;

3-({[2,2-bis(methyloxy)ethyl]amino}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,1,3,3-tetramethylbutyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,1-dimethylpropyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2,3-dihydro-1*H*-inden-1-ylamino)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[({2-[(phenylmethyl)oxy]cyclopentyl}amino)methyl]azetidin-3-ol;

3-{[(3-amino-2-hydroxypropyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-hydroxy-1-(phenylmethyl)ethyl]amino}methyl)azetidin-3-ol;

3-[(cyclooctylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-{[(1-cyclohexylethyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-[(cycloheptylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-pyridin-3-ylethyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(methylthio)propyl]amino}methyl)azetidin-3-ol;

N-cyclohexyl-N^2-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-2-methylalaninamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(tetrahydro-2*H*-pyran-4-ylmethyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-hydroxypropyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-pyridin-4-ylethyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-(phenylmethyl)pyrrolidin-3-yl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(2-thienyl)ethyl]amino}methyl)azetidin-3-ol;

3-[({2-[bis(1-methylethyl)amino]ethyl}amino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(phenyloxy)ethyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(phenylamino)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxypropyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[({2-[(1-methylethyl)oxy]ethyl}amino)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-ethylpiperidin-3-yl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(methyloxy)ethyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-nitropropyl)azetidin-3-ol;

3-(1-aminoethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1-methylpiperidin-4-yl)methyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[4-(dimethylamino)butyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-furan-2-ylethyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1-[(1,1-dimethylethyl)amino]ethyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-ethylbutyl)amino]methyl}azetidin-3-ol;

1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}pyrrolidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({(2*S*)-2-[(methyloxy)methyl]pyrrolidin-1-yl}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxyphenyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-hydroxyphenyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(phenyloxy)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1r,3r,5*R*,7*R*)-tricyclo[3.3.1.1~3,7~]dec-2-ylamino]methyl}azetidin-3-ol;

3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)propane-1,2-diol;

N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-L-alanine;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(phenylthio)methyl]azetidin-3-ol;

N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-D-alanine;

methyl *N*-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}alaninate;

3-[({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)oxy]propane-1,2-diol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-methylbutyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1-methylpropyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-methylbutyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(pentylamino)methyl]azetidin-3-ol;

3-[(cyclohexylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(ethylamino)ethyl]azetidin-3-ol;

3-[(azepan-3-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(dimethylamino)-1-methylethyl]amino}methyl)azetidin-3-ol;

N-cyclopropyl-1-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)cyclopentanecarboxamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(2,3-dihydro-1*H*-indol-3-yl)ethyl]amino}methyl)azetidin-3-ol;

N^2-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-*N*-ethyl-2-methylalaninamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2-methylhydrazino)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(hydroxyamino)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(methyloxy)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(ethyloxy)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(ethylamino)propyl]azetidin-3-ol;

3-[(azetidin-3-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1,3-thiazol-2-ylamino)methyl]azetidin-3-ol;

1,1-dimethylethyl [3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)propyl]carbamate;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(pyrrolidin-2-ylmethyl)amino]methyl}azetidin-3-ol;

1,1-dimethylethyl 4-[({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)methyl]piperidine-1-carboxylate;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(2-hydroxyphenyl)methyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(3-hydroxyphenyl)methyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(4-hydroxyphenyl)methyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(4-hydroxybutyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxyethyl)oxy]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1*S*,2*S*)-2-hydroxycyclohexyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(1,1-dimethyl-2-pyrrolidin-1-ylethyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1-methyl-1*H*-imidazol-4-yl)methyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1-methyl-1*H*-imidazol-5-yl)methyl]amino}methyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(2*S*)-2-(methyloxy)cyclopentyl]amino}methyl)azetidin-3-ol;

3-{[1,1'-bi(cyclohexyl)-2-ylamino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(methyloxy)phenyl]amino}methyl)azetidin-3-ol;

1-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)cyclopentanecarboxylic acid;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(4-fluorophenyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1,3,5-triazin-2-ylamino)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(*trans*-4-hydroxycyclohexyl)amino]methyl}azetidin-3-ol;

3-[(cyclopent-3-en-1-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

N-[4-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)phenyl]acetamide;

N-[3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)phenyl]acetamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methylpyrrolidin-2-yl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1*H*-1,2,4-triazol-3-ylamino)methyl]azetidin-3-ol;

3-[1-(diethylamino)propyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)-5-(hydroxymethyl)cyclopentane-1,2-diol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-piperidin-2-ylazetidin-3-ol

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-fluorophenyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methylpiperidin-2-yl)azetidin-3-ol;

1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}guanidine;

1-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-3-nitroguanidine;

N-{1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}acetamide;

(2*R*)-*N*-{1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(piperidin-4-ylmethyl)amino]methyl}azetidin-3-ol;

3-{[(3-aminopropyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[({[2-(4-methylpiperazin-1-yl)phenyl]methyl}amino)methyl]azetidin-3-ol;

3-{[(1,1-dimethylethyl)amino]methyl}-1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxycyclohexyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2,2,3,3,3-pentafluoropropyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3,3,3-trifluoropropyl)amino]methyl}azetidin-3-ol;

N-[3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)phenyl]methanesulfonamide;

N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}methanesulfonamide;

3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)-1*H*-pyrazol-5-ol;

(1*R*,2*S*)-4-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)cyclopentane-1,2-diol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-(hydroxymethyl)cyclohexyl]amino}methyl)azetidin-3-ol;

3-{[(3-chlorophenyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-{[(4-chlorophenyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-[(5-amino-3-methyl-1*H*-pyrazol-1-yl)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(5-methyl-1*H*-pyrazol-3-yl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-ethylpyrrolidin-2-yl)azetidin-3-ol;

(2*R*)-*N*-{(1*S*)-1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}-3,3,3-trifluoro-2-(methyloxy)-2-phenylpropanamide;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[4-(methyloxy)phenyl]amino}methyl)azetidin-3-ol;

3-(1-amino-2-methylpropyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-{[(4-aminophenyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-hydroxy-2-methylcyclopentyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1-[(4-hydroxycyclohexyl)amino]ethyl}azetidin-3-ol;

methyl (2xi)-2-deoxy-2-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)-beta-D-arabino-hexopyranoside;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-pyridin-2-ylazetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-(hydroxymethyl)cyclopentyl]amino}methyl)azetidin-3-ol;

1-cyano-3-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}guanidine;

6-({3-[(ethylamino)methyl]-3-fluoroazetidin-1-yl}carbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-nitroethyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(3-fluoro-4-hydroxyphenyl)amino]methyl}azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[(2-fluoro-4-hydroxyphenyl)amino]methyl}azetidin-3-ol;

3-(1-aminoethyl)-1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(methylamino)ethyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-imidazol-2-yl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-pyrrol-2-yl)azetidin-3-ol;

N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}benzenecarboximidamide;

3-({[(E)-1-amino-2-nitroethenyl]amino}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methyl-1-nitroethyl)azetidin-3-ol;

3-(1-amino-1-methylethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-[(1*H*-benzimidazol-2-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1*H*-imidazol-2-ylamino)methyl]azetidin-3-ol;

methyl {1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}carbamate;

3-(1*H*-benzimidazol-2-yl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(dimethylamino)ethyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(pyrimidin-2-ylamino)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(pyridin-2-ylamino)methyl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methyl-1*H*-imidazol-2-yl)azetidin-3-ol;

3-(1-aminobutyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-[amino(phenyl)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(5-methyl-1*H*-imidazol-2-yl)azetidin-3-ol;

1,1-dimethylethyl (2*S*)-2-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate;

1-({2-[(4-bromo-2-chlorophenyl)amino]-3,4-difluorophenyl}carbonyl)-3-piperidin-2-ylazetidin-3-ol;

3-(1-amino-3-hydroxypropyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1*H*-imidazol-2-ylmethyl)azetidin-3-ol;

3-(1-aminocyclopentyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-(2-aminocyclohexyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

3-(2-aminocyclopentyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-azetidin-3-ol;

1-({4-fluoro-5-[(2-fluoro-4-iodophenyl)amino]-1-methyl-1*H*-benzimidazol-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol;

1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol;

1-({2-[(4-bromo-2-fluorophenyl)amino]-3,4-difluorophenyl}carbonyl)-3-piperidin-2-ylazetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(3-methyl-1-nitrobutyl)azetidin-3-ol;

3-(2-aminopyrimidin-4-yl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;

1-({7-[(4-bromo-2-chlorophenyl)amino]-8-chloroimidazo[1,2-a]pyridin-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol;

1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol;

1-({7-[(4-bromo-2-chlorophenyl)amino]-8-chloroimidazo[1,2-a]pyridin-6-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol;

1--({4-fluoro-5-[(2-fluoro-4-iodophenyl)amino]-1-methyl-1*H*-benzimidazol-6-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol;

4-[(4-bromo-2-fluorophenyl)amino]-3-fluoro-5-({3-hydroxy-3-[(2*S*)-piperidin-2-yl]azetidin-1-yl}carbonyl)pyridin-2(1*H*)-one;

(±)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(*trans*)-2-hydroxycyclohexyl]azetidin-3-ol;

(±)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(*cis*)-2-hydroxycyclohexyl]azetidin-3-ol;

1-({3-fluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol;

1-({4-fluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol;

1-({6-[(4-bromo-2-chlorophenyl)amino]-7-fluoro-3-methyl-1,2-benzisoxazol-5-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(6-methylpiperidin-2-yl)azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-piperazin-2-ylazetidin-3-ol;

5-[(2-fluoro-4-iodophenyl)amino]-6-({3-hydroxy-3-[(2*S*)-piperidin-2-yl]azetidin-1-yl}carbonyl)-2-methylpyridazin-3(2*H*)-one;

6-({3-[(1*S*)-1-aminoethyl]-3-hydroxyazetidin-1-yl}carbonyl)-5-[(2-fluoro-4-iodophenyl)amino]-2-methylpyridazin-3(2*H*)-one; and

1-({3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol;

and wherein the JAK-2 compound is selected from one or more of the following compounds:

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2,6-dichlorobenzamide;

2,6-dichloro-*N*-(3-{[4-(2,3-dihydro-1-benzofuran-6-yl)pyrimidin-2-yl]amino}propyl)benzamide;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-fluoro-6-iodobenzamide;

N-(3-{[4-(4-aminophenyl)pyrimidin-2-yl]amino}propyl)-2,6-dichlorobenzamide;

N-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide;

N-{4-[2-({3-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(dimethylamino)ethyl]benzamide;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-fluorobenzamide;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-fluoro-6-iodobenzamide;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dimethylbenzamide;

N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]pyridine-4-carboxamide;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,3,4,5,6-pentafluorobenzamide;

