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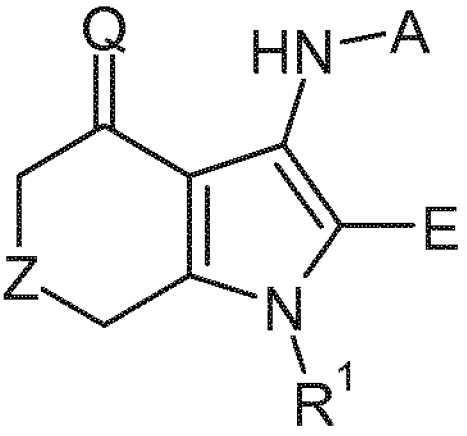
[Continued on next page]

(54) Title: HETERO-1,5,6,7-TETRAHYDRO-4H-INDOL-4-ONES

(57) Abstract: Compounds of formula (I) as described herein, processes for their production and their use as pharmaceuticals.



(I)

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— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

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Hetero-1,5,6,7-tetrahydro-4H-indol-4-ones

Field of application of the invention

The invention relates to substituted oxa-, thia- or aza-tetrahydro-4H-indol-4-one compounds, uses thereof and processes for their production.

BACKGROUND OF THE INVENTION

One of the most fundamental characteristics of cancer cells is their ability to sustain chronic proliferation whereas in normal tissues the entry into and progression through the cell divison cycle is tightly controlled to ensure a homeostasis of cell number and maintenance of normal tissue function. Loss of proliferation control was emphasized as one of the six hallmarks of cancer [Hanahan D and Weinberg RA, Cell 100, 57, 2000; Hanahan D and Weinberg RA, Cell 144, 646, 2011].

The eukaryotic cell division cycle (or cell cycle) ensures the duplication of the genome and its distribution to the daughter cells by passing through a coordinated and regulated sequence of events. The cell cycle is divided into four successive phases:

1. The G1 phase represents the time before the DNA replication, in which the cell grows and is sensitive to external stimuli.
2. In the S phase the cell replicates its DNA, and
3. in the G2 phase preparations are made for entry into mitosis.
4. In mitosis (M phase), the duplicated chromosomes get separated supported by a spindle device built from microtubules, and cell division into two daughter cells is completed.

To ensure the extraordinary high fidelity required for an accurate distribution of the chromosomes to the daughter cells, the passage through the cell cycle is strictly regulated and controlled. The enzymes that are necessary for the progression through the cycle must be activated at the correct time and are also turned off again as soon as the corresponding phase is passed. Corresponding control points ("checkpoints") stop or delay the progression through the cell cycle if DNA damage is detected, or the DNA replication or the creation of the spindle device is not yet completed. The mitotic checkpoint (also known as spindle checkpoint or spindle assembly checkpoint) controls

the accurate attachment of mircrotubules of the spindle device to the kinetochors (the attachment site for microtubules) of the duplicated chromosomes. The mitotic checkpoint is active as long as unattached kinetochores are present and generates a wait-signal to give the dividing cell the time to ensure that each kinetochore is attached to a spindle pole, and to correct attachment errors. Thus the mitotic checkpoint prevents a mitotic cell from completing cell division with unattached or erroneously attached chromosomes [Suijkerbuijk SJ and Kops GJ, Biochem. Biophys. Acta 1786, 24, 2008; Musacchio A and Salmon ED, Nat. Rev. Mol. Cell. Biol. 8, 379, 2007]. Once all kinetochores are attached with the mitotic spindle poles in a correct bipolar (amphitelic) fashion, the checkpoint is satisfied and the cell enters anaphase and proceeds through mitosis.

The mitotic checkpoint is established by a complex network of a number of essential proteins, including members of the MAD (mitotic arrest deficient, MAD 1-3) and Bub (Budding uninhibited by benzimidazole, Bub 1-3) families, Mps1 kinase, cdc20, as well as other components [reviewed in Bolanos-Garcia VM and Blundell TL, Trends Biochem. Sci. 36, 141, 2010], many of these being over-expressed in proliferating cells (*e.g.* cancer cells) and tissues [Yuan B *et al.*, Clin. Cancer Res. 12, 405, 2006]. The major function of an unsatisfied mitotic checkpoint is to keep the anaphase-promoting complex/cyclosome (APC/C) in an inactive state. As soon as the checkpoint gets satisfied the APC/C ubiquitin-ligase targets cyclin B and securin for proteolytic degradation leading to separation of the paired chromosomes and exit from mitosis.

Inactive mutations of the Ser/Thr kinase Bub1 prevented the delay in progression through mitosis upon treatment of cells of the yeast *S. cerevisiae* with microtubule-destabilizing drugs, which led to the identification of Bub1 as a mitotic checkpoint protein [Roberts BT *et al.*, Mol. Cell Biol., 14, 8282, 1994]. A number of recent publications provide evidence that Bub1 plays multiple roles during mitosis which have been reviewed by Elowe [Elowe S, Mol. Cell. Biol. 31, 3085, 2011]. In particular, Bub1 is one of the first mitotic checkpoint proteins that binds to the kinetochores of duplicated chromosomes and probably acts as a scaffolding protein to constitute the mitotic checkpoint complex. Furthermore, via phosphorylation of histone H2A, Bub1 localizes the protein shugoshin to the centromeric region of the chromosomes to prevent premature segregation of the paired chromosomes [Kawashima *et al.* Science 327, 172, 2010]. In addition, together with a Thr-3 phosphorylated Histone H3 the shugoshin protein functions as a binding site for the chromosomal passenger complex which includes the proteins survivin, borealin, INCENP and Aurora B. The chromosomal passenger complex is seen as a tension sensor within

the mitotic checkpoint mechanism, which dissolves erroneously formed microtubule-kinetochor attachments such as syntelic (both sister kinetochors are attached to one spindle pole) or merotelic (one kinetochor is attached to two spindle poles) attachments [Watanabe Y, Cold Spring Harb. Symp. Quant. Biol. 75, 419, 2010]. Recent data suggest that the phosphorylation of histone H2A at Thr 121 by Bub1 kinase is sufficient to localize AuroraB kinase to fulfill the attachment error correction checkpoint [Ricke et al. J. Cell Biol. 199, 931-949, 2012].

Incomplete mitotic checkpoint function has been linked with aneuploidy and tumourigenesis [Weaver BA and Cleveland DW, Cancer Res. 67, 10103, 2007; King RW, Biochim Biophys Acta 1786, 4, 2008]. In contrast, complete inhibition of the mitotic checkpoint has been recognised to result in severe chromosome missegregation and induction of apoptosis in tumour cells [Kops GJ *et al.*, Nature Rev. Cancer 5, 773, 2005; Schmidt M and Medema RH, Cell Cycle 5, 159, 2006; Schmidt M and Bastians H, Drug Res. Updates 10, 162, 2007]. Thus, mitotic checkpoint abrogation through pharmacological inhibition of components of the mitotic checkpoint, such as Bub1 kinase, represents a new approach for the treatment of proliferative disorders, including solid tumours such as carcinomas, sarcomas, leukaemias and lymphoid malignancies or other disorders, associated with uncontrolled cellular proliferation.

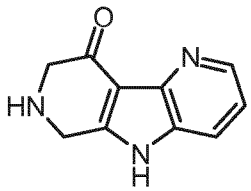
The present invention relates to chemical compounds that inhibit Bub1 kinase.

Established anti-mitotic drugs such as vinca alkaloids, taxanes or epothilones activate the mitotic checkpoint, inducing a mitotic arrest either by stabilising or destabilising microtubule dynamics. This arrest prevents separation of the duplicated chromosomes to form the two daughter cells. Prolonged arrest in mitosis forces a cell either into mitotic exit without cytokinesis (mitotic slippage or adaption) or into mitotic catastrophe leading to cell death [Rieder CL and Maiato H, Dev. Cell 7, 637, 2004]. In contrast, inhibitors of Bub1 prevent the establishment and/or functionality of the mitotic checkpoint and interfere with spindle attachment error correction, which finally results in severe chromosomal missegregation, induction of apoptosis and cell death.

These findings suggest that Bub1 inhibitors should be of therapeutic value for the treatment of proliferative disorders associated with enhanced uncontrolled proliferative cellular processes such as, for example, cancer, inflammation, arthritis, viral diseases, cardiovascular diseases, or fungal diseases in a warm-blooded animal such as man.

WO 2013/050438, WO 2013/092512, WO 2013/167698, WO 2014/147203, WO 2014/147204, WO2014202590, WO2014202588, WO2014202584, WO2014202583 WO2015/063003, disclose substituted indazoles, substituted pyrazoles, and substituted cycloalkylpyrazoles, which are Bub1 kinase inhibitors.

In SciFinder® 5,6,7,8-tetrahydro-9H-pyrrolo[3,2-b:5,4-c']dipyridin-9-one is disclosed as a commercially available compound, but no reference is given.



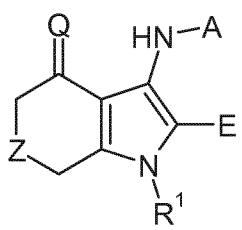
CAS 1540074-49-4

Due to the fact that especially cancer disease as being expressed by uncontrolled proliferative cellular processes in tissues of different organs of the human- or animal body still is not considered to be a controlled disease in that sufficient drug therapies already exist, there is a strong need to provide further new therapeutically useful drugs, preferably inhibiting new targets and providing new therapeutic options (e.g. drugs with improved pharmacological properties).

Description of the invention

Therefore, inhibitors of Bub1 represent valuable compounds that should complement therapeutic options either as single agents or in combination with other drugs.

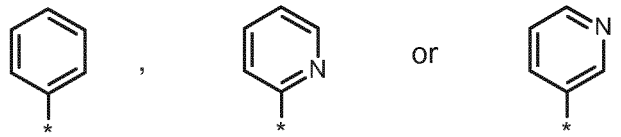
In accordance with a first aspect, the invention relates to a compound of formula (I),



(I)

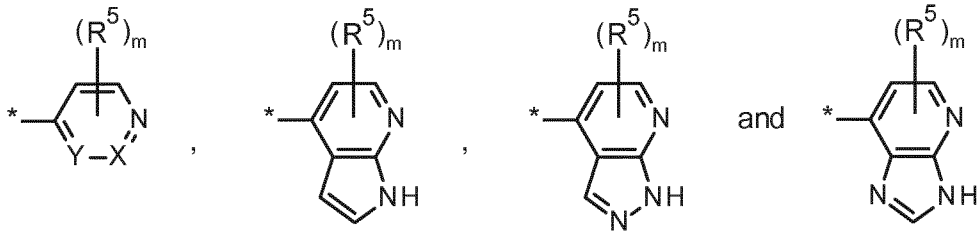
in which:

A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule and said group is optionally substituted, one, two or three times, independently from each other, with R^{3c};

E represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule;

Q represents O or N-OH;

X represents CR^{4a} or N;

Y represents CR^{4b} or N,

wherein when X represents N, Y represents CR^{4b}, and when Y represents N, X represents CR^{4a},

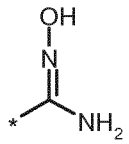
Z represents O, S, SO or NR^2;

R^1 represents hydrogen, C_1-C_4-alkyl or C_1-C_4-alkoxy-C_2-C_4-alkyl-;

R^2 represents hydrogen, C_1-C_4-alkyl, C_3-C_6-cycloalkyl, R^{8a}-C(O)-, R^{8b}O-C(O)-, R^{8c}S-C(O)-, R^6R^7N-C(O)-, $R^{10}R^{11}$N-SO_2-, R^9SO_2-, phenyl-C_1-C_3-alkyl or heteroaryl-C_1-C_3-alkyl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_4-alkyl and C_3-C_6-cycloalkyl are optionally substituted, one, two or three times, independently from each other, with R^{3b} or once with a group



wherein * indicates the point of attachment of said group with the rest of the molecule;

R^{3a}, R^{3b}, R^{3c}, R^{3d} represent, independently from each other, hydroxy, halogen, cyano, $R^{10}R^{11}N$-, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl, C_1-C_4-haloalkyl or C_1-C_4-haloalkoxy;

R^{4a}, R^{4b} represent hydrogen, halogen, hydroxy, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{10}R^{11}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}$N-C(O)-NH-;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b};

wherein C_1-C_4-alkoxy is optionally substituted, one, two or three times, independently from each other, with R^{3d};

R^5 represents, independently from each other, halogen, hydroxy, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{12a}R^{12b}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{12a}R^{12b}$N-C(O)-NH-;

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkoxy-C_2-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,
wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkoxy-C_2-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-,

C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl- and 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b}; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 4- to 7-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing groups selected from O, S, C(=O) or NR^{12a}, and which may be optionally substituted, one, two or three times, independently from each other, with R^{3a};

R^{8a} represents, independently from each other, C_1-C_6-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a}; and

wherein C_1-C_6-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{8b} represents, independently from each other, C_1-C_6-alkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a}; and

wherein C_1-C_6-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{8c} represents C_1-C_4-alkyl;

R^9 represents, independently from each other, C_1-C_4-alkyl, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, 4- to 7-membered heterocycloalkyl-C_1-C_4-alkyl, phenyl or heteroaryl,
wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a}; and

wherein C_1-C_4-alkyl, C_3-C_6-cycloalkyl and 4- to 7-membered heterocycloalkyl-C_1-C_4-alkyl groups are optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{10}, R^{11} represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, R^{12a}-O-C(O)- or phenyl,

wherein said C_1-C_6-alkyl is optionally substituted, one or more times, independently from each other, with halogen, hydroxy, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_3-C_6-cycloalkyl or $R^{12a}R^{12b}N$-,

wherein said phenyl group is optionally substituted, one or more times, independently from each other, with with halogen, hydroxy, C_1-C_3-alkyl, C_1-C_3-alkoxy or C_1-C_3-haloalkoxy;

or,

R^{10} and R^{11} together with the nitrogen atom to which they are attached form a 4- to 7-membered nitrogen containing heterocyclic ring, optionally containing one additional heteroatom selected from O, NR^{12a} and S, and which may be optionally substituted, one or more times, independently from each other, with halogen or C_1-C_3-alkyl;

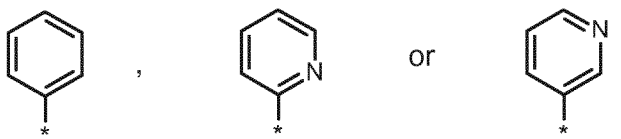
R^{12a}, R^{12b} represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl or -C(=O)-(C_1-C_6-alkyl) ;

m represents 0, 1 or 2;

or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

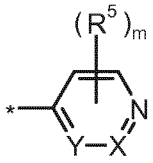
In a second aspect, the invention relates to compounds of formula (I) as described supra, wherein:

A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule and said group is optionally substituted, one, two or three times, independently from each other, with R^{3c};

E represents a group:



wherein * indicates the point of attachment of said group with the rest of the molecule;

Q represents O or N-OH;

X represents CR^{4a};

Y represents CR^{4b} or N,

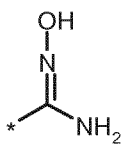
Z represents O, S, SO or NR^{2};

R^1 represents hydrogen or C_1-C_4-alkyl;

R^2 represents hydrogen, C_1-C_4-alkyl, C_3-C_6-cycloalkyl, R^{8a}-C(O)-, R^{8b}O-C(O)-, R^{8c}S-C(O)-, R^6R^7N-C(O)-, $R^{10}R^{11}$N-SO_2-, R^9SO_2-, phenyl-C_1-C_3-alkyl or heteroaryl-C_1-C_3-alkyl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_4-alkyl and C_3-C_6-cycloalkyl are optionally substituted, one, two or three times, independently from each other, with R^{3b} or once with a group



wherein * indicates the point of attachment of said group with the rest of the molecule;

R^{3a} represents, independently from each other, halogen, $R^{10}R^{11}N$-, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl;

R^{3b} represents, independently from each other, hydroxy, halogen, cyano, $R^{10}R^{11}N$-, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl;

R^{3c} represents, independently from each other, hydroxy, halogen, cyano, $R^{10}R^{11}N$-, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl, C_1-C_4-haloalkyl or C_1-C_4-haloalkoxy;

R^{3d} represents, independently from each other, halogen, $R^{10}R^{11}N$-, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl;

R^{4a} represents hydrogen, halogen, hydroxy, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{10}R^{11}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}N$-C(O)-NH-;

R^{4b} represents hydrogen, halogen, hydroxy, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{10}R^{11}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}N$-C(O)-NH-;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b};

wherein C_1-C_4-alkoxy is optionally substituted, one, two or three times, independently from each other, with R^{3d};

R^5 represents, independently from each other, halogen, hydroxy, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{12a}R^{12b}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{12a}R^{12b}N$-C(O)-NH-;

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkoxy-C_2-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,
wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkoxy-C_2-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl- and 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b}; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 4- to 6-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing groups selected from O, S, C(=O) or NR^{12a}, and which may be optionally substituted, one, two or three times, independently from each other, with R^{3a};