4-(4-chlorophenyl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

4-(2,4-dichlorophenyl)-*N*-{3-[(2-piperidin-1-ylethyl)oxy]phenyl}pyrimidin-2-amine;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-chlorobenzamide;
N-(4-{2-[(3-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(3-piperidin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-bromobenzamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-3-fluorobenzamide;
N-[3-({4-[4-(acetylamino)phenyl]-5-methylpyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide;
N-(4-{2-[(3-{[(2,6-dichlorophenyl)sulfonyl]amino}phenyl)amino]-5-methylpyrimidin-4-yl}phenyl)acetamide;
2,6-dichloro-*N*-(3-{[4-(1*H*-indol-5-yl)pyrimidin-2-yl]amino}phenyl)benzamide;
N-[3-({4-[4-(acetylamino)phenyl]-5-fluoropyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-methylbenzamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,4-dichlorobenzamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,3-dichlorobenzamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,5-dichlorobenzamide;
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-(4-{2-[(4-piperidin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(2-methyl-4-piperazin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)thiophene-2-carboxamide;
N-(4-{5-methyl-2-[(3-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)-2-(phenyloxy)acetamide;
N-(4-{6-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)-2-morpholin-4-ylacetamide;
N-[4-(2-{[3-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-[3-({4-[4-(acetylamino)-2-chlorophenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide;

2,6-dichloro-*N*-{3-[(4-phenylpyrimidin-2-yl)amino]phenyl}benzamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-difluorobenzamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,4,5-trifluorobenzamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]benzamide;
N-(4-{6-morpholin-4-yl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-3,5-difluorobenzamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-chloro-6-fluoro-3-(methyloxy)benzamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2-chloro-6-fluoro-4-methylbenzamide;
N-(4-{2-[(3-{[(2,6-dimethylphenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
4-(2,4-dichlorophenyl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;
4-(2,4-dichlorophenyl)-*N*-{3-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}pyrimidin-2-amine;
N-(3-{[4-(4-aminophenyl)pyrimidin-2-yl]amino}phenyl)-2,6-dichlorobenzamide;
4-(4-aminophenyl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;
4-[4-(ethylamino)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;
N-[4-(2-{[3-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-(4-{2-[(4-aminophenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-[4-(2-{[4-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-[4-(2-{[4-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-{4-[2-({3-[4-(pyridin-4-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;
N-[5-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-2-morpholin-4-ylphenyl]-2,6-dichlorobenzamide;
N-(4-{5-fluoro-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{[2-(4-ethylpiperazin-1-yl)-2-oxoethyl]oxy}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[3-(morpholin-4-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-5-[(4-ethylpiperazin-1-yl)carbonyl]phenyl}-2,6-dichlorobenzamide;

4-[4-(dimethylamino)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;

2,6-dichloro-*N*-(3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}phenyl)benzamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]-5-(trifluoromethyl)pyrimidin-4-yl}phenyl)acetamide;

N-(3-{2-[(3-aminophenyl)amino]pyrimidin-4-yl}phenyl)thiophene-2-carboxamide;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-1-methylpiperidine-4-carboxamide;

N-{4-[2-({3-[(phenylmethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(3-aminophenyl)amino]-5-methylpyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3-aminophenyl)amino]-5-fluoropyrimidin-4-yl}phenyl)acetamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(2-ethylphenyl)benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(phenylmethyl)benzamide;

N-{4-[2-({3-[(4-cyclopentylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[(4-phenylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(3-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(2-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({3-[(4-pyrazin-2-ylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(3-{[4-(3-chlorophenyl)piperazin-1-yl]carbonyl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(1-methyl-1*H*-benzimidazol-2-yl)methyl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-propylbenzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-cyclopropylbenzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(3-fluorophenyl)methyl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(naphthalen-1-ylmethyl)benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(dimethylamino)ethyl]-*N*-methylbenzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(2-methylphenyl)methyl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(3-chlorophenyl)methyl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(2-phenylethyl)benzamide;

N-{4-[2-({3-[(4-methylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(tetrahydrofuran-2-ylmethyl)benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[3-(2-oxopyrrolidin-1-yl)propyl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(3s,5s,7s)-tricyclo[3.3.1.1~3,7~]dec-1-yl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(methyloxy)ethyl]benzamide;

N-[4-(2-{[3-(1,3-thiazolidin-3-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({3-[(4-pyridin-2-ylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{[2-(methyloxy)phenyl]methyl}benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{[3-(methyloxy)phenyl]methyl}benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(2-fluorophenyl)methyl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(4-fluorophenyl)methyl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(3,3-dimethylbutyl)benzamide;

N-[4-(2-{[3-(thiomorpholin-4-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(2-thienylmethyl)benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[3-(dimethylamino)propyl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{[2-(trifluoromethyl)phenyl]methyl}benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{[3-(trifluoromethyl)phenyl]methyl}benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{[4-(trifluoromethyl)phenyl]methyl}benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(2,4-difluorophenyl)methyl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-ethyl-*N*-methylbenzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-({4-[(trifluoromethyl)oxy]phenyl}methyl)benzamide;

N-{4-[2-({3-[(4-acetylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(cyclopropylmethyl)benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(2-fluorophenyl)ethyl]benzamide;

N-[4-(2-{[3-(pyrrolidin-1-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({3-[(4-pyrimidin-2-ylpiperazin-1-yl)carbonyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-methyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide;
N-[4-(2-{[3-(1,3-dioxan-2-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-[4-(2-{[3-(morpholin-4-ylmethyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-{4-[2-({3-[(4-ethylpiperazin-1-yl)methyl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;
N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-3-[(2-morpholin-4-ylethyl)oxy]benzamide;
4-[4-(methylamino)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;
N-[4-(2-{[4-(4-acetylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-(4-{2-[(3-amino-2,4,5,6-tetrafluorophenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(3-{[4-(2-fluorophenyl)piperazin-1-yl]carbonyl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(phenyloxy)ethyl]benzamide;
methyl 1-{[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]carbonyl}piperidine-4-carboxylate;
N-[4-(2-{[3-({4-[3-(methyloxy)phenyl]piperazin-1-yl}carbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{2-[2-(methyloxy)phenyl]ethyl}benzamide;
N-[4-(2-{[3-(1,3-dihydro-2*H*-isoindol-2-ylcarbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(biphenyl-4-ylmethyl)benzamide;
N-(4-{2-[(3-{[4-(phenylcarbonyl)piperazin-1-yl]carbonyl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-[4-(2-{[3-({4-[4-(methyloxy)phenyl]piperazin-1-yl}carbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-methyl-*N*-{[2-(methyloxy)phenyl]methyl}benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(2-fluorophenyl)methyl]-*N*-methylbenzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(diphenylmethyl)benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(2-pyridin-2-ylethyl)benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(pyridin-2-ylmethyl)benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[2-(2-chlorophenyl)ethyl]benzamide;

N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-fluoropyrimidin-4-yl)phenyl]acetamide;

N^2-[3-(1*H*-imidazol-1-yl)propyl]-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)- N^2-(2-pyridin-3-ylethyl)glycinamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(pyridin-3-ylmethyl)benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(pyridin-4-ylmethyl)benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-methyl-*N*-(phenylmethyl)benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-cyclopentylbenzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(2-chlorophenyl)methyl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(4-chlorophenyl)methyl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-(furan-2-ylmethyl)benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-{[4-(methyloxy)phenyl]methyl}benzamide;

N-[4-(2-{[3-({4-[2-(methyloxy)phenyl]piperazin-1-yl}carbonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[3-(methyloxy)propyl]benzamide;

N-(4-{2-[(3-{[(2*R*,6*S*)-2,6-dimethylmorpholin-4-yl]carbonyl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-[(6-chloropyridin-3-yl)methyl]benzamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-butylbenzamide;

N-(4-{2-[(3-{[4-(2-chlorophenyl)piperazin-1-yl]carbonyl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-*N*-ethyl-*N*-[2-(methyloxy)ethyl]benzamide;

N-(4-(2-(3-(3-morpholinopropoxy)phenylamino)pyrimidin-4-yl)phenyl)acetamide;

N-(4-(2-(3-(2-(dimethylamino)ethoxy)phenylamino)pyrimidin-4-yl)phenyl)acetamide;

N-[3-({4-[4-(acetylamino)phenyl]-5-methylpyrimidin-2-yl}amino)phenyl]-2,6-dimethylbenzamide;

N-[4-(2-{[4-(phenyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

4-(4-aminophenyl)-*N*-[4-(phenyloxy)phenyl]pyrimidin-2-amine;

N-{4-[2-({4-[(phenylmethyl)oxy]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

4-(4-aminophenyl)-*N*-[3-(morpholin-4-ylsulfonyl)phenyl]pyrimidin-2-amine;

N-(4-{2-[(3,5-dimorpholin-4-ylphenyl)amino]-5-fluoropyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({4-[4-(phenylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(4-{4-[(5-methyl-3-phenylisoxazol-4-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(2-phenyl-1,3-thiazol-4-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[4-(4-{[6-(phenyloxy)pyridin-3-yl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({4-[4-(cyclohexylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(4-{4-[(1*S*,4*S*)-bicyclo[2.2.1]hept-5-en-2-ylmethyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[4-(4-pentylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(4-{4-[(2-chlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[4-(4-{[3,5-bis(methyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(4-{4-[(4-fluorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(1-methyl-1*H*-pyrrol-2-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(2,4-dichlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({4-[4-(9*H*-fluoren-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(4-{4-[(3-methyl-2-thienyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(5-ethylfuran-2-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(3-{[4-(1,1-dimethylethyl)phenyl]oxy}phenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({4-[4-(3-thienylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

methyl 4-({4-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperazin-1-yl}methyl)benzoate;

N-(4-{2-[(4-{4-[3-(methylthio)propyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(4-{[3-(dimethylamino)propyl]oxy}phenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[4-(4-{2-[(phenylmethyl)oxy]ethyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(4-{4-[(2-chloroquinolin-3-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(4-chloro-2,6-dimethylphenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]pyrrolidin-3-yl}acetamide;

N^2-[3-(4-methylpiperazin-1-yl)propyl]-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide;

N^2-(1-methylpiperidin-4-yl)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide;

N-{4-[2-({4-[(pyridin-4-ylmethyl)oxy]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(4-{[2-(methyloxy)ethyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

2-(dimethylamino)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)furan-2-carboxamide;

2-(methyloxy)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)cyclobutanecarboxamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)azetidine-3-carboxamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-2-carboxamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-3-carboxamide;

N-[4-(2-{[4-(dimethylamino)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(4-chlorophenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3-{[(2-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-4-carboxamide;

2-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)morpholine-2-carboxamide;

N^2-methyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-beta-alaninamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)phenylalaninamide;

N-[4-(2-{[4-(3-oxopiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-[4-(2-{[4-(4-{[5-(3-chlorophenyl)furan-2-yl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-[4-(2-{[4-(4-{[4-fluoro-2-(trifluoromethyl)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-[4-(2-{[4-(4-{[4-(1*H*-imidazol-1-yl)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-[4-(2-{[4-(4-{[2,5-bis(trifluoromethyl)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(4-{4-[(2,6-dimethylphenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(2,3-dimethylphenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[4-(4-{[2,4-bis(ethyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-[4-(2-{[4-(4-{[3-(ethyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({4-[4-(2,2'-bithien-5-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-[4-(2-{[4-(4-{[4-(2-thienyl)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(4-{4-[(4-cyanophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[4-(4-{[2,5-bis(methyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({4-[4-(2,2-diphenylethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({4-[4-(1*H*-pyrrol-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-(1*H*-indazol-6-ylamino)-5-methylpyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-(1*H*-indol-5-ylamino)-5-methylpyrimidin-4-yl]phenyl}acetamide;

N-[4-(2-{[4-(morpholin-4-ylmethyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(3-{[(3-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3-{[(4-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

4-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-*N*-ethylpiperazine-1-carboxamide;

N-{4-[2-({4-[4-(ethylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-(1*H*-indazol-5-ylamino)-5-methylpyrimidin-4-yl]phenyl}acetamide;

N-[4-(2-{[4-(4-propylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-[4-(2-{[4-(4-butylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({4-[4-(cyclopropylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

4-[4-(methylsulfonyl)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;

ethyl *N*-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-*N*-methylglycinate;

4-[3-(methylsulfonyl)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;

4-[4-(methylthio)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;

N-(4-{2-[(4-cyclohexylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({4-[(tetrahydrofuran-2-ylmethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;
N-{4-[2-({4-[(phenylmethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;
N-[4-(2-{[4-(acetylamino)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
methyl (4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)carbamate;
1-ethyl-3-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)urea;
ethyl 1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperidine-3-carboxylate;
ethyl [4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]acetate;
4-[4-(methyloxy)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;
4-[3-(methyloxy)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;
4-(1*H*-indol-5-yl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;
2-[(2-amino-2-oxoethyl)amino]-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
2-morpholin-4-yl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
2,6-dichloro-*N*-{3-[(4-{4-[(cyclopropylcarbonyl)amino]phenyl}pyrimidin-2-yl)amino]phenyl}benzamide;
N^2-(2-aminoethyl)- N^2-methyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)- N^2-1*H*-pyrazol-5-ylglycinamide;
phenylmethyl *N*-{2-[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]-2-oxoethyl}-L-alaninate;
4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzamide;
1,1-dimethylethyl [(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)methyl]carbamate;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenylacetamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-phenylpropanamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)tetrahydrofuran-2-carboxamide;

5-methyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyrazine-2-carboxamide;

2-(ethyloxy)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-(phenyloxy)acetamide;

N-[4-(2-{[4-(1*H*-pyrrol-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-[4-(2-{[4-(2,6-dimethylmorpholin-4-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

ethyl 1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperidine-4-carboxylate;

2-cyclopentyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-pyridin-3-ylpropanamide;

6-(methyloxy)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-3-carboxamide;

methyl 4-[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]-4-oxobutanoate;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)butanamide;

N-(4-{2-[(4-{bis[2-(methyloxy)ethyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[4-(morpholin-4-ylsulfonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

4-(4-(aminomethyl)phenyl)-*N*-(4-morpholinophenyl)pyrimidin-2-amine;

N-[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)methyl]acetamide;

N-(4-morpholin-4-ylphenyl)-4-{4-[(propylamino)methyl]phenyl}pyrimidin-2-amine;

N-(4-{2-[(4-piperidin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3,5-dimorpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

2-(2-methylphenyl)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)cyclopentanecarboxamide;

N,*N*-dimethyl-*N*'-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)butanediamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)- N^2-pyrimidin-4-ylglycinamide;

3-chloro-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-4-carboxamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-piperidin-1-ylacetamide;

N^2-ethyl-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-pyrrolidin-1-ylacetamide;

2-(1*H*-imidazol-1-yl)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-piperazin-1-ylacetamide;

N-[4-(2-{[4-(4-phenylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(3-chloro-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-piperazin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

'*N*-[6-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)pyridin-2-yl]-2,6-dichlorobenzamide;

'*N*-[6-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)pyrimidin-4-yl]-2,6-dichlorobenzamide;

'*N*-(4-{2-[(6-aminopyridin-2-yl)amino]pyrimidin-4-yl}phenyl)acetamide;

'*N*-(4-{2-[(6-aminopyrimidin-4-yl)amino]pyrimidin-4-yl}phenyl)acetamide;

'5-fluoro- N^4-[2-(methyloxy)phenyl]- N^2-[3-(methyloxy)phenyl]pyrimidine-2,4-diamine;

'2,6-dichloro-*N*-{3-[(4-{[3-chloro-4-(methyloxy)phenyl]oxy}pyrimidin-2-yl)amino]phenyl}benzamide;

'4-{[2-chloro-4-(methyloxy)phenyl]oxy}-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;

'*N*-[4-({2-[(4-morpholin-4-ylphenyl)amino]-7*H*-pyrrolo[2,3-d]pyrimidin-4-yl}amino)phenyl]acetamide;

'*N*-[4-({2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}oxy)phenyl]acetamide;

N-{4-[2-({4-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({4-[(2*R*,6*S*)-2,6-dimethylmorpholin-4-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(4-{4-[(2-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({4-[4-(1*H*-pyrazol-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(3-piperazin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[3-(4-{[2-(methyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({3-[4-(1,3-thiazol-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(3-bromo-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[4-{[2-(diethylamino)ethyl]oxy}-3-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzoic acid;

4-(4-furan-2-ylphenyl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;

4-[4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;

4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzonitrile;

methyl 4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzoate;

4-(4-fluorophenyl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;

N-[3-({2-[(4-morpholin-4-ylphenyl)amino]-7*H*-pyrrolo[2,3-d]pyrimidin-4-yl}amino)phenyl]acetamide;

N-(4-morpholin-4-ylphenyl)-4-[4-(pyridin-3-ylamino)phenyl]pyrimidin-2-amine;
N-(4-morpholin-4-ylphenyl)-4-[4-(pyridin-2-ylamino)phenyl]pyrimidin-2-amine;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)methanesulfonamide;
1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-(phenylmethyl)urea;
4-(2,3-dihydro-1,4-benzodioxin-6-yl)-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]-7*H*-pyrrolo[2,3-d]pyrimidin-4-yl}phenyl)acetamide;
N-(4-morpholin-4-ylphenyl)-4-quinolin-6-ylpyrimidin-2-amine;
4-[4-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl]-*N*-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;
N-(4-morpholin-4-ylphenyl)-4-(4-pyrimidin-5-ylphenyl)pyrimidin-2-amine;
N-(4-morpholin-4-ylphenyl)-4-quinoxalin-6-ylpyrimidin-2-amine;
2-chloro-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide;
2-(2-fluorophenyl)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyrimidine-5-carboxamide;
(2*S*)-*N*-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)azetidine-2-carboxamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)- N^2-phenylglycinamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-prolinamide;
N-(4-(2-(3-methoxy-4-morpholino-phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-isobutyrylpiperazin-1-yl)phenylamino)-pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-(3-methylbutanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-(cyclopropanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;

N-(4-(2-(4-(4-(cyclobutanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-(cyclopentanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-(2-methoxybenzoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-pentanoylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-picolinoylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-isonicotinoylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-(1-acetylpiperidine-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-(2-cyclopropylacetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-(2-(2-methoxyethoxy)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-(2-(pyridin-3-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-(4-(3-(pyridin-3-yl)propanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide;
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(pyridin-3-yl)acetamide;
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)isonicotinamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide;
N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide;

O-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-serinamide;

(*S*)-3-hydroxy-*N*-(4-(2-(4-morpholino-phenylamino)-pyrimidin-4-yl)-phenyl)-butanamide;

(*R*)-3-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide;

(*R*)-2-amino-3-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;

2-*H*ydroxy-2-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;

2-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-*N*-(4-(2-(4-((*R*)-3-(dimethylamino)pyrrolidin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

4-amino-1,1-dioxo-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)tetrahydro-2*H*-thiopyran-4-carboxamide;

(*R*)-4-(4-aminophenyl)-*N*-(4-(3-(dimethylamino)-pyrrolidin-1-yl)phenyl)-pyrimidin-2-amine;

(*R*)-*N*-(4-(2-(4-(3-(dimethylamino)pyrrolidin-1-yl)phenylamino)-pyrimidin-4-yl)phenyl)-3-methoxy-propanamide;

N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)piperazine-2-carboxamide;

2-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-1,2,3,4-tetrahydronaphthalene-2-carboxamide;

4-(4-(1,1-dioxo-isothiazolidin-2-yl)phenyl)-*N*-(4-morpholinophenyl)-pyrimidin-2-amine;

4-(4-(1*H*-tetrazol-1-yl)phenyl)-*N*-(4-morpholinophenyl)-pyrimidin-2-amine;

(*R*)-*N*-(4-(2-(3-(benzyloxy)-4-morpholino-phenylamino)-pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide;

(*S*)-2-amino-3-hydroxy-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;

N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(1*H*-tetrazol-1-yl)acetamide;

(*R*)-*N*-(4-(2-(3-ethoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide;

(*R*)-*N*-(4-(2-(1,2,3,4-tetrahydroquinolin-6-ylamino)-pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide;

3-hydroxy-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-3-methylbutanamide;

(3*S*,7*S*)-7-(hydroxymethyl)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)quinuclidine-3-carboxamide;

1-hydroxy-*N*-(4-(2-(4-morpholino-phenylamino)-pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;

(*S*)-2-amino-*N*-(4-(2-(3-methyl-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;

(*R*)-*N*-(4-(2-(3-methyl-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-*N*-(4-(2-(4-morpholino-3-(trifluoromethyl)-phenylamino)pyrimidin-4-yl)-phenyl)-pyrrolidine-2-carboxamide;

(*R*)-*N*-(4-(2-(4-(4-((*S*)-tetrahydrofuran-2-carbonyl)-piperazin-1-yl)-phenylamino)-pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide;

(*R*)-*N*-(4-(2-(4-(4-((*R*)-tetrahydrofuran-2-carbonyl)-piperazin-1-yl)-phenylamino)-pyrimidin-4-yl)phenyl)-pyrrolidine-2-carboxamide;

4-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)piperazine-1-carboxamide;

3-methoxy-*N*-(4-(2-(4-morpholino-3-(trifluoromethyl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;

3-methoxy-*N*-(4-(2-(4-morpholino-phenylamino)pyrimidin-4-yl)phenyl)-propane-1-sulfonamide;

2-methoxy-*N*-(4-(2-(4-morpholino-phenylamino)pyrimidin-4-yl)phenyl)-ethanesulfonamide;

(*S*)-3-hydroxy-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide;

(*R*)-3-hydroxy-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide;

N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide;

1-(3-(dimethylamino)propyl)-3-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)urea;

(*R*)-*N*-(4-(2-(4-(4-((*S*)-pyrrolidin-2-ylmethyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-2-amino-*N*-(4-(2-(4-(4-ethylpiperazin-1-yl)phenylamino)-5-methylpyrimidin-4-yl)phenyl)propanamide;

1-(3-methoxypropyl)-3-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)urea;

(*R*)-*N*-(4-(2-(4-(4-ethylpiperazin-1-yl)phenylamino)-5-methylpyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*S*)-*N*-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)-3-fluorophenylamino)pyrimidin-4-yl)phenyl)-5-oxopyrrolidine-2-carboxamide;