R^{8a} represents, independently from each other, C_1-C_6-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a}; and

wherein C_1-C_6-alkyl, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{8b} represents, independently from each other, C_1-C_6-alkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a}; and

wherein C_1-C_6-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{8c} represents C_1-C_4-alkyl;

R^9 represents, independently from each other, C_1-C_4-alkyl, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, 4- to 7-membered heterocycloalkyl-C_1-C_4-alkyl, phenyl or heteroaryl,
wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a}; and

wherein C_1-C_4-alkyl and C_3-C_6-cycloalkyl are optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{10}, R^{11} represent, independently from each other, hydrogen, C_1-C_3-alkyl, C_3-C_4-cycloalkyl, R^{12a}-O-C(O)- or phenyl,

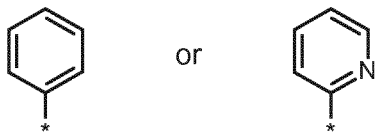
R^{12a}, R^{12b} represent, independently from each other, hydrogen, C_1-C_3-alkyl;

m represents 0 or 1;

or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

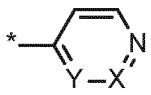
In a third aspect, the invention relates to compounds of formula (I) as described supra, wherein:

A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule and said group is optionally substituted one time with R^{3c};

E represents a group:



wherein * indicates the point of attachment of said group with the rest of the molecule;

Q represents O or N-OH;

X represents CR^{4a};

Y represents CR^{4b} or N,

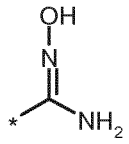
Z represents O, S, SO or NR^2;

R^1 represents hydrogen or C_1-C_4-alkyl;

R^2 represents hydrogen, C_1-C_4-alkyl, R^{8a}-C(O)-, R^{8b}O-C(O)-, R^{8c}S-C(O)-, R^6R^7N-C(O)-, $R^{10}R^{11}$N-SO_2-, R^9SO_2- or phenyl-C_1-C_3-alkyl,

wherein phenyl is optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b} or once with a group



wherein * indicates the point of attachment of said group with the rest of the molecule;

R^{3a} represents, independently from each other, halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy;

R^{3b} represents, independently from each other, hydroxy, halogen, cyano, $R^{10}R^{11}N$-, C_1-C_4-alkyl;

R^{3c} represents, independently from each other, halogen, C_1-C_2-alkyl;

R^{3d} represents, independently from each other, halogen, $R^{10}R^{11}N$-, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl;

R^{4a} represents hydrogen, C_1-C_4-alkyl, $R^{10}R^{11}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}N$-C(O)-NH-;

R^{4b} represents hydrogen, halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b},

wherein C_1-C_4-alkoxy is optionally substituted, one, two or three times, independently from each other, with R^{3d};

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_4-alkyl, C_3-C_4-cycloalkyl, methoxy-ethyl-, methoxy-ethoxy-ethyl-, methylsulfanyl-ethyl-, methylsulfinyl-ethyl-, methylsulfonyl-ethyl-, 5- to 6-membered heterocycloalkyl, or heteroaryl,;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with halogen; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 5- to 6-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing group selected from O, C(=O) or NR^{12a}, and

which may be optionally substituted, one or two times, independently from each other, with R^{3a};

R^{8a} represents, independently from each other, C_1-C_6-alkyl, C_1-alkoxy-C_1-C_2-alkyl-, methylsulfanyl-C_1-C_2-alkyl-, methylsulfinyl-C_1-C_2-alkyl-, methylsulfonyl-C_1-C_2-alkyl-, C_3-C_4-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with halogen, methyl or methoxy; and

wherein C_1-C_6-alkyl, cyclopropyl and 4- to 6-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{8b} represents, independently from each other, C_1-C_5-alkyl,

wherein C_1-C_5-alkyl is optionally substituted, one, two or three times, independently from each other, with halogen or methoxy;

R^{8c} represents C_1-C_4-alkyl;

R^9 represents, independently from each other, C_1-C_3-alkyl, C_3-C_4-cycloalkyl, 4- to 6-membered heterocycloalkyl, 4- to 6-membered heterocycloalkyl-C_1-C_2-alkyl-, or heteroaryl,
wherein heteroaryl is optionally substituted, one, two or three time, with R^{3a}; and

wherein C_1-C_3-alkyl is optionally substituted, one, two or three times, independently from each other, with hydroxy or fluoro;

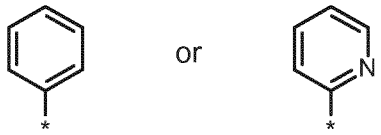
R^{10}, R^{11} represent, independently from each other, hydrogen, C_1-C_3-alkyl, C_3-C_4-cycloalkyl,

R^{12a} represents hydrogen, or C_1-C_2-alkyl;

or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

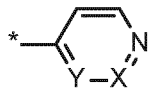
In a fourth aspect, the invention relates to compounds of formula (I) as described supra, wherein:

A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule and said group is optionally substituted once with R^{3c};

E represents a group:



wherein * indicates the point of attachment of said group with the rest of the molecule;

Q represents O or N-OH;

X represents CR^{4a};

Y represents CR^{4b} or N,

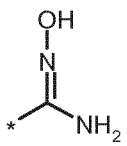
Z represents O, S, SO or NR^2;

R^1 represents hydrogen or C_1-C_4-alkyl;

R^2 represents hydrogen, C_1-C_4-alkyl, R^{8a}-C(O)-, R^{8b}O-C(O)-, R^{8c}S-C(O)-, R^6R^7N-C(O)-, $R^{10}R^{11}$N-SO_2-, R^9SO_2- or phenyl-C_1-C_3-alkyl,

wherein phenyl is optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b} or one time with a group



wherein * indicates the point of attachment of said group with the rest of the molecule;

R^{3a} represents, independently from each other, halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy;

R^{3b} represents, independently from each other, hydroxy, halogen, cyano, C_1-C_4-alkyl;

R^{3c} represents, independently from each other, halogen, C_1-C_2-alkyl,;

R^{3d} represents, independently from each other, halogen, $(CH_3)_2N$-, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl;

R^{4a} represents hydrogen, C_1-C_4-alkyl, H_2N-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}$N-C(O)-NH-;

R^{4b} represents hydrogen, halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy;

wherein C_1-C_4-alkoxy is optionally substituted, one, two or three times, independently from each other, with R^{3d};

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_4-alkyl, cyclopropyl, methoxy-ethyl-, methoxy-ethoxy-ethyl-, methylsulfanyl-ethyl-, methylsulfinyl-ethyl-, methylsulfonyl-ethyl-, tetrahydro-2H-pyran-4-yl or pyridyl;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with halogen; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 5- to 6-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing group selected from O, C(=O) or NR^{12a}, and which may be optionally substituted, one or two times, independently from each other, with methyl;

R^{8a} represents, independently from each other, C_1-C_6-alkyl, methoxymethyl-, methylsulfanyl-C_1-C_2-alkyl-, methylsulfinyl-C_1-C_2-alkyl-, methylsulfonyl-C_1-C_2-alkyl-, cyclopropyl, 4- to 6-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with fluoro, methyl or methoxy; and

wherein C_1-C_6-alkyl, cyclopropyl and 4- to 6-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with hydroxy, fluoro, methyl or $(CH_3)_2N$-;

R^{8b} represents, independently from each other, C_1-C_5-alkyl,

wherein C_1-C_5-alkyl is optionally substituted, one, two or three times, independently from each other, with fluoro or methoxy;

R^{8c} represents C_1-C_4-alkyl;

R^9 represents, independently from each other, C_1-C_3-alkyl, cyclopropyl, 4 to 6 membered heterocycloalkyl, 4 to 6 membered heterocycloalkyl-C_1-C_2-alkyl-, or heteroaryl,
wherein heteroaryl is optionally substituted, one time with methyl; and

wherein C_1-C_3-alkyl is optionally substituted, one, two or three times, independently from each other, with hydroxy or fluoro;

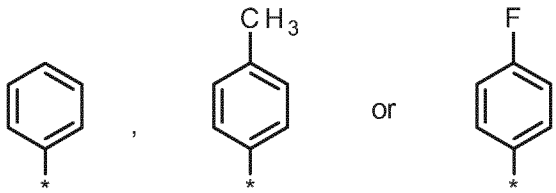
R^{10}, R^{11} represent, independently from each other, hydrogen, C_1-C_3-alkyl, C_3-C_4-cycloalkyl,

R^{12a} represents hydrogen, or C_1-C_2-alkyl;

or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

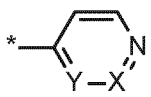
In a fifth aspect, the invention relates to compounds of formula (I) as described supra, wherein:

A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule;

E represents a group:



wherein * indicates the point of attachment of said group with the rest of the molecule;

Q represents O;

X represents CR^{4a};

Y represents CR^{4b} or N;

Z represents O, S, or NR^2;

R^1 represents hydrogen;

R^2 represents hydrogen, cyano-CH_2-, R^{8a}-C(O)-, R^{8b}O-C(O)-, R^{8c}S-C(O)-, R^6R^7N-C(O)-, $(CH_3)HN$-SO_2-, $(CH_3)_2N$-SO_2-, R^9SO_2- or phenyl-CH_2-;

R^{3c} represents fluoro;

R^{3d} represents, independently from each other, $(CH_3)_2N$-, methoxy or cyclopropyl;

R^{4a} represents hydrogen, methyl, H_2N-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}$N-C(O)-NH-;

R^{4b} represents hydrogen, fluoro, chloro, bromo, methoxy or ethoxy,

wherein methoxy and ethoxy are optionally substituted, one, two or three times with fluoro or one time with R^{3d};

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_4-alkyl, cyclopropyl, methoxy-ethyl, methoxy-ethoxy-ethyl, methylsulfanyl-ethyl, methylsulfinyl-ethyl, methylsulfonyl-ethyl, tetrahydro-2H-pyran-4-yl or pyridyl,

wherein C_1-C_4-alkyl is optionally substituted, one or two times with fluoro; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 5- to 6-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing group selected from O, C(=O) or NR^{12a};

R^{8a} represents, independently from each other, C_1-C_6-alkyl, methoxymethyl, methylsulfanyl-C_1-C_2-alkyl, methylsulfinyl-ethyl, methylsulfonyl-ethyl, cyclopropyl, phenyl, pyridyl, 1H-imidazoly, 1-methyl-1H-imidazolyl, 1H-pyrazolyl, 1H-1,2,3-triazolyl,
1,2-thiazolyl, 1,3-thiazolyl or 1,3-oxazolyl,

wherein phenyl is optionally substituted, one or two times, independently from each other, with fluoro, methyl or methoxy, and

wherein C_1-C_6-alkyl and cyclopropyl, are optionally substituted, one, two or three times, independently from each other, with hydroxy or fluoro;

R^{8b} represents, independently from each other, C_1-C_5-alkyl,

wherein C_1-C_5-alkyl is optionally substituted, one time, with fluoro or methoxy;

R^{8c} represents tert-butyl;

R^9 represents, independently from each other, C_1-C_3-alkyl, cyclopropyl, tetrahydro-2H-pyran-4-yl, tetrahydro-2H-pyran-4-ylmethyl, pyridyl, 1H-imidazoly or 1-methyl-1H-imidazolyl, and

wherein C_1-C_3-alkyl is optionally substituted one time with hydroxy or one, two or three times with fluoro;

R^{12a} represents hydrogen, or C_1-alkyl;

or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

In accordance with another aspect, the invention relates to a compound of formula (I), which is selected from the group consisting of:
6-benzyl-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-(3-chloropyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
tert-butyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
3-(phenylamino)-2-(pyridin-4-yl)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one,
6-(cyclopropylcarbonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
6-acetyl-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,

3-(phenylamino)-6-propanoyl-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(2,2-dimethylpropanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
N-ethyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide
tert-butyl 2-(3-fluoropyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-butyl 2-(2-methylpyrimidin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-(2-methylpyrimidin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
2-(2-methylpyrimidin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(2-methylpropanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
methyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
6-(methylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one 6-oxide,
2-(2-aminopyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-(2-aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
tert-butyl 2-[2-(acetylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-ethyl-2-(2-methylpyrimidin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
6-acetyl-2-(2-methylpyrimidin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
methyl 2-(2-methylpyrimidin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

2-[2-(acetylamino)pyridin-4-yl]-N-ethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
2-(2-methylpyrimidin-4-yl)-6-(methylsulfonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
N-4-[6-(cyclopropylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
methyl 2-[2-(acetylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-4-[6-(methylsulfonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
2-(3-fluoropyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylacetamide,
N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylcyclopropanecarboxamide,
3,3,3-trifluoro-N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylpropanamide,
2-(3-methylpyridin-4-yl)-3-(phenylamino)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one,
2-(3-chloropyridin-4-yl)-3-(phenylamino)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one,
2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one,
2-(3-methylpyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
2-(3-bromopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
2-(3-chloropyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylpropanamide,
2-methoxy-N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylacetamide,
2-(methylsulfanyl)-N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylacetamide,
2-(methylsulfinyl)-N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylacetamide,
2-(methylsulfonyl)-N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylacetamide,
N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl-1,3-thiazole-4-carboxamide,

N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl-1,3-oxazole-5-carboxamide,
N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl-1,3-thiazole-5-carboxamide,
4-fluoro-N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylbenzamide,
methyl 4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylcarbamate,
1-ethyl-3-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylurea,
1-cyclopropyl-3-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylurea,
6-(3-hydroxypropanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(3-hydroxy-3-methylbutanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(3,3-dimethylbutanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(1H-imidazol-5-ylcarbonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-[(1-methyl-1H-imidazol-4-yl)carbonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-2-ylcarbonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-3-ylcarbonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-4-ylcarbonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
1-methyl-6-(methylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
1-ethyl-6-(methylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(cyclopropylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-6-(propan-2-ylsulfonyl)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,

6-[(difluoromethyl)sulfonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-[(3,3,3-trifluoropropyl)sulfonyl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(tetrahydro-2H-pyran-4-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-[(tetrahydro-2H-pyran-4-ylmethyl)sulfonyl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(1H-imidazol-5-ylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-2-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-3-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
ethyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
propan-2-yl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2,2-dimethylpropyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2-fluoroethyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2-methoxyethyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate
N-methyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N,N-dimethyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-(2,2-difluoroethyl)-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-cyclopropyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-tert-butyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,

N-(2-methoxyethyl)-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-[2-(methylsulfanyl)ethyl]-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-2-[(S)-methylsulfinyl]ethyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-[2-(methylsulfonyl)ethyl]-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-[2-(2-methoxyethoxy)ethyl]-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
6-[(2-oxoimidazolidin-1-yl)carbonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(pyrrolidin-1-ylcarbonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-6-(piperidin-1-ylcarbonyl)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(morpholin-4-ylcarbonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-[(4-methylpiperazin-1-yl)carbonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-N-(tetrahydro-2H-pyran-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
4-oxo-3-(phenylamino)-N-(pyridin-3-yl)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
[4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridin-6-yl]acetonitrile,
tert-butyl 2-(3-methylpyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-butyl 2-(3-bromopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2-(3-fluoropyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
tert-butyl 2-(3-methoxypyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,

methyl 2-(3-methoxypyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
6-acetyl-2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(2,2-dimethylpropanoyl)-2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-(3-methoxypyridin-4-yl)-6-(methylsulfonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(cyclopropylcarbonyl)-2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-(3-methoxypyridin-4-yl)-3-(phenylamino)-6-(propan-2-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-[(difluoromethyl)sulfonyl]-2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-(3-methoxypyridin-4-yl)-3-(phenylamino)-6-[(3,3,3-trifluoropropyl)sulfonyl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
N-4-[6-acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-4-[6-(1H-imidazol-5-ylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-4-[4-oxo-3-(phenylamino)-6-(pyridin-2-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-4-[4-oxo-3-(phenylamino)-6-(pyridin-3-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-4-[4-oxo-3-(phenylamino)-6-(pyridin-4-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-4-[6-(1H-imidazol-5-ylsulfonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-(4-6-[(1-methyl-1H-imidazol-4-yl)carbonyl]-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-ylpyridin-2-yl)acetamide,
tert-butyl 2-2-[(2-fluoro-2-methylpropanoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-butyl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-butyl 2-[2-([(1S)-2,2-difluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

tert-butyl 4-oxo-3-(phenylamino)-2-2-[(1,3-thiazol-5-ylcarbonyl)amino]pyridin-4-yl-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
6-[(2-hydroxyethyl)sulfonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-[2-(acetylamino)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-{4-[3-anilino-6-(morpholin-4-ylcarbonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
N-4-[4-oxo-3-(phenylamino)-6-(pyrrolidin-1-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-(4-{3-anilino-6-[(4-methylpiperazin-1-yl)carbonyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide,
tert-butyl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 3-anilino-2-[2-({[(rel-1S,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate
2-fluoro-2-methyl-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylpropanamide,
tert-butyl 2-(2-[(1-fluorocyclopropyl)carbonyl]aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
1-fluoro-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
4-fluoro-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,
N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-1,3-thiazole-5-carboxamide,
(1S,2S)-2-fluoro-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
(1S)-2,2-difluoro-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
(1S,2S)-2-fluoro-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
methyl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-[4-(3-anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-4-fluoro-3-methoxybenzamide,