(*R*)-*N*-(4-(2-(3-chloro-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

1-(2-morpholinoethyl)-3-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)urea;

1-(2-(dimethylamino)ethyl)-3-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)urea;

(*S*)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(pyrrolidin-2-yl)acetamide;

2,3-dihydroxy-*N*-(4-(2-(4-morpholino-phenylamino)pyrimidin-4-yl)phenyl)-propanamide;

(*S*)-2-amino-4-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanamide;

(*R*)-2-amino-4-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanamide;

N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)isoindoline-1-carboxamide;

N-ethyl-4-(4-(4-(4-(tetrahydrofuran-2-carboxamido)phenyl)pyrimidin-2-ylamino)phenyl)piperazine-1-carboxamide;
N-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide;
(*R*)-*N*-(4-(2-(4-(4-((*R*)-2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(*R*)-*N*-(4-(2-(4-(4-((*S*)-2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
N-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide;
3-methoxy-*N*-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;
N-(4-(2-(4-(4-pivaloylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide;
(*R*)-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-1-methylpyrrolidine-2-carboxamide;
(*R*)-*N*-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(*R*)-4-(4-(4-(4-(2-aminopropanamido)phenyl)-pyrimidin-2-ylamino)phenyl)-*N*-ethylpiperazine-1-carboxamide;
(*R*)-2-amino-*N*-(4-(2-(4-(4-((*R*)-pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;
(*R*)-2-amino-*N*-(4-(2-(4-(4-((*S*)-pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;
(*R*)-2-amino-*N*-(4-(2-(4-(4-((*S*)-2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;
(*R*)-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(*S*)-*N*-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;
N-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;

(*R*)-*N*-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;

1-ethyl-3-(4-(5-methyl-2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)urea;

(*S*)-*N*-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;

(*R*)-*N*-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-methoxypropanamide;

(*S*)-3-methoxy-*N*-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;

(*R*)-*N*-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;

N-(4-(2-(4-(4-(cyclobutanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;

N-(4-(2-(4-(4-isobutyrylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;

N-(4-(2-(4-(1-butyryl-1,2,4-triazinan-4-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide;

1-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-ethylurea;

N-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-methoxypropanamide;

N-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;

N-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide;

1-ethyl-3-(4-(2-(4-(4-pivaloylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea;

1-(4-(2-(4-(4-(cyclobutanecarbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-ethylurea;

1-ethyl-3-(4-(2-(4-(4-isobutyrylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea;

N-ethyl-4-(4-(4-(4-(3-ethylureido)phenyl)pyrimidin-2-ylamino)phenyl)piperazine-1-carboxamide;

(*S*)-1-ethyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-1-(2-hydroxyethyl)-*N*-(4-(2-(4-morpholinobenzyl)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-1-isopropyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*S*)-2-(dimethylamino)-*N*-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;

1-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-ethylurea;

(*R*)-1-ethyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

4-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)tetrahydro-2*H*-pyran-4-carboxamide;

(*R*)-2-amino-*N*-(4-(2-(4-(4-isobutyrylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;

(*R*)-2-amino-*N*-(4-(2-(4-(4-((*R*)-2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;

(*R*)-*N*-(4-(5-methyl-2-(4-(4-((1-methyl-1*H*-imidazol-2-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-2-amino-*N*-(4-(5-methyl-2-(4-(4-((1-methyl-1*H*-imidazol-2-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;

(*R*)-2-(dimethylamino)-*N*-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;

(*R*)-*N*-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*S*)-*N*-(4-(5-methyl-2-(4-(4-((1-methyl-1*H*-imidazol-2-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-2-amino-*N*-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;

(2*R*)-*N*-(4-(2-(4-(4-(tetrahydrofuran-3-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*S*)-1-ethyl-3-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea;

(*S*)-1-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-ethylurea;

N-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide;

(*S*)-*N*-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide;

3-methoxy-*N*-(4-(5-methyl-2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;

(*R*)-2-amino-*N*-(4-(5-methyl-2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;

2-(dimethylamino)-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;

1-ethyl-3-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea;

3-methoxy-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;

(*R*)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-5-oxopyrrolidine-2-carboxamide;

(*S*)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-5-oxopyrrolidine-2-carboxamide;

(*S*)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-3-carboxamide;

(2*R*,3*S*)-2-amino-3-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide;

(*R*)-2-amino-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;

N-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;

N-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butyramide;
N-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide;
N-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;
(*R*)-2-amino-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;
(2*S*,3*R*)-2-amino-3-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide;
(*R*)-*N*-(4-(2-(4-((2*S*,6*R*)-2,6-dimethylmorpholino)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(*R*)-*N*-(4-(2-(4-(4-(3-hydroxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
1-ethyl-3-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea;
(*R*)-1-ethyl-3-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea;
3,3,3-trifluoro-2-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;
(*R*)-1-(4-(2-(4-(4-(2-aminopropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-ethylurea;
2-(dimethylamino)-*N*-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
(*R*)-2-amino-*N*-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;
(*R*)-*N*-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(*R*)-2-amino-*N*-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;
N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)-3-methoxypropanamide;

N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide;
N-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide;
N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide;
(*R*)-*N*-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide;
2-(dimethylamino)-*N*-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;
(*R*)-*N*-(4-(2-(4-(4-(piperidine-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
3-methoxy-*N*-(4-(2-(4-(4-(piperidine-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;
1-ethyl-3-(4-(2-(4-(4-(piperidine-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)urea;
N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropanoyl)piperazin-1-yl)benzyl)pyrimidin-4-yl)phenyl)acetamide;
(*S*)-*N*-(4-(2-(4-(4-(2-(dimethylamino)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide;
(*R*)-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide;
(4*S*)-4-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(*R*)-*N*-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide;
(*S*)-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide;
N-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;
N-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide;

(*S*)-*N*-(4-(2-(4-(4-(pyrrolidine-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)butyramide;

(2*R*)-*N*-(4-(2-(4-(4-(tetrahydrofuran-2-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-*N*-(4-(5-chloro-2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

N-(4-(2-(4-(4-(3-(diethylamino)propanoyl)piperazin-1-yl)benzyl)pyrimidin-4-yl)phenyl)acetamide;

(*S*)-1-(2-hydroxyethyl)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-3-carboxamide;

(*S*)-2-amino-*N*1-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanediamide;

(*R*)-2-amino-*N*1-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanediamide;

(*R*)-2-amino-*N*1-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)succinamide;

(*R*)-*N*-(4-(2-(4-(4-((4-chloro-1-methyl-1*H*-pyrazol-3-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*S*)-1-ethyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-3-carboxamide;

(*R*)-*N*-(4-(2-(4-(4-(2-ethoxyacetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-*N*-(4-(2-(4-(4-(2-(pyrrolidin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-*N*-(4-(2-(4-(4-(2-morpholinoacetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-1*H*-imidazole-4-carboxamide;

2-(dimethylamino)-*N*-(4-(2-(4-(4-(2-(piperazin-1-yl)acetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;

(*S*)-*N*-(4-(2-(4-(4-(3-(dimethylamino)-2,2-dimethylpropyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-2-carboxamide;

(*R*)-2-hydroxy-2-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide;
(*S*)-2-hydroxy-2-methyl-*N*-(4-(2-(4-morpholinobenzyl)pyrimidin-4-yl)phenyl)butanamide;
(*R*)-2-methoxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;
(*S*)-2-methoxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;
(*R*)-*N*-(4-(2-(4-(4-(2-methoxyacetyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(*R*)-*N*-(4-(2-(4-(4-acetylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(*S*)-2-amino-*N*-(4-(5-methyl-2-(4-(4-((1-methyl-1*H*-imidazol-2-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)propanamide;
N-(4-(2-(4-(4-(piperidine-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)tetrahydrofuran-3-carboxamide;
(2*R*,4*S*)-4-hydroxy-*N*-(4-(2-(4-(4-(3-methoxypropanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
1-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)cyclopentanecarboxamide;
(*R*)-*N*-(4-(2-(4-(4-formylpiperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(*R*)-1-(2-hydroxyethyl)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-3-carboxamide;
1-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)cyclopropanecarboxamide;
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-1*H*-pyrrole-2-carboxamide;
N-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-1*H*-imidazole-2-carboxamide;
(*S*)-2-hydroxy-3,3-dimethyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide;

(*R*)-2-cyclohexyl-2-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide;
(*S*)-2-cyclohexyl-2-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide;
(*S*)-2-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;
1-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)cyclobutanecarboxamide;
(*R*)-*N*-(4-(2-(6-morpholinopyridin-3-ylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(*S*)-*N*-(4-(2-(3-chloro-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(2*R*,3*R*)-2-amino-3-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanamide;
1-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)cyclopentanecarboxamide;
(*R*)-*N*-(4-(2-(4-(4-(4-(dimethylamino)butanoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(*R*)-*N*-(4-(2-(4-(2-methoxyethyl)-3,4-dihydro-2*H*-benzo[b][1,4]oxazin-7-ylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
(*R*)-2-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)butanamide;
(*R*)-2-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanamide;
(*R*)-2-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)hexanamide;
(*R*)-2-amino-3-methoxy-*N*-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;
(2*S*,3*R*)-2-amino-3-methyl-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pentanamide;
(*R*)-*N*-(4-(2-(3-fluoro-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;
N-(4-(2-(3-methoxy-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)-2-(1*H*-tetrazol-1-yl)acetamide;

(*S*)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)indoline-2-carboxamide;

(*R*)-tert-butyl 2-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenylcarbamoyl)pyrrolidine-1-carboxylate;

1-acetyl-4-amino-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)piperidine-4-carboxamide;

(*R*)-2-amino-3-methoxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;

(*S*)-*N*-(4-(2-(3-fluoro-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-2-amino-*N*-(4-(2-(3-fluoro-4-morpholinophenylamino)pyrimidin-4-yl)phenyl)propanamide;

2-hydroxy-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)acetamide;

(*R*)-*N*-(4-(2-(4-(4-(2-hydroxyethyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-*N*-(4-(2-(4-(4-((1-methyl-1*H*-pyrrol-2-yl)methyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(*R*)-*N*-(4-(2-(4-(4-((*R*)-pyrrolidin-2-ylmethyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)pyrrolidine-2-carboxamide;

(2*S*,3a*S*,7a*S*)-*N*-(4-(2-(4-morpholinophenylamino)pyrimidin-4-yl)phenyl)octahydro-1*H*-indole-2-carboxamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)cyclopropanecarboxamide;

N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)cyclopropanecarboxamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)valinamide;

N-(4-{2-[(4-{4-[(1-methyl-1H-imidazol-2-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3,5-dimorpholin-4-ylphenyl)amino]-5-methylpyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-alaninamide;

N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;
2-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenylacetamide;
N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
3-(methyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)prolinamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-alaninamide;
N-(4-{2-[(4-{4-[3-(dimethylamino)-2,2-dimethylpropyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(4-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1,3-thiazole-4-carboxamide;
N-(4-{2-[(2-methyl-4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(4-pyrrolidin-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-[4-(2-{[4-(diethylamino)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-(4-{2-[(4-azepan-1-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-{4-[2-({4-[methyl(2-phenylethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;
N-[4-(2-{[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-[4-(2-{[4-(2-oxopiperidin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-[4-(2-{[4-(2-methylpiperidin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-valinamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-valinamide;
2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)alaninamide
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)tryptophanamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;

O-(1,1-dimethylethyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-serinamide

3-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)tetrahydrofuran-3-carboxamide;

bis(1,1-dimethylethyl) (2R)-2-{[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]carbonyl}piperazine-1,4-dicarboxylate;

N-(4-{2-[(4-{4-[2-(2-fluorophenyl)acetyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[2-(2-methylphenyl)acetyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[2-(3-fluorophenyl)acetyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({4-[4-(3-thienylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(4-{4-[(6-chloropyridin-3-yl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(3-methylfuran-2-yl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-(2-(4-(4-(3-fluoro-2-methylbenzoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;

N-(4-(2-(4-(4-(1H-imidazole-4-carbonyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;

N-(4-(2-(4-(4-(2-methoxynicotinoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;

N-(4-(2-(4-(4-(4-fluoro-3-methylbenzoyl)piperazin-1-yl)phenylamino)pyrimidin-4-yl)phenyl)acetamide;

N-{4-[2-({4-[4-(naphthalen-2-ylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({4-[4-(quinolin-8-ylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-[4-(2-{[4-(4-{[4-(1,1-dimethylethyl)phenyl]sulfonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-[4-(2-{[4-(4-{[5-bromo-2-(methyloxy)phenyl]sulfonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(4-{4-[(phenylmethyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[4-(4-{[3-(trifluoromethyl)phenyl]sulfonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(4-{4-[(2-methylphenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(3-fluorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(2,4-difluorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({3-[4-({4-[(trifluoromethyl)oxy]phenyl}methyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(3-{4-[(1-methyl-1H-imidazol-2-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({3-[4-({2-[(trifluoromethyl)oxy]phenyl}methyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(3-{4-[(3-chlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({3-[4-(2,3-dihydroxypropyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(pyridin-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(pyridin-3-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(1H-pyrrol-2-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

4-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-N-(phenylmethyl)piperazine-1-carboxamide;

N-[4-(2-{[3-(4-{[2-(methyloxy)phenyl]carbonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({3-[4-(1H-pyrazol-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(3-pyridin-3-ylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(3-{4-[3-(methyloxy)propanoyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[3-(4-{2-[(4-fluorophenyl)oxy]acetyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({3-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(pyridin-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(pyridin-2-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(3-{4-[(2-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({3-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-3-carboxamide;

(2R)-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide;

(2S)-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide;

N-(4-{2-[(4-{4-[(2-fluorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3-{4-[(3,5-dichlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

ethyl 3-[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]-3-oxopropanoate;

N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-3-carboxamide;

N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-3-carboxamide;

N-ethyl-4-{4-[(4-{4-[(tetrahydrofuran-3-ylcarbonyl)amino]phenyl}pyrimidin-2-yl)amino]phenyl}piperazine-1-carboxamide;

N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-3-carboxamide;

N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-3-carboxamide;

N-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-3-carboxamide;

N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-3-carboxamide;

N-{4-[2-(1H-benzimidazol-6-ylamino)-5-methylpyrimidin-4-yl]phenyl}acetamide;

4-(4-furan-2-ylphenyl)-N-(4-morpholin-4-ylphenyl)pyrimidin-2-amine;

N-(4-morpholin-4-ylphenyl)-4-[4-(pyrimidin-2-ylamino)phenyl]pyrimidin-2-amine;

N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-methylpyrimidin-4-yl)phenyl]cyclopropanecarboxamide;

N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]cyclopropanecarboxamide;

N-(4-{2-[(3,5-dimorpholin-4-ylphenyl)amino]-5-methylpyrimidin-4-yl}phenyl)- N^2, N^2-dimethylglycinamide;

N^2, N^2-dimethyl-N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)glycinamide;

N-(4-{5-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide;

N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide;

N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide;

N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-prolinamide;

N-ethyl-4-[4-({4-[4-(D-prolylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperazine-1-carboxamide;

N-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide;

N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide;

1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-2-carboxamide;

N-{4-[2-({4-[4-(piperidin-4-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-prolinamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-pyridin-4-ylacetamide;

2-(3-fluorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

3-(4-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide;

2-(3-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-phenylpropanamide;

(1R,2R)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenylcyclopropanecarboxamide;

2-(4-fluorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

3-(2-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide;

3-(3-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide;

3-(2-fluorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)propanamide;

Nalpha,Nalpha-dimethyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-phenylalaninamide;

2-(2-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-pyridin-2-ylacetamide;

2-(4-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-{4-[(trifluoromethyl)oxy]phenyl}acetamide;

2-[2-(methyloxy)phenyl]-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

2-[3-(methyloxy)phenyl]-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

2-[4-(methyloxy)phenyl]-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-alaninamide;

N-{4-[2-({4-[4-(N,N-dimethylglycyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-3-(methyloxy)propanamide;

(2R)-2-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenylethanamide;

N^2, N^2-dimethyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-alaninamide;

1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-prolinamide;

N^2, N^2-dimethyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-alaninamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1-phenylcyclopropanecarboxamide;

2-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)butanamide;

(2S)-1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)azetidine-2-carboxamide;

2,4,6-trichloro-N-(3-{[4-(4-methyl-2-thienyl)pyrimidin-2-yl]amino}propyl)benzamide;

N-[3-({4-[3,4-bis(methyloxy)phenyl]pyrimidin-2-yl}amino)propyl]-2,6-dichlorobenzamide;

2,6-dichloro-N-[3-({4-[(4-morpholin-4-ylphenyl)amino]pyrimidin-2-yl}amino)propyl]benzamide;

2,6-dichloro-N-(3-{[4-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-fluoropyrimidin-2-yl]amino}propyl)benzamide;

2,6-dichloro-N-{3-[(4-{3-[(dimethylamino)methyl]phenyl}pyrimidin-2-yl)amino]propyl}benzamide;

2,6-dichloro-N-[3-({4-[3-(1-methylethyl)phenyl]pyrimidin-2-yl}amino)propyl]benzamide;

2,6-dichloro-N-{3-[(4-{4-[(1-methylethyl)oxy]phenyl}pyrimidin-2-yl)amino]propyl}benzamide;

N-[3-({4-[3-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2,6-dichlorobenzamide;

2,6-dichloro-N-[3-({4-[(E)-2-phenylethenyl]pyrimidin-2-yl}amino)propyl]benzamide;

phenyl (4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)carbamate;

phenylmethyl (4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)carbamate;

N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-3-(methyloxy)propanamide;

N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}cyclopropanecarboxamide;

4-{4-[(4-{4-[(cyclopropylcarbonyl)amino]phenyl}pyrimidin-2-yl)amino]phenyl}-N-ethylpiperazine-1-carboxamide;

N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-3-(methyloxy)propanamide;

3-(methyloxy)-N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}propanamide;

N-ethyl-4-(4-{[4-(4-{[3-(methyloxy)propanoyl]amino}phenyl)pyrimidin-2-yl]amino}phenyl)piperazine-1-carboxamide;

N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-2-phenylacetamide;

1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyrrolidin-2-one;

N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-alaninamide;

N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-alaninamide;

(2S)-2-hydroxy-3-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)butanamide;

(2R)-2-hydroxy-3-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)butanamide;

N-{4-[2-({4-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-D-alaninamide;

(2S)-2-amino-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-2-phenylethanamide;

2-amino-2-(4-chlorophenyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)morpholine-3-carboxamide;

1-ethyl-3-[4-(2-{[4-(4-ethylpiperazin-1-yl)-3-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]urea;

N-[4-(2-{[4-(4-ethylpiperazin-1-yl)-3-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide;

N-[4-(2-{[4-(4-ethylpiperazin-1-yl)-3-(methyloxy)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

1-(2,6-dichlorophenyl)-3-(3-{[4-(4-methyl-2-thienyl)pyrimidin-2-yl]amino}propyl)urea;

1-[2-fluoro-5-(trifluoromethyl)phenyl]-3-(3-{[4-(4-methyl-2-thienyl)pyrimidin-2-yl]amino}propyl)urea;

2,6-dichloro-N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]benzenesulfonamide;

N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2,6-difluorobenzenesulfonamide;

N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]naphthalene-2-sulfonamide;

N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]-3,4-bis(methyloxy)benzenesulfonamide;

3-chloro-N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]propane-1-sulfonamide;

N-[3-({4-[4-(dimethylamino)phenyl]pyrimidin-2-yl}amino)propyl]propane-1-sulfonamide;

methyl (3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}propyl)carbamate;

1-methylethyl (3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}propyl)carbamate;

phenylmethyl (3-{[4-(2,4-dichlorophenyl)pyrimidin-2-yl]amino}propyl)carbamate;

N-{4-[2-({[3-(3-chlorophenyl)isoxazol-5-yl]methyl}amino)pyrimidin-4-yl]phenyl}acetamide;

ethyl 4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)piperidine-1-carboxylate;

1,1-dimethylethyl 4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)piperidine-1-carboxylate;

N-(4-{2-[(4-cyanophenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyridin-4-yl}phenyl)acetamide;
1,1-dimethylethyl {1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperidin-4-yl}carbamate;
N-{4-[2-({4-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}cyclopropanecarboxamide;
N-{1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperidin-4-yl}acetamide;
4-(4-aminophenyl)-N-[4-(4-aminopiperidin-1-yl)phenyl]pyrimidin-2-amine;
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-methylpyrimidin-4-yl)phenyl]-3-(methyloxy)propanamide;
N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-2-carboxamide;
N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-2-carboxamide;
N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}tetrahydrofuran-2-carboxamide;
N-cyclopropyl-4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzamide;
N-[2-(methyloxy)ethyl]-4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}benzamide;
2,6-dichloro-N-{3-[(4-pyridin-3-ylpyrimidin-2-yl)amino]propyl}benzamide;
2,6-dichloro-N-(3-{[4-(4-methyl-3,4-dihydro-2H-1,4-benzoxazin-7-yl)pyrimidin-2-yl]amino}propyl)benzamide;
2,6-dichloro-N-(3-{[4-(2,3-dihydro-1,4-benzodioxin-6-yl)-6-methylpyrimidin-2-yl]amino}propyl)benzamide;
N-(4-{2-[(3-{[(2,6-dichlorophenyl)carbonyl]amino}propyl)amino]pyrimidin-4-yl}phenyl)morpholine-4-carboxamide;
2,6-dichloro-N-{3-[(4-{4-[(cyclopropylcarbonyl)amino]phenyl}pyrimidin-2-yl)amino]propyl}benzamide;
N-(4-{2-[(3-{[(2,6-dichlorophenyl)carbonyl]amino}propyl)amino]pyrimidin-4-yl}phenyl)thiophene-2-carboxamide;