methyl 3-anilino-2-[2-({[(1R,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
(1S,2R)-N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide,
methyl 3-anilino-2-[2-({[(1S,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
methyl 3-anilino-2-{2-[(2-fluoro-2-methylpropanoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-[4-(3-anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-1H-pyrazole-5-carboxamide
methyl 3-anilino-2-[2-({[(1RS)-2,2-difluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
methyl 3-anilino-2-(2-{[(1-fluorocyclopropyl)carbonyl]amino}pyridin-4-yl)-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
rel-(1R,2R)-N-{4-[3-anilino-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2-fluorocyclopropanecarboxamide,
(1RS)-N-{4-[3-anilino-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2,2-difluorocyclopropanecarboxamide,
N-{4-[3-anilino-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-1-fluorocyclopropanecarboxamide,
N-{4-[3-anilino-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-1,3-thiazole-5-carboxamide,
N-[4-(3-anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-2-hydroxy-2-methylpropanamide,
N-[4-(3-anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-N2,N2-dimethylglycinamide,
N-[4-(3-Anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-3,4-difluorobenzamide,
isopropyl 3-anilino-2-{2-[(2-fluoro-2-methylpropanoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
isopropyl 3-anilino-4-oxo-2-{2-[(1,3-thiazol-5-ylcarbonyl)amino]pyridin-4-yl}-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
isopropyl 3-anilino-2-[2-({[rel-(1R,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
isopropyl 3-anilino-2-[2-({[(1RS)-2,2-difluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

isopropyl 3-anilino-2-(2-{[(1-fluorocyclopropyl)carbonyl]amino}pyridin-4-yl)-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-{4-[3-anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-4-fluorobenzamide,
N-{4-[3-anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-1,3-thiazole-5-carboxamide,
N-{4-[3-anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2-fluoro-2-methylpropanamide,
rel-(1R,2R)-N-{4-[3-anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2-fluorocyclopropanecarboxamide,
(1RS)-N-{4-[3-anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2,2-difluorocyclopropanecarboxamide,
N-{4-[3-anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-1-fluorocyclopropanecarboxamide,
N-{4-[3-anilino-4-oxo-6-(piperidin-1-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
2-(2-acetamidopyridin-4-yl)-3-anilino-N,N-diethyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
2-(2-acetamidopyridin-4-yl)-3-anilino-N-methyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-{4-[3-anilino-4-oxo-6-(3,3,3-trifluoropropanoyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
N-[4-(3-anilino-6-isobutyryl-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]acetamide,
N-{4-[3-anilino-6-(isopropylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
N-{4-[3-anilino-6-(cyclopropylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide
N-{4-[3-anilino-4-oxo-6-(tetrahydro-2H-pyran-4-ylsulfonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide
N-{4-[3-anilino-6-(3,3-dimethylbutanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
N-{4-[3-anilino-4-oxo-6-(1,3-thiazol-5-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
N-{4-[3-anilino-6-(1,3-oxazol-5-ylcarbonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-{4-[3-anilino-6-(3-hydroxy-3-methylbutanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-(4-{3-anilino-4-oxo-6-[(2RS)-3,3,3-trifluoro-2-methylpropanoyl]-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide,

N-{4-[3-anilino-6-(4,4-dimethylpentanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-[4-(3-anilino-4-oxo-6-propionyl-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]acetamide,

N-{4-[3-anilino-6-(2,2-dimethylpropanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-(4-{3-anilino-4-oxo-6-[(3,3,3-trifluoropropyl)sulfonyl]-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamideide,

ethyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

2-fluoroethyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

isopropyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

2-(2-acetamidopyridin-4-yl)-3-anilino-N-isopropyl-N-methyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,

2-(2-acetamidopyridin-4-yl)-3-anilino-N-methyl-4-oxo-N-propyl-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

N-(4-{3-anilino-6-[(2-hydroxyethyl)sulfonyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide

N-{4-[3-anilino-6-(3-hydroxypropanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-{4-[3-anilino-4-oxo-6-(4,4,4-trifluorobutanoyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-(4-{3-anilino-6-[(1-methylpiperidin-4-yl)carbonyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide,

N-(4-{3-anilino-6-[3-(methylsulfanyl)propanoyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide,

N-{4-[3-anilino-4-oxo-6-(1,2-thiazol-4-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-{4-[3-anilino-4-oxo-6-(1,3-thiazol-4-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-{4-[3-anilino-6-(1,3-oxazol-4-ylcarbonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

tert-butyl 3-anilino-2-[2-({[(1S,2S)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

(1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide,

(1S,2S)-2-fluoro-N-4-[4-oxo-3-(phenylamino)-6-propanoyl-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,

N-4-[6-(1,3-oxazol-2-ylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,

(1S,2S)-2-fluoro-N-4-[4-oxo-3-(phenylamino)-6-(pyridin-4-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,

(1S,2S)-2-fluoro-N-4-[6-(3-hydroxy-3-methylbutanoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,

(1S,2S)-2-fluoro-N-4-[6-(3-hydroxypropanoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide

(1S,2S)-2-fluoro-N-4-[6-(methylsulfonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,

(1S,2S)-2-fluoro-N-4-[6-(1H-imidazol-5-ylsulfonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,

methyl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-N-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,

2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,

N-ethyl-2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,

(1S,2S)-2-fluoro-N-(4-6-[(4-methylpiperazin-1-yl)carbonyl]-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-ylpyridin-2-yl)cyclopropanecarboxamide,

N-(4-6-[3-(methylsulfonyl)propanoyl]-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-ylpyridin-2-yl)acetamide,

N-4-[6-(3-fluoropropanoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,

(1S,2S)-N-4-[6-(cyclopropylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-2-fluorocyclopropanecarboxamide,

(1S,2S)-N-4-[6-(2,2-dimethylpropanoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-2-fluorocyclopropanecarboxamide,
(1S,2S)-2-fluoro-N-4-[4-oxo-3-(phenylamino)-6-(propan-2-ylsulfonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
ethyl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
propan-2-yl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N,N-diethyl-2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
(1E/Z)-N'-hydroxy-2-[(4E/Z)-4-(hydroxyimino)-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridin-6-yl]ethanimidamide,
N-{4-[3-Anilino-4-oxo-6-(4,4,4-trifluoro-3,3-dimethylbutanoyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
tert-Butyl 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 3-anilino-4-oxo-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 3-anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 3-anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
3-Anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-Anilino-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-Anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-Anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-Acetyl-3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-Acetyl-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-Acetyl-2-[3-(2-methoxyethoxy)pyridin-4-yl]-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,

6-Acetyl-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-Anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-6-(methylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(Methylsulfonyl)-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-[3-(2-Methoxyethoxy)pyridin-4-yl]-6-(methylsulfonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-[3-(Cyclopropylmethoxy)pyridin-4-yl]-6-(methylsulfonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one
Methyl 2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate
2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-N-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide
2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide
2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-6-(morpholin-4-ylcarbonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one
2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-6-[(4-methylpiperazin-1-yl)carbonyl]-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one
2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-3-(phenylamino)-6-(propan-2-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one
Methyl 4-oxo-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate
N-Methyl-4-oxo-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide
N,N-Dimethyl-4-oxo-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide
6-(Morpholin-4-ylcarbonyl)-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one
6-[(4-Methylpiperazin-1-yl)carbonyl]-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one
3-(Phenylamino)-6-(propan-2-ylsulfonyl)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one
Methyl 2-[3-(2-methoxyethoxy)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

2-[3-(2-Methoxyethoxy)pyridin-4-yl]-N-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

Methyl 2-[3-(cyclopropylmethoxy)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

2-[3-(Cyclopropylmethoxy)pyridin-4-yl]-N-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

2-[3-(Cyclopropylmethoxy)pyridin-4-yl]-6-[(4-methylpiperazin-1-yl)carbonyl]-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

tert-Butyl 2-2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,

N-4-[6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]carbonyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,

tert-Butyl 2-2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl-1-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

4-Fluoro-3-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,

N-4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-3-methoxybenzamide,

N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-3-methoxybenzamide,

4-Fluoro-3-methoxy-N-4-[6-(morpholin-4-ylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,

N-4-[6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]carbonyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-3-methoxybenzamide,

4-Fluoro-3-methoxy-N-4-[4-oxo-3-(phenylamino)-6-(pyrrolidin-1-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,

tert-Butyl 2-2-[(4-fluoro-2-methylbenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

4-Fluoro-2-methyl-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,

N-4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-2-methylbenzamide,

tert-Butyl 2-2-[(4-methoxy-2-methylbenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

4-Methoxy-2-methyl-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,

tert-Butyl 2-2-[(5-fluoro-2-methylbenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

5-Fluoro-2-methyl-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,

tert-Butyl 2-2-[(4-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

N-4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluorobenzamide,

(1S,2S)-N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-2-fluorocyclopropanecarboxamide,

N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-1-fluorocyclopropanecarboxamide,

tert-Butyl 4-oxo-3-(phenylamino)-2-2-[(1H-1,2,3-triazol-5-ylcarbonyl)amino]pyridin-4-yl-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

N-4-[4-Oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-1H-1,2,3-triazole-5-carboxamide,

tert-Butyl 2-3-[2-(dimethylamino)ethoxy]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

2-3-[2-(Dimethylamino)ethoxy]pyridin-4-yl-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,

6-Acetyl-2-3-[2-(dimethylamino)ethoxy]pyridin-4-yl-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,

2-3-[2-(Dimethylamino)ethoxy]pyridin-4-yl-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-sulfonamide,

2-[3-(2-Methoxyethoxy)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-sulfonamide,

3-Anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-N,N-dimethyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-sulfonamide,

2-[3-(Cyclopropylmethoxy)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-sulfonamide,

tert-Butyl 2-2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

3-Fluoro-4-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,

N-4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide,
tert-Butyl 2-2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl-1-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
3-Fluoro-4-methoxy-N-4-[1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide
N-4-[6-Acetyl-1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide,
N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide,
N-4-[6-(Dimethylsulfamoyl)-1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide,
3-Fluoro-4-methoxy-N-4-[6-(morpholin-4-ylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,
N-4-[6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]carbonyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide,
3-Fluoro-4-methoxy-N-4-[4-oxo-3-(phenylamino)-6-(pyrrolidin-1-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,
tert-butyl 2-(2-Aminopyridin-4-yl)-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 2-(2-acetamidopyridin-4-yl)-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 2-(2-aminopyridin-4-yl)-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 2-(2-acetamidopyridin-4-yl)-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 4-oxo-3-(phenylamino)-2-[3-(trifluoromethyl)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
3-(Phenylamino)-2-[3-(trifluoromethyl)pyridin-4-yl]-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one,
3-(Phenylamino)-2-[3-(trifluoromethyl)pyridin-4-yl]-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
S-tert-butyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate,
N-(4-{3-[(4-Fluorophenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide,

N-(4-{3-[(4-methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide,

S-tert-butyl 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate,

S-tert-butyl 3-anilino-2-{2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate,

S-tert-butyl 3-anilino-2-{2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate,

S-tert-butyl 3-anilino-2-(2-{[(1-fluorocyclopropyl)carbonyl]amino}pyridin-4-yl)-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate,

S-tert-butyl 3-anilino-2-[2-({[(1S,2S)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate,

tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(pyridin-2-ylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

tert-butyl 2-(2-acetamidopyridin-4-yl)-4-oxo-3-(pyridin-2-ylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

N-(4-(3-[(4-fluorophenyl)amino]-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide,

N-(4-(6-acetyl-3-[(4-fluorophenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide,

2-[2-(acetylamino)pyridin-4-yl]-3-[(4-fluorophenyl)amino]-N-methyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,

methyl 2-[2-(acetylamino)pyridin-4-yl]-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

N-(4-(3-[(4-fluorophenyl)amino]-6-(methylsulfamoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide,

propan-2-yl 2-[2-(acetylamino)pyridin-4-yl]-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

2-[2-(acetylamino)pyridin-4-yl]-N,N-dimethyl-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,

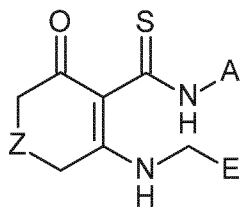
N-(4-(3-[(4-methylphenyl)amino]-4-oxo-6-(propan-2-ylsulfonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide,

N-(4-(6-acetyl-3-[(4-methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide,

2-[2-(acetylamino)pyridin-4-yl]-N-methyl-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,

methyl 2-[2-(acetylamino)pyridin-4-yl]-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-(4-(3-[(4-methylphenyl)amino]-6-(methylsulfamoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide,
propan-2-yl 2-[2-(acetylamino)pyridin-4-yl]-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate
or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

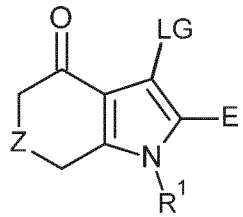
One special aspect of the invention is intermediate (1-2) ,



1-2

whereby A, E and Z have the meaning according to any of claims 1 to 5 or as defined in the aspects and embodiments described herein.

One special aspect of the invention is intermediate (I-h) ,



I-h

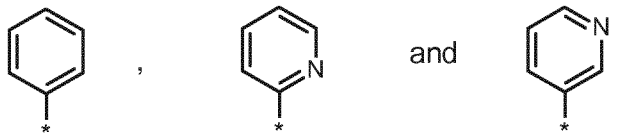
whereby R^1, E and Z have the meaning according to any of claims 1 to 5 or as defined in the aspects and embodiments described herein, and LG represents a leaving group, such as, Cl, Br, I, aryl sulfonates, such as p-toluene sulfonate, or alkyl sulfonates, such as methane sulfonate or trifluoromethane sulfonate.

Another aspect of the invention relates to any of the intermediates described herein and to their use for preparing a compound of formula (I) as defined herein or an N-oxide, a salt, a

tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

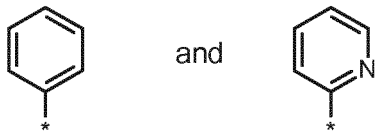
A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule and said group is optionally substituted, one, two or three times, independently from each other, with R^{3c}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

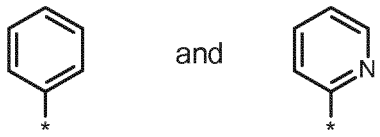
A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule and said group is optionally substituted, one, two or three times, independently from each other, with R^{3c}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

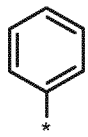
A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule and said group is optionally substituted, one, two or three times, independently from each other, with halogen or C_1-C_3-alkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

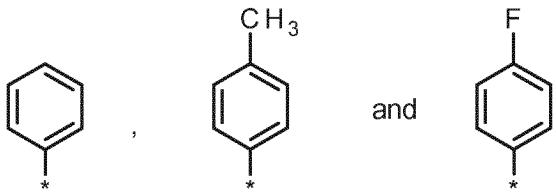
A represents a group:



wherein * indicates the point of attachment of said group with the rest of the molecule and said group is optionally substituted, one, two or three times, independently from each other, with R^{3c}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

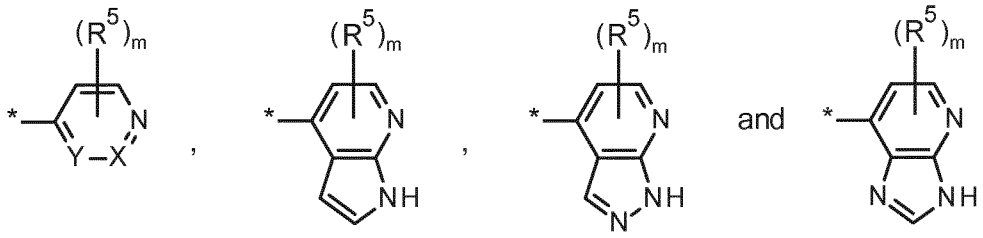
A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

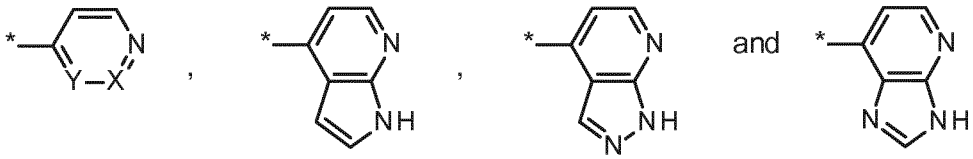
E represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

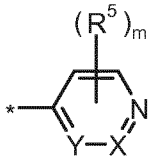
E represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

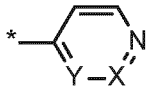
E represents a group:



wherein * indicates the point of attachment of said group with the rest of the molecule.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