2,6-dichloro-N-(3-{[4-(4-{[N-(2-morpholin-4-ylethyl)glycyl]amino}phenyl)pyrimidin-2-yl]amino}propyl)benzamide;

1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)ethanone;

(1E)-1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)ethanone oxime;

N-{4-[2-({4-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-2-phenylacetamide;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-bromobenzamide;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-fluorobenzamide;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)propyl]-2-chlorobenzamide;

N-[4-(2-{[3-(morpholin-4-ylsulfonyl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({3-[(cyclohexylmethyl)amino]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(3-{[(5-bromo-2-fluorophenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3-{[(2,5-dimethylphenyl)methyl]amino}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3,4-dimorpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({4-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}cyclopropanecarboxamide;

N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}butanamide;

N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}butanamide;

N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}butanamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-2-carboxamide;

2-hydroxy-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide;

3-(methyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide;
4-(methyloxy)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide;
4-chloro-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide;
(2R)-N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide;
(2S)-N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide;
1-(2-hydroxyethyl)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-prolinamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)thiophene-2-carboxamide;
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-3-carboxamide;
2-phenyl-N-{4-[2-({4-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;
3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-N-(diphenylmethyl)benzamide;
N-[4-(2-{[4-(4-methylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;
N-{4-[2-({4-[4-(phenylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;
N-{4-[2-({4-[4-(2-cyclopentylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;
N-{4-[2-({4-[4-(cyclohexylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;
N-(4-{2-[(4-{4-[(2-chlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(4-{4-[(3-fluorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;
N-(4-{2-[(4-{4-[(3-fluoro-4-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(3,4-dichlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(3,5-dichlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[4-(4-{[3-(methyloxy)phenyl]carbonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(4-{4-[(4-chlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(4-methylphenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({4-[4-(furan-2-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-[4-(2-{[4-(4-{2-[(4-fluorophenyl)oxy]acetyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)furan-3-carboxamide;

N-{4-[2-({4-[4-(phenylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({4-[4-(2-thienylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(4-{4-[(4-fluorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[4-(4-{[4-(methyloxy)phenyl]sulfonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-(4-{2-[(4-{4-[(4-chlorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-{4-[(3-chlorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({4-[4-(biphenyl-4-ylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({4-[4-(naphthalen-1-ylsulfonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(3-{4-[(2-chlorophenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[4-(2-{[3-(4-{[3-(methyloxy)phenyl]methyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({3-[4-(3-methylbutyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(2,3-dihydro-1,4-benzodioxin-6-ylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(cyclopropylmethyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(3-{4-[3-(methylthio)propyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3-{4-[(4-{[3-(dimethylamino)propyl]oxy}phenyl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({3-[4-({3-[(trifluoromethyl)oxy]phenyl}methyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

4-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-N-phenylpiperazine-1-carboxamide;

N-[4-(2-{[3-(4-propanoylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({3-[4-(phenylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(2-phenylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(cyclopentylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide

N-{4-[2-({3-[4-(2-pyridin-3-ylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(2-cyclopentylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-(4-{2-[(3-{4-[(2-chlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3-{4-[(4-chlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3-{4-[(3,4-dichlorophenyl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3-{4-[(1-methyl-1H-pyrrol-2-yl)carbonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N^2, N^2-dimethyl-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]glycinamide;

3-(methyloxy)-N-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]propanamide;

N-(4-{2-[(4-{4-[(2-chlorophenyl)sulfonyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-{4-[2-({3-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({3-[4-(2-cyclopropylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-[4-(2-{[3-(4-{[3-(methyloxy)phenyl]carbonyl}piperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

1-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]piperidine-3-carboxylic acid;

1,1-dimethylethyl methyl{2-[(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)amino]-2-oxoethyl}carbamate;

1,1-dimethylethyl [4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]carbamate;

N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-N^2, N^2-dimethylglycinamide;

4-(4-aminophenyl)-N-[4-(4-ethylpiperazin-1-yl)phenyl]pyrimidin-2-amine;

Nalpha-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-phenylalaninamide;
Nalpha-{[(1,1-dimethylethyl)oxy]carbonyl}-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-phenylalaninamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-D-phenylalaninamide;
N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-L-phenylalaninamide;
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-L-valinamide;
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-valinamide;
1-ethyl-3-[4-(2-{[3-(methyloxy)-4-morpholin-4-ylphenyl]amino}pyrimidin-4-yl)phenyl]urea;
(2R)-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)piperidine-2-carboxamide;
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-5-methylpyrimidin-4-yl)phenyl]acetamide;
4-{4-[(4-{4-[(N,N-dimethylglycyl)amino]phenyl}pyrimidin-2-yl)amino]phenyl}-N-ethylpiperazine-1-carboxamide;
N-{4-[2-({4-[4-(2,2-dimethylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-N^2, N^2-dimethylglycinamide;
N-{4-[2-({4-[4-(cyclobutylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-N^2, N^2-dimethylglycinamide;
N^2, N^2-dimethyl-N-{4-[2-({4-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}glycinamide;
N-{4-[2-({4-[4-(cyclopropylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}-N^2,N^2-dimethylglycinamide;
N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-N^2, N^2-dimethylglycinamide;
N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-N^2, N^2-dimethylglycinamide;

N-(4-{2-[({1-[(2,6-dichlorophenyl)carbonyl]azetidin-3-yl}methyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(3-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-[3-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)cyclohexyl]-2,6-dichlorobenzamide;

N-{4-[2-({[4-(4-methylpiperazin-1-yl)phenyl]methyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-[4-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)phenyl]-2,6-dichlorobenzamide;

N-{4-[2-(piperidin-4-ylamino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({1-[(2,6-dichlorophenyl)carbonyl]piperidin-4-yl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-{4-[2-({4-[(2-hydroxyethyl)oxy]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

1-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-3-phenylurea;

N-[5-({4-[4-(acetylamino)phenyl]pyrimidin-2-yl}amino)-2-(4-ethylpiperazin-1-yl)phenyl]-2,6-dichlorobenzamide;

1-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-3-(phenylmethyl)urea;

N^2, N^2-dimethyl-N-{4-[2-({4-[4-(pyridin-3-ylcarbonyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}glycinamide;

N-(3-fluoro-4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)cyclopropanecarboxamide;

N-(4-{2-[(4-{4-[(1-methyl-1H-imidazol-2-yl)methyl]piperazin-1-yl}phenyl)amino]pyrimidin-4-yl}phenyl)cyclopropanecarboxamide;

N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]acetamide;

N-{4-[2-({4-[4-(2-piperazin-1-ylacetyl)piperazin-1-yl]phenyl}amino)pyrimidin-4-yl]phenyl}acetamide;

N-[4-(2-{[4-(4-L-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide;

N-[4-(2-{[4-(4-L-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide;

N-[4-(2-{[4-(4-D-alanylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide;

N-[4-(2-{[4-(4-D-prolylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]tetrahydrofuran-2-carboxamide;

1-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)-1H-pyrrole-2-carboxamide;

3-fluoro-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-4-carboxamide;

6-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-3-carboxamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridazine-4-carboxamide;

2-cyclopropyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)acetamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)isoxazole-5-carboxamide;

N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)pyridine-3-carboxamide;

4-methyl-N-(4-{2-[(4-morpholin-4-ylphenyl)amino]pyrimidin-4-yl}phenyl)benzamide;

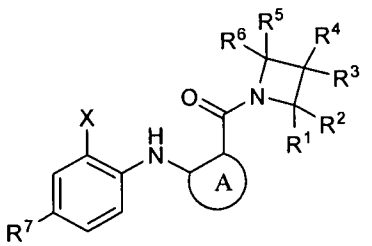
N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]-D-prolinamide;

N-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]butanamide; and

1-ethyl-3-[4-(2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}pyrimidin-4-yl)phenyl]urea.

14. The method according to claim 1, further comprising one or more additional treatments selected from one or more chemotherapeutic agents, one or more antibodies, radiation therapy, surgery, hormone therapy, and hypothermia therapy, wherein the chemotherapeutic agent is selected from one or more taxanes, one or more platin(s), one or more topoisomerase inhibitor(s), one or more alkylating agent(s), one or more antimetabolite(s), one or more antimicrotubule agent(s), one or more bcr-abl inhibitor(s), rapamycin, carboplatin, cisplatin, oxaliplatin, gemcitabine, dacarbazine, topotecan, irinotecan, one or more AKT inhibitors, one or more c-Met inhibitors, one or more EGFR inhibitors, one or more ErbB2 inhibitors, one or more HSP90 inhibitors, one or more IGF1R inhibitors, one or more VEGFR inhibitors, one or more VEGF inhibitors, and one or more Raf inhibitors.

15. A method of treating a disease in a mammal, comprising administering to the mammal a therapeutically effective amount of a MEK compound of Formula I(M), or a pharmaceutical composition comprising a therapeutically effective amount of the MEK compound of Formula I(M) and a pharmaceutically acceptable carrier, in combination with a therapeutically effective amount of a JAK-2 inhibitor, or a pharmaceutical composition comprising a therapeutically effective amount of a JAK-2 inhibitor and a pharmaceutically acceptable carrier, wherein the MEK compound of Formula I(M) is defined as follows:



I(M)

or a pharmaceutically acceptable salt or solvate thereof, wherein A, X, R^1, R^2, R^3, R^4, R^5, R^6, and R^7 are as defined in Group A, Group B, Group C, or Group D:

Group A

A is phenylene optionally substituted with one or two groups selected from R^{10}, R^{12}, R^{14}, and R^{16} wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen or halo;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen, halo, hydroxy, alkoxy, or amino;

R^4 is hydrogen, $-NR^8R^{8'}$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, cycloalkyl, heterocycloalkyl, or heteroaryl; wherein the alkyl is optionally substituted with one, two, or three groups independently selected from $-OR^8$, halo, nitro, $-S(O)_mR^9$, optionally substituted heterocycloalkyl, $-NR^8R^{8'}$, $-NR^8C(O)R^{8'}$, $-NR^8S(O)_2R^9$, $-NR^8C(O)OR^{8'}$, and aryl; wherein the cycloalkyl is optionally substituted with one or two groups selected from $-OR^8$ and $-NR^8R^{8'}$; wherein the heterocycloalkyl is optionally substituted with one or two groups independently selected from alkyl and $-C(O)OR^8$; and wherein the heteroaryl is optionally substituted with $-NR^8R^{8'}$; or

R^3 and R^4 together with the carbon to which they are attached form C(O) or C(=NOH);

m is 0;

R^7 is halo;