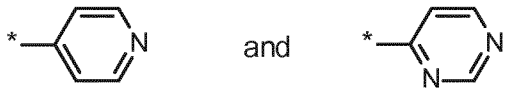
E represents a group:



wherein * indicates the point of attachment of said group with the rest of the molecule.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

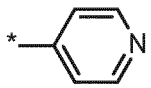
E represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

E represents a group:



wherein * indicates the point of attachment of said group with the rest of the molecule.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

Q represents O or N-OH.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

Q represents O.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

X represents CR^{4a} or N.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

X represents CR^{4a}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

Y represents CR^{4b} or N.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

Y represents CR^{4b}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

Z represents O, S, SO or NR^2.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

Z represents O, S or NR^2.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

Z represents NR^2.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^1 represents hydrogen, C_1-C_4-alkyl or C_1-C_4-alkoxy-C_2-C_4-alkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^1 represents hydrogen or C_1-C_4-alkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

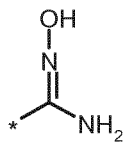
R^1 represents hydrogen.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^2 represents hydrogen, C_1-C_4-alkyl, C_3-C_6-cycloalkyl, R^{8a}-C(O)-, R^{8b}O-C(O)-, R^{8c}S-C(O)-, R^6R^7N-C(O)-, $R^{10}R^{11}$N-SO_2-, R^9SO_2-, phenyl-C_1-C_3-alkyl or heteroaryl-C_1-C_3-alkyl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_4-alkyl and C_3-C_6-cycloalkyl are optionally substituted, one, two or three times, independently from each other, with R^{3b} or once with a group



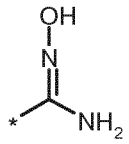
wherein * indicates the point of attachment of said group with the rest of the molecule.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^2 represents hydrogen, C_1-C_4-alkyl, R^{8a}-C(O)-, R^{8b}O-C(O)-, R^{8c}S-C(O)-, R^6R^7N-C(O)-, $R^{10}R^{11}$N-SO_2-, R^9SO_2- or phenyl-C_1-C_3-alkyl,

wherein phenyl is optionally substituted, one, two or three times, independently from each other, with R^{3a},

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b} or one time with a group



wherein * indicates the point of attachment of said group with the rest of the molecule.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^2 represents hydrogen, cyano-CH_2-, R^{8a}-C(O)-, R^{8b}O-C(O)-, R^{8c}S-C(O)-, R^6R^7N-C(O)-, (CH_3)HN-SO_2-, $(CH_3)_2$N-SO_2-, R^9SO_2- or phenyl-CH_2-.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3a}, R^{3b}, R^{3c}, R^{3d} represent, independently from each other, hydroxy, halogen, cyano, $R^{10}R^{11}$N-, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl, C_1-C_4-haloalkyl or C_1-C_4-haloalkoxy.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3a} represents, independently from each other, halogen, $R^{10}R^{11}$N-, C_1-C_4-alkyl, C_1-C_4-alkoxy or C_3-C_6-cycloalkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3a} represents, independently from each other, halogen, C_1-C_4-alkyl or C_1-C_4-alkoxy.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3b} represents, independently from each other, hydroxy, halogen, cyano, $R^{10}R^{11}N$-, C_1-C_4-alkyl, C_1-C_4-alkoxy or C_3-C_6-cycloalkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3b} represents, independently from each other, hydroxy, halogen, cyano, $R^{10}R^{11}N$- or C_1-C_4-alkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3b} represents, independently from each other, hydroxy, halogen, cyano, or C_1-C_4-alkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3c} represents, independently from each other, hydroxy, halogen, cyano, $R^{10}R^{11}N$-, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl, C_1-C_4-haloalkyl or C_1-C_4-haloalkoxy.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3c} represents, independently from each other, halogen or C_1-C_2-alkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3c} represents fluoro.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3d} represents, independently from each other, halogen, $R^{10}R^{11}N$-, C_1-C_4-alkyl, C_1-C_4-alkoxy or C_3-C_6-cycloalkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3d} represents, independently from each other, halogen, $R^{10}R^{11}N$-, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl;

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3d} represents, independently from each other, halogen, $(CH_3)_2N$-, C_1-C_4-alkoxy or C_3-C_6-cycloalkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{3d} represents, independently from each other, $(CH_3)_2N$-, methoxy or cyclopropyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{4a}, R^{4b} represent hydrogen, halogen, hydroxy, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{10}R^{11}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}N$-C(O)-NH-,

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b},

wherein C_1-C_4-alkoxy is optionally substituted, one, two or three times, independently from each other, with R^{3d}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{4a} represents hydrogen, halogen, hydroxy, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{10}R^{11}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}N$-C(O)-NH-.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{4a} represents hydrogen, C_1-C_4-alkyl, $R^{10}R^{11}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}N$-C(O)-NH-.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{4a} represents hydrogen, C_1-C_4-alkyl, H_2N-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}N$-C(O)-NH-.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{4a} represents hydrogen, methyl, H_2N-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}N$-C(O)-NH-.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{4b} represents hydrogen, halogen, hydroxy, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{10}R^{11}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}N$-C(O)-NH-,

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b},

wherein C_1-C_4-alkoxy is optionally substituted, one, two or three times, independently from each other, with R^{3d}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{4b} represents hydrogen, halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b},

wherein C_1-C_4-alkoxy is optionally substituted, one, two or three times, independently from each other, with R^{3d}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{4b} represents hydrogen, halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy,

wherein C_1-C_4-alkoxy is optionally substituted, one, two or three times, independently from each other, with R^{3d}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{4b} represents hydrogen, fluoro, chloro, bromo, methoxy or ethoxy,

wherein methoxy and ethoxy are optionally substituted, one, two or three times with fluoro or oce time with R^{3d}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^5 represents, independently from each other, halogen, hydroxy, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{12a}R^{12b}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{12a}R^{12b}$N-C(O)-NH-.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkoxy-C_2-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,
wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a},

wherein C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkoxy-C_2-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl- and 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b}; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 4- to 7-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing group selected from O, S, C(=O) or NR^{12a}, and which may be optionally substituted, one, two or three times, independently from each other, with R^{3a}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^6 and R^7 together with the nitrogen atom to which they are attached form a 4- to 6-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing groups selected from O, S, C(=O) or NR^{12a}, and which may be optionally substituted, one, two or three times, independently from each other, with R^{3a}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_4-alkyl, C_3-C_4-cycloalkyl, methoxy-ethyl-, methoxy-ethoxy-ethyl-, methylsulfanyl-ethyl-, methylsulfinyl-ethyl-, methylsulfonyl-ethyl-, 5- to 6-membered heterocycloalkyl, or heteroaryl;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with halogen; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 5- to 6-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing group selected from O, C(=O) or NR^{12a}, and which may be optionally substituted, one or two times, independently from each other, with R^{3a};

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_4-alkyl, C_3-C_4-cycloalkyl, methoxy-ethyl-, methoxy-ethoxy-ethyl-, methylsulfanyl-ethyl-, methylsulfinyl-ethyl-, methylsulfonyl-ethyl-, 5- to 6-membered heterocycloalkyl, or heteroaryl;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with halogen.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^6 and R^7 together with the nitrogen atom to which they are attached form a 5- to 6-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing group selected from O, C(=O) or NR^{12a}, and which may be optionally substituted, one or two times, independently from each other, with R^{3a}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_4-alkyl, cyclopropyl, methoxy-ethyl-, methoxy-ethoxy-ethyl-, methylsulfanyl-ethyl-, methylsulfinyl-ethyl-, methylsulfonyl-ethyl-, tetrahydro-2H-pyran-4-yl or pyridyl,

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with halogen; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 5- to 6-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing group selected from O, C(=O) or NR^{12a}, and which may be optionally substituted, one or two times, independently from each other, with methyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_4-alkyl, cyclopropyl, methoxy-ethyl, methoxy-ethoxy-ethyl, methylsulfanyl-ethyl, methylsulfinyl-ethyl, methylsulfonyl-ethyl, tetrahydro-2H-pyran-4-yl or pyridyl,

wherein C_1-C_4-alkyl is optionally substituted, one or two times with fluoro; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 5- to 6-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing group selected from O, C(=O) or NR^{12a}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^6, represents hydrogen, C_1-C_6-alkyl, or C_3-C_6-cycloalkyl,

R^7 represents hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkoxy-C_2-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a},

wherein C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkoxy-C_2-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl- and 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^6 represents hydrogen, C_1-C_4-alkyl, or C_3-C_4-cycloalkyl,

R^7 represents hydrogen, C_1-C_4-alkyl, C_3-C_4-cycloalkyl, methoxy-ethyl-, methoxy-ethoxy-ethyl-, methylsulfanyl-ethyl-, methylsulfinyl-ethyl-, methylsulfonyl-ethyl-, 5- to 6-membered heterocycloalkyl, or heteroaryl;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with halogen.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{8a} represents, independently from each other, C_1-C_6-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a},

wherein C_1-C_6-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{8a} represents, independently from each other, C_1-C_6-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a},

wherein C_1-C_6-alkyl, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{8a} represents, independently from each other, C_1-C_6-alkyl, methoxymethyl-, methylsulfanyl-C_1-C_2-alkyl-, methylsulfinyl-C_1-C_2-alkyl-, methylsulfonyl-C_1-C_2-alkyl-, cyclopropyl, 4 to 6-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with fluoro, methyl or methoxy,

wherein C_1-C_6-alkyl, cyclopropyl and 6-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with hydroxy, fluoro, methyl or $(CH_3)_2N$-.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{8a} represents, independently from each other, C_1-C_6-alkyl, methoxymethyl, methylsulfanyl-C_1-C_2-alkyl, methylsulfinyl-ethyl, methylsulfonyl-ethyl, cyclopropyl, phenyl, pyridyl, 1H-imidazoly, 1-methyl-1H-imidazolyl, 1H-pyrazolyl, 1H-1,2,3-triazolyl, 1,2-thiazolyl, 1,3-thiazolyl or 1,3-oxazolyl,

wherein phenyl is optionally substituted, one or two times, independently from each other, with fluoro, methyl or methoxy,

wherein C_1-C_6-alkyl and cyclopropyl, are optionally substituted, one, two or three times, independently from each other, with hydroxy or fluoro.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{8b} represents, independently from each other, C_1-C_6-alkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a},

wherein C_1-C_6-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{8b} represents, independently from each other, C_1-C_6-alkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a},

wherein C_1-C_6-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{8b} represents, independently from each other, C_1-C_5-alkyl,

wherein C_1-C_5-alkyl is optionally substituted, one, two or three times, independently from each other, with halogen or methoxy.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{8b} represents, independently from each other, C_1-C_5-alkyl,

wherein C_1-C_5-alkyl is optionally substituted, one, two or three times, independently from each other, with fluoro or methoxy.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{8b} represents, independently from each other, C_1-C_5-alkyl,

wherein C_1-C_5-alkyl is optionally substituted one time with fluoro or methoxy.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{8c} represents C_1-C_4-alkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{8c} represents tert-butyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^9 represents, independently from each other, C_1-C_4-alkyl, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, 4- to 7-membered heterocycloalkyl-C_1-C_4-alkyl, phenyl or heteroaryl,
wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a},

wherein C_1-C_4-alkyl, C_3-C_6-cycloalkyl and 4- to 7-membered heterocycloalkyl-C_1-C_4-alkyl groups are optionally substituted, one, two or three times, independently from each other, with R^{3b}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^9 represents, independently from each other, C_1-C_4-alkyl, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, 4- to 7-membered heterocycloalkyl-C_1-C_4-alkyl, phenyl or heteroaryl,
wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a},

wherein C_1-C_4-alkyl and C_3-C_6-cycloalkyl are optionally substituted, one, two or three times, independently from each other, with R^{3b}.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^9 represents, independently from each other, C_1-C_3-alkyl, C_3-C_4-cycloalkyl, 4- to 6-membered heterocycloalkyl, 4- to 6-membered heterocycloalkyl-C_1-C_2-alkyl-, or heteroaryl,
wherein heteroaryl is optionally substituted, one, two or three time, with R^{3a}; and

wherein C_1-C_3-alkyl is optionally substituted, one, two or three times, independently from each other, with hydroxy or fluoro.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^9 represents, independently from each other, C_1-C_3-alkyl, cyclopropyl, 4 to 6 membered heterocycloalkyl, 4 to 6 membered heterocycloalkyl-C_1-C_2-alkyl- or heteroaryl,
wherein heteroaryl is optionally substituted one time with methyl,

wherein C_1-C_3-alkyl is optionally substituted, one, two or three times, independently from each other, with hydroxy or fluoro.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^9 represents, independently from each other, C_1-C_3-alkyl, cyclopropyl, tetrahydro-2H-pyran-4-yl, tetrahydro-2H-pyran-4-ylmethyl, pyridyl, 1H-imidazoly or 1-methyl-1H-imidazolyl,

wherein C_1-C_3-alkyl is optionally substituted one time with hydroxy or one, two or three times with fluoro.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

m represents 0, 1 or 2.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

m represents 0 or 1.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

m represents 0.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{10}, R^{11} represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, R^{12a}-O-C(O)- or phenyl,

wherein said C_1-C_6-alkyl is optionally substituted, one or more times, independently from each other, with halogen, hydroxy, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_3-C_6-cycloalkyl or $R^{12a}R^{12b}N$-,

wherein said phenyl group is optionally substituted, one or more times, independently from each other, with with halogen, hydroxy, C_1-C_3-alkyl, C_1-C_3-alkoxy or C_1-C_3-haloalkoxy;

or,

R^{10} and R^{11} together with the nitrogen atom to which they are attached form a 4- to 7-membered nitrogen containing heterocyclic ring, optionally containing one additional heteroatom selected from O, NR^{12a} and S, and which may be optionally substituted, one or more times, independently from each other, with halogen or C_1-C_3-alkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{10}, R^{11} represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, R^{12a}-O-C(O)- or phenyl,

wherein said C_1-C_6-alkyl is optionally substituted, one or more times, independently from each other, with halogen, hydroxy, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_3-C_6-cycloalkyl or $R^{12a}R^{12b}N$-.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{10} represents hydrogen, C_1-C_6-alkyl, or C_3-C_6-cycloalkyl.

R^{11} represents hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, R^{12a}-O-C(O)- or phenyl,

wherein said C_1-C_6-alkyl is optionally substituted, one or more times, independently from each other, with halogen, hydroxy, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_3-C_6-cycloalkyl or $R^{12a}R^{12b}N$-,

wherein said phenyl group is optionally substituted, one or more times, independently from each other, with with halogen, hydroxy, C_1-C_3-alkyl, C_1-C_3-alkoxy or C_1-C_3-haloalkoxy.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{10} and R^{11} together with the nitrogen atom to which they are attached form a 4- to 7-membered nitrogen containing heterocyclic ring, optionally containing one additional heteroatom selected from O, NR^{12a} and S, and which may be optionally substituted, one or more times, independently from each other, with halogen or C_1-C_3-alkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{10}, R^{11} represent, independently from each other, hydrogen, C_1-C_3-alkyl, C_3-C_4-cycloalkyl, R^{12a}-O-C(O)- or phenyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{12a}, R^{12b} represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl or -C(=O)-(C_1-C_6-alkyl).

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{12a}, R^{12b} represent, independently from each other, hydrogen, C_1-C_3-alkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{12a}, R^{12b} represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl or -C(=O)-(C_1-C_6-alkyl).

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{10}, R^{11} represent, independently from each other, hydrogen, C_1-C_3-alkyl, C_3-C_4-cycloalkyl.

R^{12a}, R^{12b} represent, independently from each other, hydrogen, C_1-C_3-alkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{12a}, R^{12b} represent, independently from each other, hydrogen, C_1-C_2-alkyl.

In a further embodiment of the above-mentioned aspects, the invention relates to compounds of formula (I), wherein:

R^{12a} represents hydrogen, or C_1-alkyl.

One aspect of the invention are compounds of formula (I) as described in the examples, as characterized by their names in the title, as claimed in claims 1 to 5, and their structures as well as the subcombinations of all residues specifically disclosed in the compounds of the examples.

Another aspect of the present invention are the intermediates as used for their synthesis.

A further aspect of the invention are compounds according to the invention, which are present as their salts.

It is to be understood that the present invention relates to any sub-combination within any embodiment or aspect of the present invention of compounds of formula (I) according to the invention, supra.

More particularly still, the present invention covers compounds of formula (I) according to the invention which are disclosed in the Example section of this text, infra.

In accordance with another aspect, the present invention covers methods of preparing compounds of formula (I) of the present invention, said methods comprising the steps as described in the Experimental Section herein.

Another embodiment of the invention are compounds according to the claims as disclosed in the Claims section wherein the definitions are limited according to the preferred or more preferred definitions as disclosed below or specifically disclosed residues of the exemplified compounds and subcombinations thereof.