R^8 and $R^{8'}$ are independently selected from hydrogen, hydroxy, alkyl, alkenyl, alkynyl, aryl, heterocycloalkyl, heteroaryl, and cycloalkyl;

wherein the R^8 and $R^{8'}$ alkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, $-NR^{30}R^{30'}$ (wherein R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), optionally substituted heteroaryl, optionally substituted cycloalkyl), optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, $-C(O)NR^{33}R^{33a}$ (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), optionally substituted aryloxy, $-S(O)_nR^{31}$ (wherein n is 0 and R^{31} is alkyl), carboxy, alkoxycarbonyl, and $-NR^{32}C(O)R^{32a}$ (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl); or wherein the alkyl is optionally substituted with one, two, three, four, or five halo;

wherein the R^8 and $R^{8'}$ heteroaryl are independently optionally substituted with one or two groups indendently selected from amino and alkyl;

wherein the R^8 and $R^{8'}$ heterocycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from alkyl, alkoxycarbonyl, optionally substituted arylalkyl, hydroxy, alkoxy, and hydroxyalkyl;

wherein the R^8 and $R^{8'}$ aryl are independently optionally substituted with one or two groups indendently selected from hydroxy, alkoxy, halo, $-NR^{32}C(O)R^{32a}$ (wherein R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl), and $-NR^{34}SO_2R^{34a}$ (wherein R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl); and

wherein the R^8 and $R^{8'}$ cycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, hydroxyalkyl, alkoxy, carboxy, $-C(O)NR^{33}R^{33a}$ (wherein R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), and optionally substituted cycloalkyl; and

R^9 is alkyl or aryl;

Group B

A is thien-3,4-diyl, benzo[*d*]isoxazol-5,6-diyl, 1*H*-indazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), benzo[*d*]oxazol-5,6-diyl, 1*H*-benzo[d]imidazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), 1*H*-benzo[*d*][1,2,3]triazol-5,6-diyl (optionally substituted at the N1 position with R^{19} wherein R^{19} is alkyl or alkenyl), imidazo[1,2-*a*]pyridin-6,7-diyl, cinnolin-6,7-diyl, quinolin-6,7-diyl, pyridin-3,4-diyl, 1-oxido-pyridin-3,4-diyl, [1,2,4]triazolo[4,3-a]pyridin-6,7-diyl, or 2,3-dihydroimidazo[1,2-a]pyridin-6,7-diyl; wherein A is optionally substituted with one, two, or three groups independently selected from R^{10}, R^{12}, R^{14}, R^{16} and R^{19} wherein R^{10}, R^{12}, R^{14} and R^{16} are independently hydrogen, alkyl, halo, or amino; and R^{19} is hydrogen or alkyl;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

R^4 is $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ and wherein the heteroaryl is optionaly substituted with alkyl;

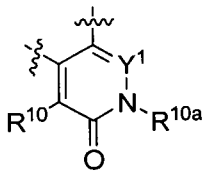
R^7 is halo;

R^8 is hydrogen or alkyl; and

$R^{8'}$ is hydrogen, alkyl, or cycloalkyl; wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl;

Group C

A is



(a)

R^{10} is hydrogen or halo;

R^{10a} is hydrogen or alkyl;

Y^1 is =CH- or =N-;

X is halo;

R^1, R^2, R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

R^4 is $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; wherein the alkyl is optionally substituted with $-NR^8R^{8'}$ and wherein the heteroaryl is optionaly substituted with alkyl;

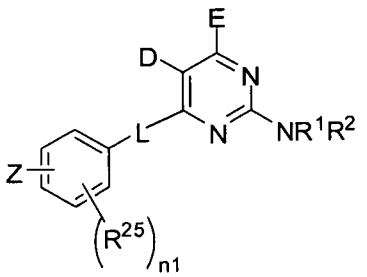
R^7 is halo;

R^8 is hydrogen or alkyl; and

$R^{8'}$ is hydrogen, alkyl, or cycloalkyl; wherein the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl;

wherein the mammal is in need of the treatment.

15. A method of treating a disease in a mammal, comprising administering to the mammal a therapeutically effective amount of a MEK inhibitor, or a pharmaceutical composition comprising a therapeutically effective amount of the MEK inhibitor and a pharmaceutically acceptable carrier, in combination with a therapeutically effective amount of a JAK-2 compound of Formula I(J), or a pharmaceutical composition comprising a therapeutically effective amount of the JAK-2 compound of Formula I(J) and a pharmaceutically acceptable carrier, wherein the JAK-2 compound of Formula I(J) is defined as follows:



I(J)

or a pharmaceutically acceptable salt or solvate thereof, wherein

D is hydrogen, halo, $-CF_3$, heterocycloalkyl or alkyl;

E is hydrogen, halo, $-CF_3$, heterocycloalkyl or alkyl; or

D and E, together with the carbon atoms to which they are attached, form a 5-7 membered heteroaryl or a 5-7 membered heterocycloalkyl, wherein the 5-7 membered heteroaryl or 5-7 membered heterocycloalkyl are each fused to the pyrimidinyl moiety to which D and E are attached;

L is a bond, -O- or -N(H)-;

Z is selected from alkoxy, cycloalkyl, heteroaryl optionally substituted with alkyl, halo,

$-C(O)OR^{26}$, $-C(=N\text{-}OH)$alkyl, $-C(O)R^{8}$, $-C(O)NR^{30}R^{30a}$, $-CH_2R^{2}$, $-(CH_2)_{n5}NR^{26}R^{26a}$, $-CF_3$, -CN, $-SO_2R^{12}$, $-S\text{-}R^{12a}$, $-OR^{32a}$, $-NHC(O)R^{32}$, aryl, and heterocycloalkyl optionally substituted with 1 or 2 oxo, or

Z and R^{25}, together with the carbon atoms to which they are attached, join to form a 5 or 6 membered heterocycloalkyl, a 5 or 6 membered heteroaryl, or a 5 or 6 membered cycloalkyl ring, wherein the 5 or 6 membered heterocycloalkyl, 5 or 6 membered heteroaryl, or 5 or 6 membered cycloalkyl ring are fused to the phenyl moiety to which Z and R^{25} are attached, and wherein the 5 or 6 membered heterocycloalkyl, 5 or 6 membered heteroaryl, or 5 or 6 membered cycloalkyl ring are each optionally substituted with 1, 2, or 3 groups independently selected from oxo, alkyl, alkoxy and halo;

n1 is 0, 1, 2, 3, or 4, and each n1 is independently selected when more than one n1 is present;

n2 is 0, 1, 2, 3, or 4, and each n2 is independently selected when more than one n2 is present;

n3 is 0, 1, 2, or 3, and each n3 is independently selected when more than one n3 is present;

n4 is 0, 1, 2, 3 or 4, and each n4 is independently selected when more than one n4 is present;

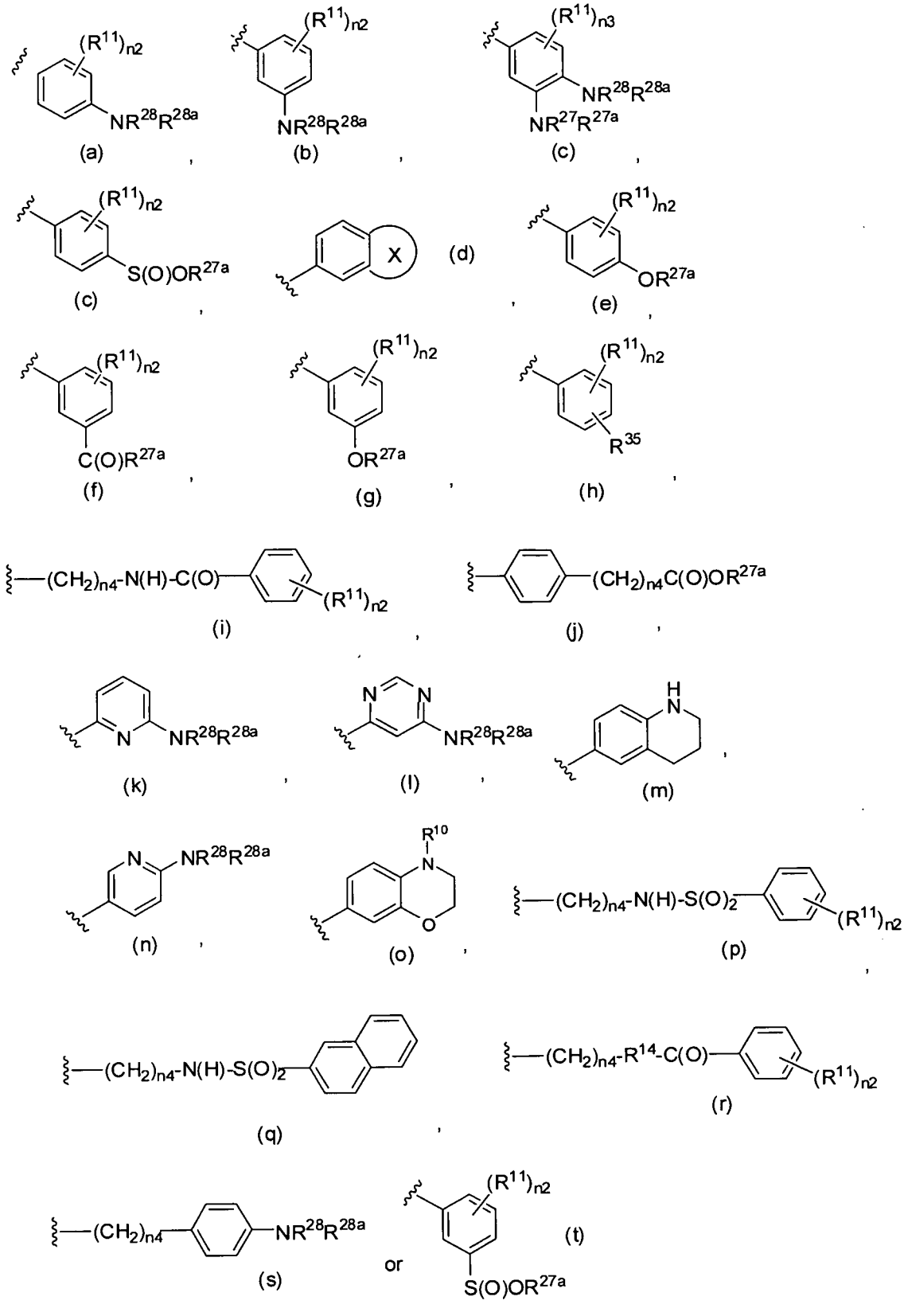
n5 is 0, 1, 2, 3 or 4, and each n5 is independently selected when more than one n5 is present;

p is 0-3;

r is 1-3;

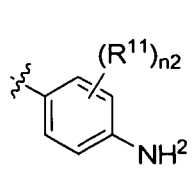
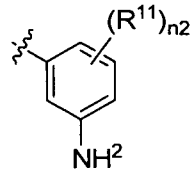
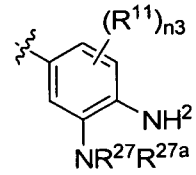
R^1 is hydrogen;

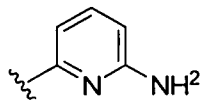
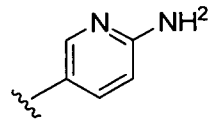
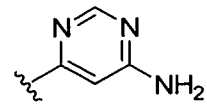
R^2 is selected from one of the following groups:



;

or R^2 is selected from one of the following groups:


(u) ,

(v) ,

(w) ,


(x) ,

(y) , or

(z) ;

ring X in formula (d) of R^2 is a 5 or 6 membered unsaturated heterocyclic ring fused to the two carbon atoms of the phenyl moiety to which ring X is attached, wherein ring X contains 1 or 2 nitrogen atoms;

R^7, $R^{7'}$, R^9, R^{10}, R^{12} and R^{15} are each independently hydrogen, alkyl, alkoxy, or alkoxyalkyl;

R^8 is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, hydroxyalkyl, alkoxyalkyl, dihydroxyalkyl, alkylamino, dialkylamino, aminoalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, alkylaminoalkyl, dialkylaminoalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl;

each R^{11}, when R^{11} is present, is independently selected from alkyl, alkenyl, lower alkynyl,

$-CF_3$, alkoxy, halo, haloalkoxy, haloalkyl, aminoalkyl, aminoalkoxy, alkylaminoalkyl, alkylaminoalkoxy, dialkylaminoalkyl, dialkylaminoalkoxy, oxo, thioalkyl, alkylthioalkyl, $-(CH_2)_p-OR^{17}$, -CN, $-O-CH_2-C(O)-R^{17}$,

$-C(O)R^{16}$, $-(CH_2)_p-C(O)OR^{17}$, $-S(O)_2R^{17}$, $-S(O)_2NR^{15}R^{17}$, aryl, heteroaryl, cycloalkyl, arylalkyl, arylalkoxy, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at any ring position with 1, 2, 3 or 4 R^{21};

R^{12} is hydrogen or alkyl;

R^{12a} is hydrogen or alkyl;

R^{13} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with 1, 2, 3, 4 or 5 groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl are independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

R^{14} is a bond, heterocycloalkyl or cycloalkyl;

R^{16} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, dialkylaminoalkyl,
$-(CH_2)_r-C(O)OR^7$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and

heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl is optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

R^{17} is selected from hydrogen, hydroxy, alkyl, alkenyl, lower alkynyl, hydroxyamino, haloalkyl, alkyl substituted with halo and hydroxy, hydroxyalkyl, alkoxyalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, dialkylaminoalkyl, $-(CH_2)_r-C(O)OR^7$, $-(CH_2)_r-C(O)NR^7R^{7'}$, aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, heteroaryl, cycloalkyl, arylalkyl, diarylalkyl, aryloxyalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at the ring position with one, two, three, four or five groups independently selected from alkyl, alkenyl, lower alkynyl, halo, hydroxy, hydroxyalkyl, alkoxycarbonyl, alkylcarbonyl, haloalkyl, haloalkoxy, lower alkoxy, amino, aryl, alkylamino, dialkylamino, heterocyclylalkoxy, oxo and haloalkyl; and wherein the alkyl of cycloalkylalkyl, heterocycloalkylalkyl, arylalkyl, and heteroarylalkyl is optionally substituted with 1, 2, 3, 4, or 5 groups selected from halo and hydroxy;

each R^{21}, when R^{21} is present, is independently selected from alkyl, alkenyl, lower alkynyl, cyano, halo, haloalkoxy, haloalkyl, hydroxyalkyl, amino, alkylamino, dialkylamino, dialkylaminoalkyl, dialkylaminoalkyloxy, haloalkyl, oxo, $-OR^{13}$, $-NHS(O)_2R^{17}$, $-S(O)_2R^{17}$, $-C(O)R^{17}$, $-C(O)OR^{17}$, $-C(O)NR^{15}R^{17}$, $-NR^{15}C(O)R^{17}$, aryl, arylalkyl, heteroarylalkyl, aryloxy, and heteroaryl; wherein each of the aryl, arylalkyl, heteroarylalkyl, aryloxy, and heteroaryl within R^{21} are optionally substituted at any ring position with 1, 2, or 3 groups

selected from alkyl, lower alkoxy halo, phenyl, heteroaryl and alkylheteroalkyl;

R^{25} is selected from alkyl, alkenyl, lower alkyl, halo, haloalkyl, haloalkoxy, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, $-OR^{12}$, cyano, $-CH_2NHC(O)OR^7$, $-CH_2NHC(O)R^7$, $-SR^7$, $-S(O)_2R^7$, $-S(O)_2NR^7R^8$, $-C(O)OR^8$, $-C(O)NR^7R^8$, cycloalkyl, heterocycloalkyl, aryl and heteroaryl; wherein the cycloalkyl, heterocycloalkyl, aryl and heteroaryl are each optionally substituted with one, two or three groups independently selected from alkyl, alkenyl, halo, haloalkoxy, haloalkyl, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, $-OR^8$, $-NHS(O)_2R^8$, cyano, $-C(O)R^8$, $-CH_2NHC(O)OR^7$, $-CH_2NHC(O)R^7$, $-SR^7$, $-S(O)_2R^7$, $-S(O)_2NR^7R^8$, $-C(O)OR^8$, $-C(O)NR^7R^8$, $-NR^{7'}C(O)-CHR^3-OR^8$, $-NR^{7'}C(O)-CHR^3-NR^7-R^8$, and $-NR^7C(O)R^8$;

R^{26} is hydrogen, -C(O)-phenyl or alkyl, wherein the -C(O)-phenyl is optionally substituted at any ring position with 1, 2 or 3 halo;

R^{26a} is hydrogen, alkyl, heteroaryl, $-C(O)R^{32}$, $-C(O)NHR^{32a}$, $-S(O)_2R^9$, $-SR^9$, $-C(O)OR^{32}$, or $-C(O)NR^{32a}R^{32}$;

R^{27} and R^{28} are each independently selected from alkyl, alkenyl, hydroxy, alkoxy, and alkoxyalkyl;

R^{27a} and R^{28a} are independently selected from hydrogen, alkyl, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, dialkylaminoalkyl, arylcarbonylalkyl, aryloxyalkyl, dialkylaminoalkyl, alkyl-O-C(O)heterocylcoalkyl, $-(CH_2)_{n4}$heterocycloalkyl, heterocycloalkylalkyl, heteroaryl, heteroarylalkyl, $-(CH_2)_{n4}-C(O)R^{29}$, $-(CH_2)_{n4}NR^{28}R^{28a}$, $-(CH_2)_{n4}NHR^{28a}$, $-CH(phenyl)_2$, $-S(O)_2R^{29}$, $-C(O)R^{29}$, $-C(O)OR^{29}$, and $-C(O)NR^{29a}R^{29}$, wherein the aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{27a} and R^{28a} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkylcarbonyl, phenyl, phenoxy, arylcarbonyl, $-CF_3$, oxo, $-OCF_3$, alkoxyphenyl, and heteroaryl optionally substituted with alkyl or halo;

or R^{27} and R^{27a}, together with the nitrogen to which they are attached, form heterocycloalkylamino, heterocycloalkyl or heteroaryl, wherein the heterocycloalkylamino and heteroaryl are each independently optionally substituted with 1, 2, 3, 4, or 5 R^{31};

or R^{28} and R^{28a} together with the nitrogen to which they are attached form heterocycloalkyl or heteroaryl, wherein the heterocycloalkyl and heteroaryl are each optionally substituted with 1, 2, 3, 4, or 5 R^{31};

R^{29a} is hydrogen or alkyl;

R^{29} is selected from alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{29} are each optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkylcarbonyl, phenyl, phenoxy, arylcarbonyl, $-CF_3$, oxo, $-OCF_3$, alkoxyphenyl, and heteroaryl optionally substituted with alkyl or halo;

R^{30a} is hydrogen or alkyl;

R^{30} is selected from hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkoxycarbonylalkyl, amino, alkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, aryl, arylalkyl, phenoxyalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, arylheteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl; wherein the aryl, arylalkyl, phenoxyalkyl, cycloalkyl, arylheteroarylalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{30} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, alkoxy, alkoxyalkyl, $-C(O)OCH_3$, $-CF_3$, $-OCF_3$, alkylcarbonyl, phenyl, phenoxy, alkylphenoxy, dialkylaminoalkoxy and heteroaryl;

R^{31} is selected from alkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkylthioalkyl, $-C(O)R^{30}$, $-C(O)NR^{30}R^{30a}$, $-C(O)OR^{30}$, $-S(O)_2R^{30}$, amino, dihydroxyalkyl, arylcarbonyl, alkylcarbonylamino, alkoxyphenyl, phenylalkoxyalkyl, arylheteroarylalkyl, alkylamino,

-O-dialkylamino, dialkylamino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, dialkylaminoalkoxy, oxo, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, spirocyclic cycloalkyl, spirocyclic heterocycloalkyl, and heterocycloalkylalkyl, wherein the aryl, arylalkyl, cycloalkyl, arylheteroarylalkyl, arylalkoxyalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl groups within R^{31} are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from halo, alkyl, $-CF_3$, $-OCF_3$, cyano, alkoxy, alkoxyalkyl, $-C(O)OCH_3$, alkylcarbonyl, phenyl optionally substituted at any ring position with halo, phenoxy, alkylphenoxy, arylalkoxyalkyl, dialkylaminoalkoxy and heteroaryl;

R^{32a} is hydrogen, $-OCF_3$, $-CF_3$, or alkyl;

R^{32} is selected from aryl, arylalkyl, arylalkoxy, arylcycloalkyl, alkoxycarbonylalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkylhydroxyalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl, wherein the aryl, arylalkyl, cycloalkyl, arylcycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, and heterocycloalkylalkyl are each independently optionally substituted at any ring position with 1, 2, 3, 4, or 5 groups selected from hydroxy, oxo, alkyl, alkoxy, amino, hydroxyalkyl, alkylcarbonyl, alkoxycarbonyl, halo, $-CF_3$, $-OCF_3$, aminoalkyl, alkylaminoalkyl, aryl and dialkylaminoalkyl, and wherein the alkyl portion of the heteroarylalkyl can be substituted with amino;

or R^{32} is alkyl optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from hydroxy, alkoxycarbonyl, alkoxy, $-CF_3$, halo, aminocarbonyl, alkylaminocarbonyl, alkoxycarbonylalkylamino, dialkylaminocarbonyl, $-NR^{34}R^{34a}$ and phenyl optionally substituted with 1, 2, or 3 halo;

or R^{32} is alkylamino or arylalkylamino;

R^{34} is hydrogen or alkyl;

R^{34a} is selected from hydrogen, alkyl, heteroaryl, aryl, aminoalkyl, aminocarbonylalkyl, heteroarylalkyl, arylalkoxy and arylalkyloxycarbonylalkyl; wherein the heteroaryl, aryl, heteroarylalkyl, arylalkoxy or arylalkyloxycarbonylalkyl are each independently optionally substituted at any

ring position with 1, 2, 3, 4, or 5 groups selected from hydroxy, oxo, alkyl, amino, hydroxyalkyl, alkylcarbonyl, alkoxycarbonyl, halo, aminoalkyl, alkylaminoalkyl, and dialkylaminoalkyl; and

R^{35} is selected from halo, $-(CH_2)_pC(O)OR_{17}$, cycloalkyl, heterocycloalkyl, and heterocycloalklylalkyl; wherein the heterocycloalkyl and heterocycloalklylalkyl are each optionally substituted with 1, 2, 3, 4, or 5 groups each independently selected from alkyl, alkoxy, and halo,

wherein the mammal is in need of the treatment.