Definitions

Constituents which are optionally substituted as stated herein, may be substi-tuted, unless otherwise noted, one or more times, independently from one another at any possible position. When any variable occurs more than once in any constituent, each definition is independent. For example, when R^1, R^2, R^{3a}, R^{3b}, R^{3c}, R^{3d},R^{4a}, R^{4b},R^5, R^6, R^7, R^{8a}, R^{8b}, R^{8c}, R^9, R^{10}, R^{11}, R^{12a}, and/or R^{12b}, occur more than once in any compound of formula (I) each

definition of R^1, R^2, R^{3a}, R^{3b}, R^{3c}, R^{3d},R^{4a}, R^{4b},R^5, R^6, R^7, R^{8a}, R^{8b}, R^{8c}, R^9, R^{10}, R^{11}, R^{12a}, and R^{12b} is independent.

Should a constituent be composed of more than one part, e.g. C_1-C_4-alkoxy-C_1-C_4-alkyl-, the position of a possible substituent can be at any of these parts at any suitable position.

A hyphen at the beginning of the constituent marks the point of attachment with the rest of the molecule. Should a ring be substituted the substitutent could be at any suitable position of the ring, also on a ring nitrogen atom if suitable, unless indicated otherwise.

The term "comprising" when used in the specification includes "consisting of".

If it is referred to "as mentioned above" or "mentioned above" within the description it is referred to any of the disclosures made within the specification in any of the preceding pages.

"suitable" within the sense of the invention means chemically possible to be made by methods within the knowledge of a skilled person.

The terms as mentioned in the present text have preferably the following meanings:

The term "halogen atom", "halo-" or "Hal-" is to be understood as meaning a fluorine, chlorine, bromine or iodine atom, preferably a fluorine, chlorine or bromine atom.

The term "C_1-C_6-alkyl" is to be understood as preferably meaning a linear or branched, saturated, monovalent hydrocarbon group having 1, 2, 3, 4, 5 or carbon atoms, *e.g.* a methyl, ethyl, propyl, butyl, pentyl, hexyl, iso-propyl, iso-butyl, sec-butyl, tert-butyl, iso-pentyl, 2-methylbutyl, 1-methylbutyl, 1-ethylpropyl, 1,2-dimethylpropyl, neo-pentyl, 1,1-dimethylpropyl, 4-methylpentyl, 3-methylpentyl, 2-methylpentyl, 1-methylpentyl, 2-ethylbutyl, 1-ethylbutyl, 3,3-dimethylbutyl, 2,2-dimethylbutyl, 1,1-dimethylbutyl, 2,3-dimethylbutyl, 1,3-dimethylbutyl or 1,2-dimethylbutyl group, or an isomer thereof, particularly 1, 2, 3 or 4 carbon atoms ("C_1-C_4-alkyl"), *e.g.* a methyl, ethyl, propyl, butyl, iso-propyl, iso-butyl, sec-butyl, tert-butyl group, more particularly 1, 2, or 3 carbon atoms ("C_1-C_3-alkyl") *e.g.* a methyl, ethyl, n-propyl- or iso-propyl group.

The term "C_2-C_4-alkenyl" is to be understood as meaning a linear or branched, monovalent hydrocarbon group, which contains one or two double bonds, and which has 2, 3 or 4 carbon atoms, particularly 2 or 3 carbon atoms ("C_2-C_3-alkenyl"), it being understood that in the case in which said alkenyl group contains more than one double bond, then said double bonds may be isolated from, or conjugated with, each other. Said alkenyl group is, for example, a vinyl, allyl, (*E*)-2-methylvinyl, (*Z*)-2-methylvinyl, homoallyl, (*E*)-but-2-enyl, (*Z*)-but-2-enyl, (*E*)-but-1-enyl, (*Z*)-but-1-enyl, *iso*-propenyl, 2-methylprop-2-enyl, 1-methylprop-2-enyl, 2-methylprop-1-enyl, (*E*)-1-methylprop-1-enyl, (*Z*)-1-methylprop-1-enyl, or buta-1,3-dienyl group. Particularly, said group is vinyl or allyl.

The term "C_1-C_4-haloalkyl" is to be understood as preferably meaning a linear or branched, saturated, monovalent hydrocarbon group in which the term "C_1-C_4-alkyl" is defined *supra*, and in which one or more hydrogen atoms is replaced by a halogen atom, in identically or differently, *i.e.* one halogen atom being independent from another. Particularly, said halogen atom is F. Said C_1-C_4-haloalkyl group is, for example, $-CF_3$, $-CHF_2$, $-CH_2F$, $-CF_2CF_3$ or $-CH_2CF_3$.

The term "C_1-C_4-alkoxy" is to be understood as preferably meaning a linear or branched, saturated, monovalent, hydrocarbon group of formula –O-alkyl, in which the term "alkyl" is defined *supra*, *e.g.* a methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, iso-butoxy, tert-butoxy or sec-butoxy group, or an isomer thereof.

The term "C_1-C_4-haloalkoxy" is to be understood as preferably meaning a linear or branched, saturated, monovalent C_1-C_4-alkoxy group, as defined *supra*, in which one or more of the hydrogen atoms is replaced, in identically or differently, by a halogen atom. Particularly, said halogen atom is F. Said C_1-C_4-haloalkoxy group is, for example, $–OCF_3$, $-OCHF_2$, $-OCH_2F$, $-OCF_2CF_3$ or $-OCH_2CF_3$.

The term "C_3-C_6-cycloalkyl" is to be understood as meaning a saturated, monovalent, mono-, or bicyclic hydrocarbon ring which contains 3, 4, 5 or 6 carbon atoms ("C_3-C_6-cycloalkyl"). Said C_3-C_6-cycloalkyl group is for example, a monocyclic hydrocarbon ring, *e.g.* a cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, or a bicyclic hydrocarbon ring.

The term "heteroaryl" is understood as meaning a monovalent, monocyclic, aromatic ring system having 5, or 6, ring atoms (a "5- to 6-membered heteroaryl" group), which contains at least one ring heteroatom atom and optionally one, two or three further ring

heteroatoms from the series N, NR^{12a}, O and/or S, and which is bound via a ring carbon atom or, unless otherwise defined, optionally via a ring nitrogen atom (when allowed by valency). R^{12a} is as defined herein. Optionally, said 5- to 6-membered heteroaryl can be fused with a benzene ring (benzofused). Preferred heteroaryl benzofused groups include, but are not limited to, 1,3-benzothiazolyl.

Said heteroaryl group can be a 5-membered heteroaryl group, such as, for example, thienyl, furanyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl or tetrazolyl; or a 6-membered heteroaryl group, such as, for example, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl or triazinyl. In general, and unless otherwise mentioned, the heteroarylic or heteroarylenic radicals include all the possible isomeric forms thereof, *e.g.*: tautomers and positional isomers with respect to the point of linkage to the rest of the molecule. Thus, for some illustrative non-restricting example, the term pyridinyl includes pyridin-2-yl, pyridin-3-yl and pyridin-4-yl; or the term thienyl includes thien-2-yl and thien-3-yl.

The term "4- to 7-membered heterocycloalkyl" or "4- to 7-membered heterocyclic ring", is to be understood as meaning a saturated or partially unsaturated, monovalent, mono- or bicyclic hydrocarbon ring which contains 3, 4, 5 or 6, carbon atoms, and one or more heteroatom-containing groups selected from O, S, S(=O), $S(=O)_2$, and NR^{12a}, in which R^{12a} is as defined herein; optionally one ring carbon atom is replaced with a C(=O) group, it being possible for said heterocycloalkyl group to be attached to the rest of the molecule via any one of the carbon atoms or, if present, the nitrogen atom.

For the avoidance of doubt, when R^{8a} and/or R^{9} represent a heterocycloalkyl group according to the present invention, said heterocycloakyl group is connected with the rest of the molecule via a carbon atom of the heterocycloalkyl ring.

Particularly, said 4- to 7-membered heterocycloalkyl can contain 3, 4, or 5 carbon atoms, and one or more of the above-mentioned heteroatom-containing groups (a "4- to 6-membered heterocycloalkyl"), more particularly said heterocycloalkyl can contain 4 or 5 carbon atoms, and one or more of the above-mentioned heteroatom-containing groups (a "5- to 6-membered heterocycloalkyl").

Particularly, without being limited thereto, said heterocycloalkyl can be a 4-membered ring, such as an azetidinyl, oxetanyl, or a 5-membered ring, such as tetrahydrofuranyl, dioxolinyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, pyrrolinyl, or a 6-membered ring, such

as tetrahydropyranyl, piperidinyl, morpholinyl, dithianyl, thiomorpholinyl, piperazinyl, or trithianyl, or a 7-membered ring, such as a diazepanyl ring, for example. Optionally, said heterocycloalkyl can be benzo fused.

Said heterocyclyl can be bicyclic, such as, without being limited thereto, a 5,5-membered ring, e.g. a hexahydrocyclopenta[c]pyrrol-2(1H)-yl ring, or a 5,6-membered bicyclic ring, e.g. a hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl ring.

As mentioned *supra*, said nitrogen atom-containing ring can be partially unsaturated, *i.e.* it can contain one or more double bonds, such as, without being limited thereto, a 2,5-dihydro-1H-pyrrolyl, 4H-[1,3,4]thiadiazinyl, 4,5-dihydrooxazolyl, or 4H-[1,4]thiazinyl ring, for example, or, it may be benzo-fused, such as, without being limited thereto, a dihydroisoquinolinyl ring, for example.

The term "C_1-C_6", as used throughout this text, *e.g.* in the context of the definition of "C_1-C_6-alkyl" or "C_1-C_6-alkoxy" is to be understood as meaning an alkyl group having a finite number of carbon atoms of 1 to 6, *i.e.* 1, 2, 3, 4, 5, or 6 carbon atoms. It is to be understood further that said term "C_1-C_6" is to be interpreted as any sub-range comprised therein, *e.g.* C_1-C_6, C_2-C_5, C_3-C_4, C_1-C_2, C_1-C_3, C_1-C_4, C_1-C_5, C_1-C_6; particularly C_1-C_2, C_1-C_3, C_1-C_4, C_1-C_5, C_1-C_6; more particularly C_1-C_4; in the case of "C_1-C_4-haloalkyl", "C_1-C_4-alkoxy" or "C_1-C_4-haloalkoxy" even more particularly C_1-C_2.

Further, as used herein, the term "C_3-C_6", as used throughout this text, *e.g.* in the context of the definition of "C_3-C_6-cycloalkyl", is to be understood as meaning a cycloalkyl group having a finite number of carbon atoms of 3 to 6, *i.e.* 3, 4, 5 or 6 carbon atoms. It is to be understood further that said term "C_3-C_6" is to be interpreted as any sub-range comprised therein, *e.g.* C_3-C_6, C_4-C_5, C_3-C_5, C_3-C_4, C_4-C_6, C_5-C_6; particularly C_3-C_6.

The term "substituted" means that one or more hydrogens on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency under the existing circumstances is not exceeded, and that the substitution results in a stable compound. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

The term "optionally substituted" means optional substitution with the specified groups, radicals or moieties.

Ring system substituent means a substituent attached to an aromatic or nonaromatic ring system which, for example, replaces an available hydrogen on the ring system.

As used herein, the term “one or more”, *e.g.* in the definition of the substituents of the compounds of the general formulae of the present invention, is understood as meaning “one, two, three, four or five, particularly one, two, three or four, more particularly one, two or three, even more particularly one or two”.

The invention also includes all suitable isotopic variations of a compound of the invention. An isotopic variation of a compound of the invention is defined as one in which at least one atom is replaced by an atom having the same atomic number but an atomic mass different from the atomic mass usually or predominantly found in nature. Examples of isotopes that can be incorporated into a compound of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, sulphur, fluorine, chlorine, bromine and iodine, such as ^{2}H (deuterium), ^{3}H (tritium), ^{11}C, ^{13}C, ^{14}C, ^{15}N, ^{17}O, ^{18}O, ^{32}P, ^{33}P, ^{33}S, ^{34}S, ^{35}S, ^{36}S, ^{18}F, ^{36}Cl, ^{82}Br, ^{123}I, ^{124}I, ^{129}I and ^{131}I, respectively. Certain isotopic variations of a compound of the invention, for example, those in which one or more radioactive isotopes such as ^{3}H or ^{14}C are incorporated, are useful in drug and/or substrate tissue distribution studies. Tritiated and carbon-14, i.e., ^{14}C, isotopes are particularly preferred for their ease of preparation and detectability. Further, substitution with isotopes such as deuterium may afford certain therapeutic advantages resulting from greater metabolic stability, for example, increased in vivo half-life or reduced dosage requirements and hence may be preferred in some circumstances. Isotopic variations of a compound of the invention can generally be prepared by conventional procedures known by a person skilled in the art such as by the illustrative methods or by the preparations described in the examples hereafter using appropriate isotopic variations of suitable reagents.

Where the plural form of the word compounds, salts, polymorphs, hydrates, solvates and the like, is used herein, this is taken to mean also a single compound, salt, polymorph, isomer, hydrate, solvate or the like.

By "stable compound' or "stable structure" is meant a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

The compounds of this invention may contain one or more asymmetric centre, depending upon the location and nature of the various substituents desired. Asymmetric carbon atoms may be present in the (R) or (S) configuration, resulting in racemic mixtures in the case of a single asymmetric centre, and diastereomeric mixtures in the case of multiple asymmetric centres. In certain instances, asymmetry may also be present due to restricted rotation about a given bond, for example, the central bond adjoining two substituted aromatic rings of the specified compounds.

Substituents on a ring may also be present in either cis or trans form. It is intended that all such configurations (including enantiomers and diastereomers), are included within the scope of the present invention.

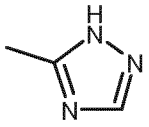
Preferred compounds are those which produce the more desirable biological activity. Separated, pure or partially purified isomers and stereoisomers or racemic or diastereomeric mixtures of the compounds of this invention are also included within the scope of the present invention. The purification and the separation of such materials can be accomplished by standard techniques known in the art.

The optical isomers can be obtained by resolution of the racemic mixtures according to conventional processes, for example, by the formation of diastereoisomeric salts using an optically active acid or base or formation of covalent diastereomers. Examples of appropriate acids are tartaric, diacetyltartaric, ditoluoyltartaric and camphorsulfonic acid. Mixtures of diastereoisomers can be separated into their individual diastereomers on the basis of their physical and/or chemical differences by methods known in the art, for example, by chromatography or fractional crystallisation. The optically active bases or acids are then liberated from the separated diastereomeric salts. A different process for separation of optical isomers involves the use of chiral chromatography (*e.g.*, chiral HPLC columns), with or without conventional derivatisation, optimally chosen to maximise the separation of the enantiomers. Suitable chiral HPLC columns are manufactured by Daicel, *e.g.*, Chiracel OD and Chiracel OJ among many others, all routinely selectable. Enzymatic separations, with or without derivatisation, are also useful. The optically active compounds of this invention can likewise be obtained by chiral syntheses utilizing optically active starting materials.

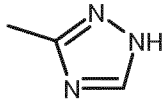
In order to limit different types of isomers from each other reference is made to IUPAC Rules Section E (Pure Appl Chem 45, 11-30, 1976).

The present invention includes all possible stereoisomers of the compounds of the present invention as single stereoisomers, or as any mixture of said stereoisomers, *e.g.* R- or S- isomers, or E- or Z-isomers, in any ratio. Isolation of a single stereoisomer, *e.g.* a single enantiomer or a single diastereomer, of a compound of the present invention may be achieved by any suitable state of the art method, such as chromatography, especially chiral chromatography, for example.

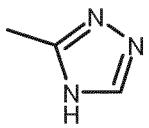
Further, the compounds of the present invention may exist as tautomers. For example, any compound of the present invention which contains a pyrazole moiety as a heteroaryl group for example can exist as a 1H tautomer, or a 2H tautomer, or even a mixture in any amount of the two tautomers, or a triazole moiety for example can exist as a 1H tautomer, a 2H tautomer, or a 4H tautomer, or even a mixture in any amount of said 1H, 2H and 4H tautomers, namely:



1H-tautomer



2H-tautomer



4H-tautomer.

The present invention includes all possible tautomers of the compounds of the present invention as single tautomers, or as any mixture of said tautomers, in any ratio.

Further, the compounds of the present invention can exist as N-oxides, which are defined in that at least one nitrogen of the compounds of the present invention is oxidised. The present invention includes all such possible N-oxides.

The present invention also relates to useful forms of the compounds as disclosed herein, such as metabolites, hydrates, solvates, prodrugs, salts, in particular pharmaceutically acceptable salts, and co-precipitates.

The compounds of the present invention can exist as a hydrate, or as a solvate, wherein the compounds of the present invention contain polar solvents, in particular water, methanol or ethanol for example as structural element of the crystal lattice of the compounds. The amount of polar solvents, in particular water, may exist in a stoichiometric or non-stoichiometric ratio. In the case of stoichiometric solvates, *e.g.* a

hydrate, hemi-, (semi-), mono-, sesqui-, di-, tri-, tetra-, penta- *etc.* solvates or hydrates, respectively, are possible. The present invention includes all such hydrates or solvates.

Further, the compounds of the present invention can exist in free form, *e.g.* as a free base, or as a free acid, or as a zwitterion, or can exist in the form of a salt. Said salt may be any salt, either an organic or inorganic addition salt, particularly any pharmaceutically acceptable organic or inorganic addition salt, customarily used in pharmacy.

The term "pharmaceutically acceptable salt" refers to a relatively non-toxic, inorganic or organic acid addition salt of a compound of the present invention. For example, see S. M. Berge, *et al*. "Pharmaceutical Salts," J. Pharm. Sci. **1977**, 66, 1-19.

A suitable pharmaceutically acceptable salt of the compounds of the present invention may be, for example, an acid-addition salt of a compound of the present invention bearing a nitrogen atom, in a chain or in a ring, for example, which is sufficiently basic, such as an acid-addition salt with an inorganic acid, such as hydrochloric, hydrobromic, hydroiodic, sulfuric, bisulfuric, phosphoric, or nitric acid, for example, or with an organic acid, such as formic, acetic, acetoacetic, pyruvic, trifluoroacetic, propionic, butyric, hexanoic, heptanoic, undecanoic, lauric, benzoic, salicylic, 2-(4-hydroxybenzoyl)-benzoic, camphoric, cinnamic, cyclopentanepropionic, digluconic, 3-hydroxy-2-naphthoic, nicotinic, pamoic, pectinic, persulfuric, 3-phenylpropionic, picric, pivalic, 2-hydroxyethanesulfonate, itaconic, sulfamic, trifluoromethanesulfonic, dodecylsulfuric, ethansulfonic, benzenesulfonic, para-toluenesulfonic, methansulfonic, 2-naphthalenesulfonic, naphthalinedisulfonic, camphorsulfonic acid, citric, tartaric, stearic, lactic, oxalic, malonic, succinic, malic, adipic, alginic, maleic, fumaric, D-gluconic, mandelic, ascorbic, glucoheptanoic, glycerophosphoric, aspartic, sulfosalicylic, hemisulfuric, or thiocyanic acid, for example.

Further, another suitably pharmaceutically acceptable salt of a compound of the present invention which is sufficiently acidic, is an alkali metal salt, for example a sodium or potassium salt, an alkaline earth metal salt, for example a calcium or magnesium salt, an ammonium salt or a salt with an organic base which affords a physiologically acceptable cation, for example a salt with N-methyl-glucamine, dimethyl-glucamine, ethyl-glucamine, lysine, dicyclohexylamine, 1,6-hexadiamine, ethanolamine, glucosamine, sarcosine, serinol, tris-hydroxy-methyl-aminomethane, aminopropandiol, sovak-base, 1-amino-2,3,4-butantriol. Additionally, basic nitrogen containing groups may be quaternised with such

agents as lower alkyl halides such as methyl, ethyl, propyl, and butyl chlorides, bromides and iodides; dialkyl sulfates like dimethyl, diethyl, and dibutyl sulfate; and diamyl sulfates, long chain halides such as decyl, lauryl, myristyl and strearyl chlorides, bromides and iodides, aralkyl halides like benzyl and phenethyl bromides and others.

Those skilled in the art will further recognise that acid addition salts of the claimed compounds may be prepared by reaction of the compounds with the appropriate inorganic or organic acid via any of a number of known methods. Alternatively, alkali and alkaline earth metal salts of acidic compounds of the invention are prepared by reacting the compounds of the invention with the appropriate base via a variety of known methods.

The present invention includes all possible salts of the compounds of the present invention as single salts, or as any mixture of said salts, in any ratio.

In the present text, in particular in the Experimental Section, for the synthesis of intermediates and of examples of the present invention, when a compound is mentioned as a salt form with the corresponding base or acid, the exact stoichiometric composition of said salt form, as obtained by the respective preparation and/or purification process, is, in most cases, unknown.

Unless specified otherwise, suffixes to chemical names or structural formulae such as "hydrochloride", "trifluoroacetate", "sodium salt", or "x HCl", "x CF3COOH", "x Na+", for example, are to be understood as not a stoichiometric specification, but solely as a salt form.

This applies analogously to cases in which synthesis intermediates or example compounds or salts thereof have been obtained, by the preparation and/or purification processes described, as solvates, such as hydrates with (if defined) unknown stoichiometric composition.

The salts include water-insoluble and, particularly, water-soluble salts.

Furthermore, derivatives of the compounds according to the invention and the salts thereof which are converted into a compound according to the invention or a salt thereof in a biological system (bioprecursors or pro-drugs) are covered by the invention. Said biological system is e.g. a mammalian organism, particularly a human subject. The

bioprecursor is, for example, converted into the compound according to the invention or a salt thereof by metabolic processes.

As used herein, the term "*in vivo* hydrolysable ester" is understood as meaning an *in vivo* hydrolysable ester of a compound of the present invention containing a carboxy or hydroxy group, for example, a pharmaceutically acceptable ester which is hydrolysed in the human or animal body to produce the parent acid or alcohol. Suitable pharmaceutically acceptable esters for carboxy include for example alkyl, cycloalkyl and optionally substituted phenylalkyl, in particular benzyl esters, C_1-C_6 alkoxymethyl esters, *e.g.* methoxymethyl, C_1-C_6 alkanoyloxymethyl esters, *e.g.* pivaloyloxymethyl, phthalidyl esters, C_3-C_8 cycloalkoxy-carbonyloxy-C_1-C_6 alkyl esters, *e.g.* 1-cyclohexylcarbonyloxyethyl; 1,3-dioxolen-2-onylmethyl esters, *e.g.* 5-methyl-1,3-dioxolen-2-onylmethyl; and C_1-C_6-alkoxycarbonyloxyethyl esters, *e.g.* 1-methoxycarbonyloxyethyl, and may be formed at any carboxy group in the compounds of this invention.

An *in vivo* hydrolysable ester of a compound of the present invention containing a hydroxy group includes inorganic esters such as phosphate esters and [alpha]-acyloxyalkyl ethers and related compounds which as a result of the *in vivo* hydrolysis of the ester breakdown to give the parent hydroxy group. Examples of [alpha]-acyloxyalkyl ethers include acetoxymethoxy and 2,2-dimethylpropionyloxymethoxy. A selection of *in vivo* hydrolysable ester forming groups for hydroxy include alkanoyl, benzoyl, phenylacetyl and substituted benzoyl and phenylacetyl, alkoxycarbonyl (to give alkyl carbonate esters), dialkylcarbamoyl and N-(dialkylaminoethyl)-N-alkylcarbamoyl (to give carbamates), dialkylaminoacetyl and carboxyacetyl. The present invention covers all such esters.

Furthermore, the present invention includes all possible crystalline forms, or polymorphs, of the compounds of the present invention, either as single polymorphs, or as a mixture of more than one polymorphs, in any ratio.

In the context of the properties of the compounds of the present invention the term "pharmacokinetic profile" means one single parameter or a combination thereof including permeability, bioavailability, exposure, and pharmacodynamic parameters such as duration, or magnitude of pharmacological effect, as measured in a suitable experiment. Compounds with improved pharmacokinetic profiles can, for example, be used in lower doses to achieve the same effect, may achieve a longer duration of action, or a may achieve a combination of both effects.

The term “combination” in the present invention is used as known to persons skilled in the art and may be present as a fixed combination, a non-fixed combination or kit-of-parts.

A “fixed combination” in the present invention is used as known to persons skilled in the art and is defined as a combination wherein the said first active ingredient and the said second active ingredient are present together in one unit dosage or in a single entity. One example of a “fixed combination” is a pharmaceutical composition wherein the said first active ingredient and the said second active ingredient are present in admixture for simultaneous administration, such as in a formulation. Another example of a “fixed combination” is a pharmaceutical combination wherein the said first active ingredient and the said second active ingredient are present in one unit without being in admixture.

A non-fixed combination or “kit-of-parts” in the present invention is used as known to persons skilled in the art and is defined as a combination wherein the said first active ingredient and the said second active ingredient are present in more than one unit. One example of a non-fixed combination or kit-of-parts is a combination wherein the said first active ingredient and the said second active ingredient are present separately. The components of the non-fixed combination or kit-of-parts may be administered separately, sequentially, simultaneously, concurrently or chronologically staggered. Any such combination of a compound of the present invention with an anti-cancer agent as defined below is an embodiment of the invention.

The term “(chemotherapeutic) anti-cancer agents”, includes but is not limited to 131I-chTNT, abarelix, abiraterone, aclarubicin, adalimumab, ado-trastuzumab emtansine, afatinib, aflibercept, aldesleukin, alectinib, alemtuzumab, alendronic acid, alitretinoin, altretamine, amifostine, aminoglutethimide, hexyl aminolevulinate, amrubicin, amsacrine, anastrozole, ancestim, anethole dithiolethione, anetumab ravtansine, angiotensin II, antithrombin III, aprepitant, arcitumomab, arglabin, arsenic trioxide, asparaginase, atezolizumab, axitinib, azacitidine, basiliximab, belotecan, bendamustine, besilesomab, belinostat, bevacizumab, bexarotene, bicalutamide, bisantrene, bleomycin, blinatumomab, bortezomib, buserelin, bosutinib, brentuximab vedotin, busulfan, cabazitaxel, cabozantinib, calcitonine, calcium folinate, calcium levofolinate, capecitabine, capromab, carbamazepine carboplatin, carboquone, carfilzomib, carmofur, carmustine, catumaxomab, celecoxib, celmoleukin, ceritinib, cetuximab, chlorambucil, chlormadinone, chlormethine, cidofovir, cinacalcet, cisplatin, cladribine, clodronic acid, clofarabine,

cobimetinib, copanlisib , crisantaspase, crizotinib, cyclophosphamide, cyproterone, cytarabine, dacarbazine, dactinomycin, daratumumab, darbepoetin alfa, dabrafenib, dasatinib, daunorubicin, decitabine, degarelix, denileukin diftitox, denosumab, depreotide, deslorelin, dianhydrogalactitol, dexrazoxane, dibrospidium chloride, dianhydrogalactitol, diclofenac, dinutuximab, docetaxel, dolasetron, doxifluridine, doxorubicin, doxorubicin + estrone, dronabinol, eculizumab, edrecolomab, elliptinium acetate, elotuzumab, eltrombopag, endostatin, enocitabine, enzalutamide, epirubicin, epitiostanol, epoetin alfa, epoetin beta, epoetin zeta, eptaplatin, eribulin, erlotinib, esomeprazole, estradiol, estramustine, ethinylestradiol, etoposide, everolimus, exemestane, fadrozole, fentanyl, filgrastim, fluoxymesterone, floxuridine, fludarabine, fluorouracil, flutamide, folinic acid, formestane, fosaprepitant, fotemustine, fulvestrant, gadobutrol, gadoteridol, gadoteric acid meglumine, gadoversetamide, gadoxetic acid, gallium nitrate, ganirelix, gefitinib, gemcitabine, gemtuzumab, Glucarpidase, glutoxim, GM-CSF, goserelin, granisetron, granulocyte colony stimulating factor, histamine dihydrochloride, histrelin, hydroxycarbamide, I-125 seeds, lansoprazole, ibandronic acid, ibritumomab tiuxetan, ibrutinib, idarubicin, ifosfamide, imatinib, imiquimod, improsulfan, indisetron, incadronic acid, ingenol mebutate, interferon alfa, interferon beta, interferon gamma, iobitridol, iobenguane (123I), iomeprol, ipilimumab, irinotecan, Itraconazole, ixabepilone, ixazomib, lanreotide, lansoprazole, lapatinib, lasocholine, lenalidomide, lenvatinib, lenograstim, lentinan, letrozole, leuprorelin, levamisole, levonorgestrel, levothyroxine sodium, lisuride, lobaplatin, lomustine, lonidamine, masoprocol, medroxyprogesterone, megestrol, melarsoprol, melphalan, mepitiostane, mercaptopurine, mesna, methadone, methotrexate, methoxsalen, methylaminolevulinate, methylprednisolone, methyltestosterone, metirosine, mifamurtide, miltefosine, miriplatin, mitobronitol, mitoguazone, mitolactol, mitomycin, mitotane, mitoxantrone, mogamulizumab, molgramostim, mopidamol, morphine hydrochloride, morphine sulfate, nabilone, nabiximols, nafarelin, naloxone + pentazocine, naltrexone, nartograstim, necitumumab, nedaplatin, nelarabine, neridronic acid, netupitant/palonosetron, nivolumab, pentetreotide, nilotinib, nilutamide, nimorazole, nimotuzumab, nimustine, nintedanib, nitracrine, nivolumab, obinutuzumab, octreotide, ofatumumab, olaparib, olaratumab, omacetaxine mepesuccinate, omeprazole, ondansetron, oprelvekin, orgotein, orilotimod, osimertinib, oxaliplatin, oxycodone, oxymetholone, ozogamicine, p53 gene therapy, paclitaxel, palbociclib, palifermin, palladium-103 seed, palonosetron, pamidronic acid, panitumumab, panobinostat, pantoprazole, pazopanib, pegaspargase, PEG-epoetin beta (methoxy PEG-epoetin beta), pembrolizumab, pegfilgrastim, peginterferon alfa-2b, pembrolizumab, pemetrexed, pentazocine, pentostatin, peplomycin, Perflubutane, perfosfamide, Pertuzumab, picibanil,

pilocarpine, pirarubicin, pixantrone, plerixafor, plicamycin, poliglusam, polyestradiol phosphate, polyvinylpyrrolidone + sodium hyaluronate, polysaccharide-K, pomalidomide, ponatinib, porfimer sodium, pralatrexate, prednimustine, prednisone, procarbazine, procodazole, propranolol, quinagolide, rabeprazole, racotumomab, radium-223 chloride, radotinib, raloxifene, raltitrexed, ramosetron, ramucirumab, ranimustine, rasburicase, razoxane, refametinib , regorafenib, risedronic acid, rhenium-186 etidronate, rituximab, rolapitant, romidepsin, romiplostim, romurtide, roniciclib , samarium (153Sm) lexidronam, sargramostim, satumomab, secretin, siltuximab, sipuleucel-T, sizofiran, sobuzoxane, sodium glycididazole, sonidegib, sorafenib, stanozolol, streptozocin, sunitinib, talaporfin, talimogene laherparepvec, tamibarotene, tamoxifen, tapentadol, tasonermin, teceleukin, technetium (99mTc) nofetumomab merpentan, 99mTc-HYNIC-[Tyr3]-octreotide, tegafur, tegafur + gimeracil + oteracil, temoporfin, temozolomide, temsirolimus, teniposide, testosterone, tetrofosmin, thalidomide, thiotepa, thymalfasin, thyrotropin alfa, tioguanine, tocilizumab, topotecan, toremifene, tositumomab, trabectedin, trametinib, tramadol, trastuzumab, trastuzumab emtansine, treosulfan, tretinoin, trifluridine + tipiracil, trilostane, triptorelin, trametinib, trofosfamide, thrombopoietin, tryptophan, ubenimex, valatinib , valrubicin, vandetanib, vapreotide, vemurafenib, vinblastine, vincristine, vindesine, vinflunine, vinorelbine, vismodegib, vorinostat, vorozole, yttrium-90 glass microspheres, zinostatin, zinostatin stimalamer, zoledronic acid, zorubicin.

It has now been found, and this constitutes the basis of the present invention, that said compounds of the present invention have surprising and advantageous properties.

In particular, said compounds of the present invention have surprisingly been found to effectively inhibit Bub1 kinase and may therefore be used for the treatment or prophylaxis of diseases of uncontrolled cell growth, proliferation and/or survival, inappropriate cellular immune responses, or inappropriate cellular inflammatory responses or diseases which are accompanied with uncontrolled cell growth, proliferation and/or survival, inappropriate cellular immune responses, or inappropriate cellular inflammatory responses, particularly in which the uncontrolled cell growth, proliferation and/or survival, inappropriate cellular immune responses, or inappropriate cellular inflammatory responses is mediated by Bub1 kinase, such as, for example, haematological tumours, solid tumours, and/or metastases thereof, *e.g.* leukaemias and myelodysplastic syndrome, malignant lymphomas, head and neck tumours including brain tumours and brain metastases, tumours of the thorax including non-small cell and small cell lung tumours, gastrointestinal tumours, endocrine

tumours, mammary and other gynaecological tumours, urological tumours including renal, bladder and prostate tumours, skin tumours, and sarcomas, and/or metastases thereof.

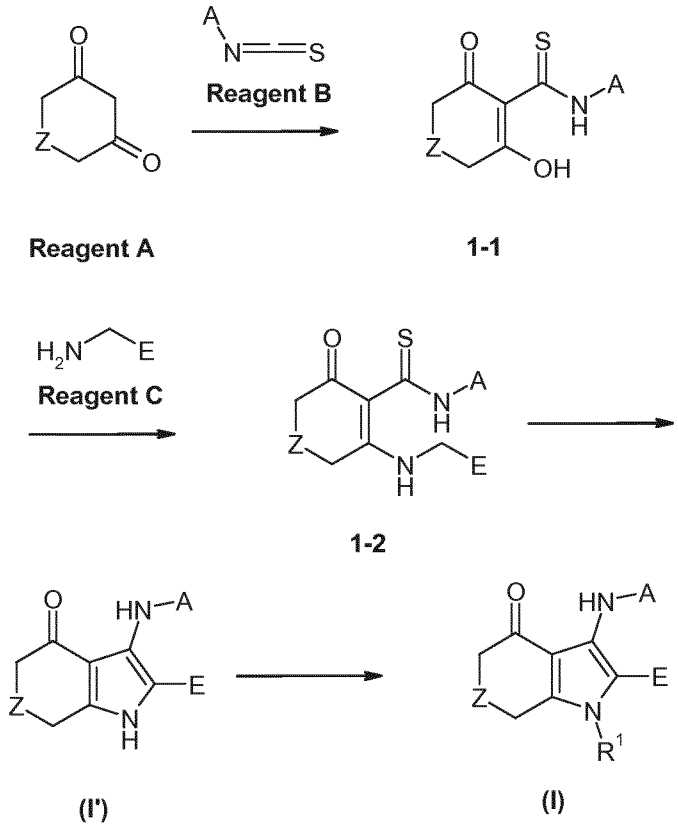
The intermediates used for the synthesis of the compounds of the claims as described below, as well as their use for the synthesis of the compounds of claims described below, are one further aspect of the present invention. Preferred intermediates are the Intermediate Examples as disclosed below.

General Procedures

The compounds according to the invention can be prepared according to the following Schemes 1 through 5.

The Schemes and procedures described below illustrate synthetic routes to the compounds of general formula (I) of the invention and are not intended to be limiting. It is obvious to the person skilled in the art that the order of transformations as exemplified in the Schemes can be modified in various ways. The order of transformations exemplified in the Schemes is therefore not intended to be limiting. In addition, interconversion of any of the substituents R^1, A, E, Q and Z can be achieved before and/or after the exemplified transformations. These modifications can be such as the introduction of protecting groups, cleavage of protecting groups, reduction or oxidation of functional groups, halogenation, metallation, substitution or other reactions known to the person skilled in the art. These transformations include those which introduce a functionality which allows for further interconversion of substituents. Appropriate protecting groups and their introduction and cleavage are well-known to the person skilled in the art (see for example T.W. Greene and P.G.M. Wutts in *Protective Groups in Organic Synthesis*, 3rd edition, Wiley 1999). Specific examples are described in the subsequent paragraphs.

Scheme 1



Scheme 1: Route for the preparation of compounds of general formula (I), wherein R^1, A, E and Z have the meaning as given for general formula (I), supra. In addition, interconversion of any of the substituents R^1, A, E and Z can be achieved before and/or after the exemplified transformations. These modifications can be such as the introduction of protecting groups, cleavage of protecting groups, reduction or oxidation of functional groups, halogenation, metallation, substitution or other reactions known to the person skilled in the art. These transformations include those which introduce a functionality which allows for further interconversion of substituents. Appropriate protecting groups and their introduction and cleavage are well-known to the person skilled in the art (see for example T.W. Greene and P.G.M. Wutts in Protective Groups in Organic Synthesis, 3rd edition, Wiley 1999). Specific examples are described in the subsequent paragraphs.

Reagent A, reagent B, and reagent C are either commercially available or can be prepared according to procedures available from the public domain, as understandable to the person skilled in the art. Specific examples are described in the subsequent paragraphs.

For reagent A whereby Z is oxygen can be synthesized accordingly to literature methods, e.g. Li *et al.*, *J. Org. Chem.*, 2006, 71, 1725. For reagent A whereby Z is sulphur can be

synthesized accordingly to literature methods, e.g. Ghosh *et al.*, *J. Med. Chem.*, 2013, 56, 6792. For reagent A whereby Z is nitrogen (preferably protected with a suitable protecting group) can be synthesized accordingly to literature methods, e.g. *tert*-butoxycarbonyl protected WO2006/3096 and benzyl protected Olofsson *et al.*, *J. Org. Chem.*, 2006, 71, 8256.

A suitably substituted dione of general formula (reagent A), such as, for example, 2H-pyran-3,5(4H,6H)-dione, can be reacted with a suitably substituted isothiocyanate (reagent B), such as, for example, phenylisothiocyanate, in a suitable solvent system, such as, for example, acetonitrile, in the presence of a suitable base, such as, for example, triethylamine or DBU, at temperatures ranging from -78℃ to +100℃, preferably the reaction is carried out at 0℃ or +100℃, to fu rnish general formula (**1-1**). Similar reactions have been performed in the literature (D. E. Worrall, *J. Am. Chem. Soc.*, 1940, 62, 675).

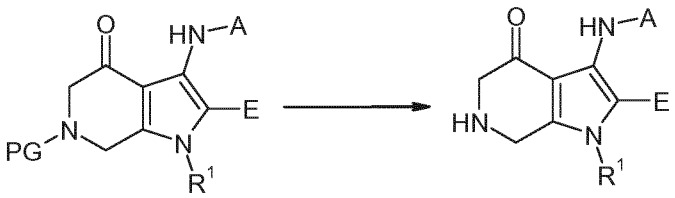
Intermediates of general formula (**1-1**) can be converted to Intermediates of general formula (**1-2**) by reaction with a suitable amine, such as, for example 4-(aminomethyl)pyridine, in a suitable solvent system, such as, for example, ethanol and ethyl acetate, at a temperature between room temperature and the boiling point of the respective solvents, preferably the reaction is carried out at the boiling point of the respective solvents, whereby the water formed in the reaction is removed from the reaction by methods known to those skilled in the art, such as, for example, azeotropic removal of water (Dean-Stark conditions) or with molecular sieves, to furnish general formula (**1-2**).

Intermediates of general formula (**1-2**) are reacted with a base and/or oxidizing reagent, preferably an oxidizing agent, such as, for example hydrogen peroxide or SIBX (stabilized iodoxybenoic acid), in a suitable solvent system, such as, for example, methanol, in a temperature range from -30℃ to the boiling point o f the respective solvent, preferably the reaction is carried out at the boiling point of the respective solvent, to furnish Intermediates of general formula (**I'**).

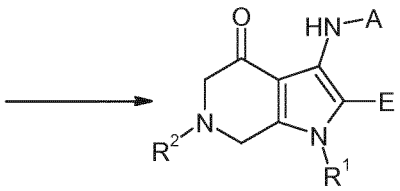
Intermediates of general formula (**I'**) are reacted with an alkylating agent which contain a suitable leaving group, such as, for example, Cl, Br, aryl sulfonates such as for example *para* -toluene sulfonate, or alkyl sulfonates such as for example methane sulfonate or trifluoromethane sulfonate, in the presence of a base, such as, for example sodium

hydride, potassium carbonate, caesium carbonate, in a suitable solvent system, such as, for example, dimethylformamide, in a temperature range from 0℃ to the boiling point of the respective solvent, to furnish Intermediates of general formula (**I**). Alternatively, intermediates of general formula (**I'**) are reacted with a nucleophile, for example, an alcohol, using Mitsunobu reactions conditions known to those skilled the art, which conditions use, for example, a phosphine, such as, for example, triphenylphosphine, in the presence of an azodicarboxylate, such as, for example, diisopropyl azodicarboxylate), in a suitable solvent system, such as, for example, tetrahydrofuran, in a temperature range from -30℃ to the boiling point of the respective solvent, preferably the reaction is carried out at room temperature, to furnish compounds of general formula (**I**).

Scheme 2



Wherein
PG = protecting group



(I)

Scheme 2: Route for the preparation of compounds of general formula (Ib), wherein R^1, R^2, A and E have the meaning as given for general formula (I), supra. In addition, interconversion of any of the substituents R^1, R^2, A and E can be achieved before and/or after the exemplified transformation. These modifications can be such as the introduction of protecting groups, cleavage of protecting groups, reduction or oxidation of functional groups, halogenation, metallation, substitution or other reactions known to the person skilled in the art. These transformations include those which introduce a functionality which allows for further interconversion of substituents. Appropriate protecting groups and their introduction and cleavage are well-known to the person skilled in the art (see for example T.W. Greene and P.G.M. Wutts in Protective Groups in Organic Synthesis, 3rd edition, Wiley 1999). Specific examples are described in the subsequent paragraphs.

Intermediates of general formula (**II**) whereby the nitrogen of the six-membered ring is protected with a suitable protecting group, such as, for example, *N-tert*-butoxycarbonyl or benzyl, are deprotected using methods known to those skilled in the art (see for example T.W. Greene and P.G.M. Wutts in Protective Groups in Organic Synthesis, 3rd edition, Wiley 1999). One such protecting groups would be *N-tert*-butoxycarbonyl and this can be removed under various varying conditions, such as, for example, using an acid, such as, for example, trifluoroacetic acid, optionally in a suitable solvent, such as, for example, dichloromethane, in a temperature range from 0℃ to the boiling point of the respective solvent, to furnish Intermediates of general formula (**III**) or salts thereof.

Intermediates of general formula (**III**) are reacted with an acylating reagent, a sulfonylating reagent or an acylated agent which can be generated *in situ*, to furnish Intermediates of general formula (**I**), these types of reactions are well-known to those skilled in the art (selected literature examples are: V. Tai, *et al.*, Bioorg. Med. Chem. Lett., 2006, 16, 4554 – 4558; K. Nishijima, *et al.*, Eur. J. Med. Chem., 2000, 35, 227 – 240; C. Tamura *et al.*, J. Heterocyclic Chem., 1980, 17, 1 – 4; G. S. Basarab, *et al.*, J. Med. Chem., 2014, 57, 6060 – 6082; Y-B. Yhang, *et al.*, Archiv der Pharmazie, 2010, 343, 143 – 151; G. Samala, *et al.*, Bioorg. Med. Chem., 2014, 22, 1938 – 1947; L. Ingrassia, *et al.*, J. Med. Chem., 2009, 52, 1100 – 1114).

Not-limiting examples of these types of reagents can be:

i) carboxylic acid with dehydrating reagents typically used in amide bond formation, such as, for example (HBTU, HATU, PyBOP, BOP, T3P, EDC, DIC, DCC)

ii) acid fluorides, acid chlorides, acid bromides, preferably in the presence of a base

iii) acid anhydrides, preferably in the presence of a base

iv) chloroformates, preferably in the presence of a base

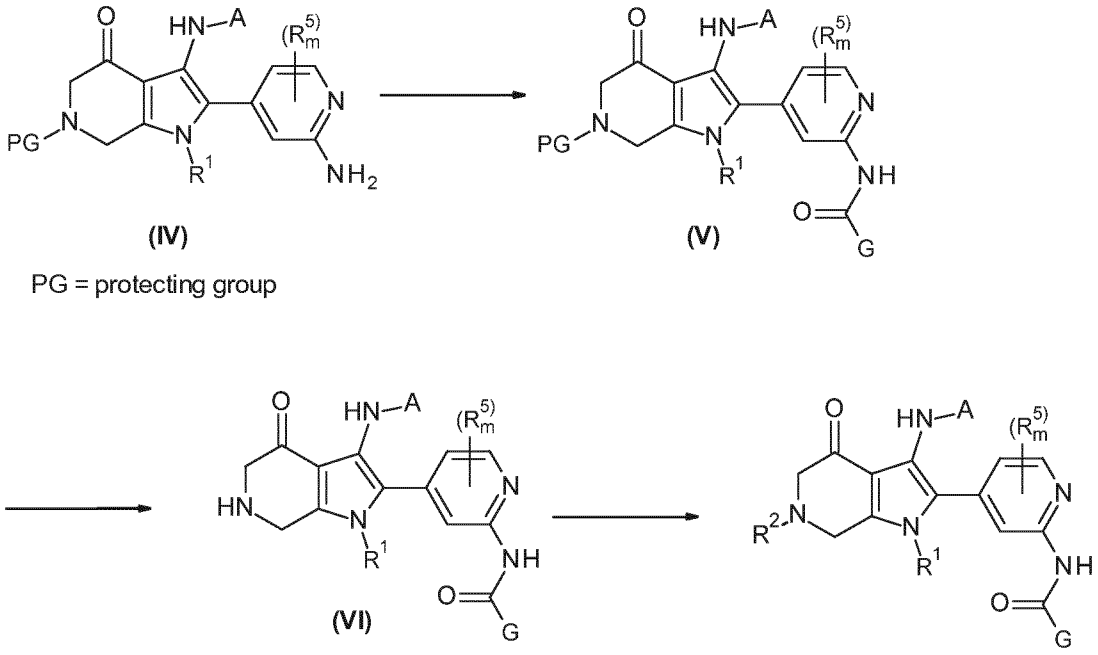
v) isocyanates, preferably in the presence of a base

Intermediates of general formula (**III**) are reacted with an alkylating agent which contain a suitable leaving group, such as, for example, Cl, Br, aryl sulfonates such as for example *para*-toluene sulfonate, or alkyl sulfonates such as for example methane sulfonate or trifluoromethane sulfonate, in the presence of a base, such as, for example sodium hydride, potassium carbonate, caesium carbonate, in a suitable solvent system, such as, for example, dimethylformamide, in a temperature range from 0℃ to the boiling point of

the respective solvent, to furnish Intermediates of general formula (**I**), these types of reactions are well-known to those skilled in the art (selected literature examples are: J. Yu, *et al.*, Org. Lett., 2002, 4, 4681 – 4684; M. Magnus, *et al.*, J. Am. Chem. Soc., 1989, 111, 786 – 789; A.J. Da Silva Goes *et al.*, Tetrahedron Lett., 1998, 39, 1339 – 1340; C. R. Edwankar *et al.*, J. Org. Chem., 2013, 78, 6471 – 6487).

Intermediates of general formula (**III**) are treated with a carbonyl containing carbonyl containing reagent, such as, for example, aldehydes or ketones, in a suitable solvent system, such as, for example, methanol, ethanol, tetrahydrofuran, which optionally contains an acid, such as, for example, acetic acid, in a temperature range from 0℃ to the boiling point of the respective solvent, to the reaction mixture is added of a reducing agent, such as, for example, sodium borohydride or sodium cyanoborohydride or sodium tris(acetoxy)borohydride, to furnish Intermediates of general formula (**I**), these types of reactions are well-known to those skilled in the art (selected literature examples are: L. A. Thompson, *et al.*, Bioorg. Med. Chem. Lett., 2011, 21 6909 – 6915; G. Rai, *et al.*, J. Med. Chem., 2012, 55, 3101 – 3112; U. M. Battisti *et al.*, Tetrahedron Lett., 2012, 53, 1122 – 1125).

Scheme 3



Scheme 3: Route for the preparation of compounds of general formula (**Ia**), wherein R^1, R^2, R^5 and A have the meaning as given for general formula (I), supra and G represents a group selected from R^{8a}, $R^{8b}O$- or R^6R^7N-. In addition, interconversion of any of the substituents R^1, R^2, R^5, A, and G can be achieved before and/or after the exemplified transformation. These modifications can be such as the introduction of protecting groups, cleavage of protecting groups, reduction or oxidation of functional groups, halogenation, metallation, substitution or other reactions known to the person skilled in the art. These transformations include those which introduce a functionality which allows for further interconversion of substituents. Appropriate protecting groups and their introduction and cleavage are well-known to the person skilled in the art (see for example T.W. Greene and P.G.M. Wutts in Protective Groups in Organic Synthesis, 3rd edition, Wiley 1999). Specific examples are described in the subsequent paragraphs.

Intermediates of general formula (**IV**) are reacted with an acylating reagent or an acylated agent which can be generated *in situ*, to furnish intermediates of general formula (**V**), these types of reactions are well-known to those skilled in the art (selected literature examples are: S. Miwatashi, *et al.*, J. Med. Chem., 2005, 48, 5966 – 5979; J. Zhao, *et al.*, Bioorg. Med. Chem. Lett., 2014, 24,. 2802 – 2806; M. P. Hay, *et al.*, J. Med. Chem., 2010, 53, 787 – 797; J. M. Keith, *et al.*, Med. Chem. Lett, 2012, 3, 823 – 827; J. Liang, *et al.*, Eur.. J. Med. Chem., 2013, 67, 175 – 187; D. Lesuisse, *et al.*, Bioorg. Med. Chem. Lett., 2011, 21, 2224 - 2228).

Not-limiting examples of these types of reagents can be:

i) carboxylic acid with dehydrating reagents typically used in amide bond formation, such as, for example (HBTU, HATU, PyBOP, BOP, T3P, EDC, DIC, DCC)

ii) acid fluorides, acid chlorides, acid bromides, preferably in the presence of a base

iii) acid anhydrides, preferably in the presence of a base

iv) chloroformates, preferably in the presence of a base

v) isocyanates, preferably in the presence of a base

Intermediates of general formula (**V**) whereby the nitrogen of the six-membered ring is protected with a suitable protecting group, such as, for example, N-tert-butoxycarbonyl or benzyl, are deprotected using methods known to those skilled in the art (see for example T.W. Greene and P.G.M. Wutts in Protective Groups in Organic Synthesis, 3rd edition, Wiley 1999). One such protecting groups would be N-tert-butoxycarbonyl and this can be

removed under various varying conditions, such as, for example, using an acid, such as, for example, trifluoroacetic acid, optionally in a suitable solvent, such as, for example, dichloromethane, in a temperature range from 0℃ to the boiling point of the respective solvent, to furnish Intermediates of general formula (**VI**) or salts thereof.

Intermediates of general formula (**VI**) are reacted with an acylating reagent, a sulfonylating reagent or an acylated agent which can be generated in situ, to furnish Intermediates of general formula (**I**), these types of reactions are well-known to those skilled in the art (selected literature examples are: V. Tai, *et al.*, Bioorg. Med. Chem. Lett., 2006, 16, 4554 – 4558; K. Nishijima, *et al.*, Eur. J. Med. Chem., 2000, 35, 227 – 240; C. Tamura *et al.*, J. Heterocyclic Chem., 1980, 17, 1 – 4; G. S. Basarab, *et al.*, J. Med. Chem., 2014, 57, 6060 – 6082; Y-B. Yhang, *et al.*, Archiv der Pharmazie, 2010, 343, 143 – 151; G. Samala, *et al.*, Bioorg. Med. Chem., 2014, 22, 1938 – 1947; L. Ingrassia, *et al.*, J. Med. Chem., 2009, 52, 1100 – 1114).

Not-limiting examples of these types of reagents can be:

i) carboxylic acid with dehydrating reagents typically used in amide bond formation, such as, for example (HBTU, HATU, PyBOP, BOP, T3P, EDC, DIC, DCC)

ii) acid fluorides, acid chlorides, acid bromides, preferably in the presence of a base

iii) acid anhydrides, preferably in the presence of a base

iv) chloroformates, preferably in the presence of a base

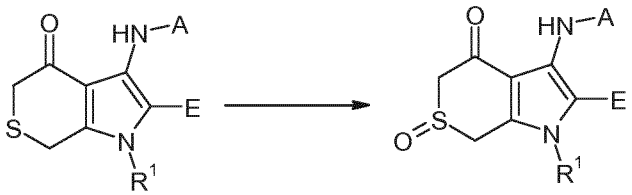
v) isocyanates, preferably in the presence of a base

Intermediates of general formula (**VI**) are reacted with an alkylating agent which contain a suitable leaving group, such as, for example, Cl, Br, aryl sulfonates such as for example para-toluene sulfonate, or alkyl sulfonates such as for example methane sulfonate or trifluoromethane sulfonate, in the presence of a base, such as, for example sodium hydride, potassium carbonate, caesium carbonate, in a suitable solvent system, such as, for example, dimethylformamide, in a temperature range from 0℃ to the boiling point of the respective solvent, to furnish Intermediates of general formula (I), these types of reactions are well-known to those skilled in the art (selected literature examples are: J. Yu, *et al.*, Org. Lett., 2002, 4, 4681 – 4684; M. Magnus, *et al.*, J. Am. Chem. Soc., 1989, 111, 786 – 789; A.J. Da Silva Goes *et al.*, Tetrahedron Lett., 1998, 39, 1339 – 1340; C. R. Edwankar *et al.*, J. Org. Chem., 2013, 78, 6471 – 6487).

Intermediates of general formula (**VI**) are treated with a carbonyl containing reagent, such as, for example, aldehydes or ketones, in a suitable solvent system, such as, for example,

methanol, ethanol, tetrahydrofuran, which optionally contains an acid, such as, for example, acetic acid, in a temperature range from 0℃ to the boiling point of the respective solvent, to the reaction mixture is added of a reducing agent, such as, for example, sodium borohydride or sodium cyanoborohydride or sodium tris(acetoxy)borohydride, to furnish Intermediates of general formula (**I**), these types of reactions are well-known to those skilled in the art (selected literature examples are: L. A. Thompson, *et al.*, Bioorg. Med. Chem. Lett., 2011, 21 6909 – 6915; G. Rai, *et al.*, J. Med. Chem., 2012, 55, 3101 – 3112; U. M. Battisti *et al.*, Tetrahedron Lett., 2012, 53, 1122 – 1125).

Scheme 4

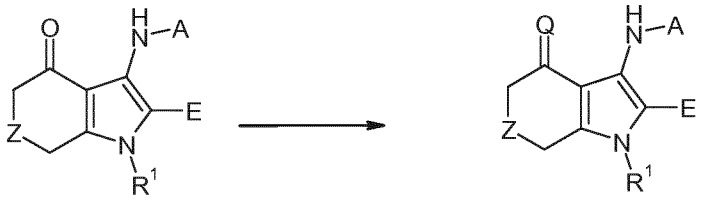


(**I'**) (**I**)

Scheme 4: Route for the preparation of compounds of general formula (**I**), wherein R^1, A and E have the meaning as given for general formula (I), supra. In addition, interconversion of any of the substituents R^1, A and E can be achieved before and/or after the exemplified transformation. These modifications can be such as the introduction of protecting groups, cleavage of protecting groups, reduction or oxidation of functional groups, halogenation, metallation, substitution or other reactions known to the person skilled in the art. These transformations include those which introduce a functionality which allows for further interconversion of substituents. Appropriate protecting groups and their introduction and cleavage are well-known to the person skilled in the art (see for example T.W. Greene and P.G.M. Wutts in Protective Groups in Organic Synthesis, 3rd edition, Wiley 1999). Specific examples are described in the subsequent paragraphs.

Intermediates of general formula (**I'**) can be reacted with an oxidizing agent, such as, for example, meta-chloroperbenzoic acid, hydrogen peroxide, dimethyl dioxirane in a suitable solvent system, such as, for example, dichloromethane, chloroform, acetone in a temperature range from -78℃ to the boiling point of the respective solvent, to furnish Intermediates of general formula (**I**), these types of reactions are well-known to those skilled in the art (selected literature examples are: C. J. Moody et al., Terahedron., 1990, 46, 6525 – 6544; K. Matsumoto, et al., Heterocycles, 2008, 76, 191 – 196).

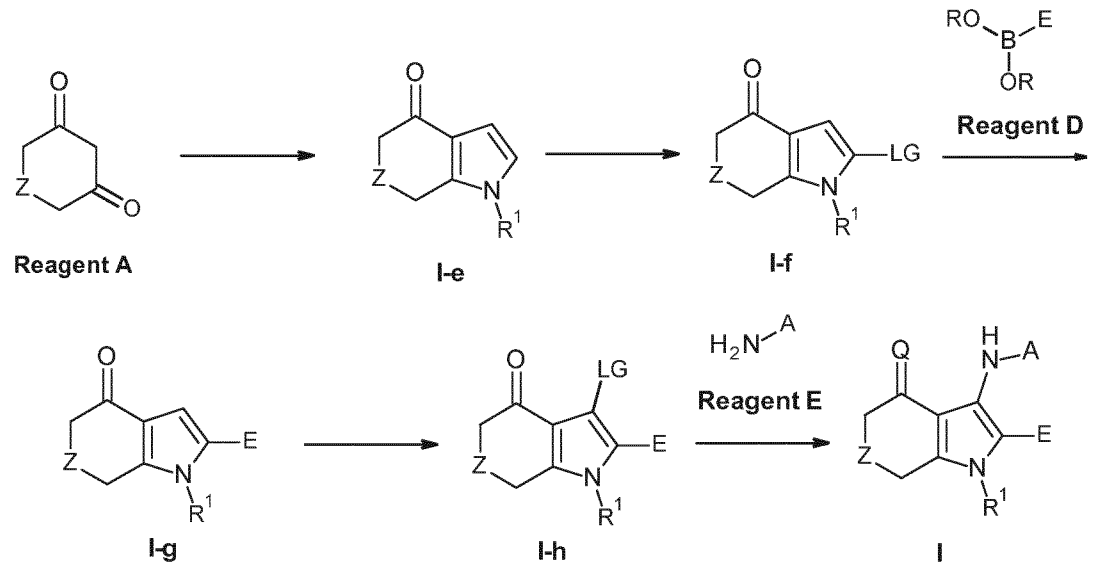
Scheme 5



I-c **I-d**

Scheme 5 Process for the preparation of compounds of general formula **(I-d)**, wherein R^1, A, E and Z have the meaning as given for general formula (**I**) and Q represents (=NOH). Compounds of general formula (**I-c**) wherein Q represents O can be converted to compounds of general formula (**I-d**) wherein Q represents (=NOH) by treatment with a suitable reagent containing one or more NH_2 group, such as for example, amines, oxyamines, hydroxylamines, hydrazones or hydrazines, preferably hydroxylamine, in a suitable solvent, such as, for example, ethanol, methanol, water, DMF, tetrahydrofuran (THF), preferably, ethanol, in a temperature range from -78℃ to the boiling point of the respective solvent, preferably the reaction is carried out RT to the boiling point of the respective solvent, to furnish general formula (**I**). Such transformations have been previously reported (Kesten *et al.*, J. Med. Chem., 1992, 35, 3429 – 3447; Bisejieks *et al.*, Heterocyclic Comunn., 2005, 11, 9 – 12; Maillard *et al.*, Eur. J. Med. Chem., 1984, 19, 451 – 456; Hassan, Molecules, 2013, 18, 2683 – 2711).

Scheme 6



Scheme 6 Route for the preparation of compounds of general formula (**I**), wherein R^1, A, E and Z have the meaning as given for general formula (**I**), supra. In addition,

interconversion of any of the substituents, R^1, A, E and Z could be achieved before and/or after the exemplified transformation. The R in reagent D could be hydrogen to represent boronic acids or alkyl groups to represent boronic esters, optionally both R groups could be attached to each other to represent, for example, pincacol boronic esters. The substituent LG in the intermediates of general formulae **1-f** and **1-h** could be a suitable leaving group, such as, for example, Cl, Br, I, aryl sulfonates such as for example p-toluene sulfonate, or alkyl sulfonates such as for example methane sulfonate or trifluoromethane sulfonate, preferably Br.

These modifications could be such as the introduction of protecting groups, cleavage of protecting groups, reduction or oxidation of functional groups, halogenation, metallation, substitution or other reactions known to the person skilled in the art. These transformations include those which introduce a functionality which allows for further interconversion of substituents. Appropriate protecting groups and their introduction and cleavage are well-known to the person skilled in the art (see for example T.W. Greene and P.G.M. Wutts in Protective Groups in Organic Synthesis, 3rd edition, Wiley 1999). Specific examples are described in the subsequent paragraphs.

Compounds reagent A, reagent D and reagent E, are either commercially available or could be prepared according to procedures available from the public domain, as understandable to the person skilled in the art.

Intermediates of general formula (**I-e**) could be synthesized using the teachings of, for example, Menichincheri et al., WO2014/72220 A1; Clark et al., J. Heterocyclic Chem., 1993, 30, 829 – 831; Clark et al., J. Med. Chem., 1993, 36, 2645 – 2657; Schneller et al., J. Med. Chem., 1978, 21, 990 – 993.

Intermediates of general formula (**I-e**) could be reacted to introduce a substituent LG, which is preferably a halide, such reactions are known to those skilled in the art (see Menichincheri et al., WO2014/72220 A1 (introduction of bromide and iodide); Smith et al., Bioorg. Med. Chem. Lett., 2007, 17, 673 – 678 (introduction of bromide) Cee et al., WO2014/22752 A1 (introduction of bromide)) to furnish intermediates of the formula (**I-f**).

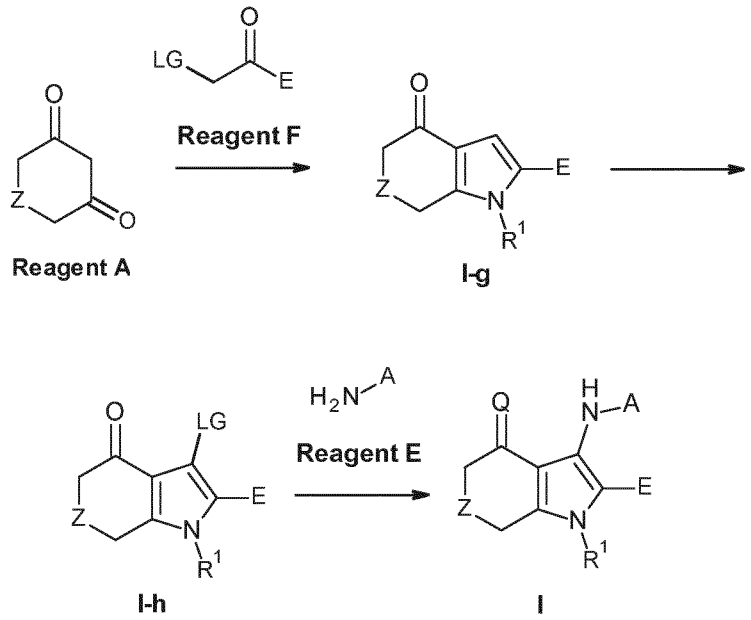
Intermediates of general formula **I-f** could be reacted to introduce the substituent E, such as, for example, an aryl or heteroaryl group using metal-catalyzed reactions, such as, for example, the Suzuki reaction. Such reactions are known to those skilled in the art (WO2007/39740 A2; Cee et al., WO2014/22752 A1; Smith et al., Bioorg. Med. Chem. Lett., 2007, 17, 673 – 678) and could be used to furnish intermediates of the formula **I-g**.

Intermediates of general formula (**I-g**) could be reacted with a suitable halogenating reagent, such as, for example, copper(I) bromide and N-bromosuccinimide, preferably N-bromosuccinimide, in a suitable solvent system, such as, for example, acetonitrile, in a

temperature range from 0℃ to the boiling point of the respective solvent, preferably the reaction would be carried out at room temperature, to furnish general formula (**I-h**). Similar examples for the bromination of pyrroles have been previously published using lactams (Aiello, E. et al., J. Heterocyclic Chem., 1982, 19, 977 – 979; Duranti, A. et al., Bioorg. Med. Chem., 2003, 11, 3965 – 3973).

Intermediates of general formula (**I-h**) could be reacted with a suitable primary amines, such as, for example, primary aromatic amines and primary amines, preferably primary aromatic amines, such as, for example aniline or 3-aminothiophene, in the presence of a base, such as, for example, lithium bis(trimethylsilyl)amide (LHMDS), in the presence of a catalyst, such as, for example a suitable ligand, preferably 2-(di-tert-butylphosphino)-2′,4′,6′- triisopropyl-3,6-dimethoxy-1,1′-biphenyl (tBuBrettPhos) and in the presence of a pre-catalyst, such as, for example a palladium pre-catalyst, preferably chloro[2-(dicyclohexylphosphino)-3,6-dimethoxy-2′,4′,6′-triisopropyl-1,1′-biphenyl][2-(2-aminoethyl)phenyl]palladium(II) (BrettPhos-PreCat MTBE ether adduct) in a suitable solvent system, such as, for example, tetrahydrofuran (THF), in a temperature range from 0℃ to the 200℃, preferably the reactio n is carried out at 80℃, to furnish compounds of general formula (**I**).

Scheme 7



Scheme 7 Route for the preparation of compounds of general formula (**I**), wherein R^1, A, E and Z have the meaning as given for general formula (**I**), supra. In addition, interconversion of any of the substituents, R^1, A, E and Z could be achieved before and/or

after the exemplified transformation. The substituent LG in intermediates of general formula **1-h** can be a suitable leaving group, such as, for example, Cl, Br, I, aryl sulfonates such as for example p-toluene sulfonate, or alkyl sulfonates such as for example methane sulfonate or trifluoromethane sulfonate. These modifications could be such as the introduction of protecting groups, cleavage of protecting groups, reduction or oxidation of functional groups, halogenation, metallation, substitution or other reactions known to the person skilled in the art. These transformations include those which introduce a functionality which allows for further interconversion of substituents. Appropriate protecting groups and their introduction and cleavage are well-known to the person skilled in the art (see for example T.W. Greene and P.G.M. Wuts in Protective Groups in Organic Synthesis, 3rd edition, Wiley 1999). Specific examples are described in the subsequent paragraphs.

Compounds reagent A, reagent E and reagent F, are either commercially available or could be prepared according to procedures available from the public domain, as understandable to the person skilled in the art.

A suitably substituted 1,3-dicarbonyl compound (Reagent A) could be reacted with suitably substituted compounds of general formula (Reagent F) where LG is a suitable leaving group, such as, for example, bromide, chloride, which in the presence of an ammonium salt, such as, for example, ammonium acetate can furnish intermediates of general formula (**I-g**). Similar examples for the formation of a pyrrole ring in this manner have been previously published using lactams (Anderson, D. R. et al., J. Med. Chem., 2007, 50, 2647 – 2654; Amici, R. et al., J. Med. Chem., 2008, 51, 487 – 501; Bargiotti, A. et al., J. Med. Chem., 2009, 52, 293 – 307; Voss etal., WO 2015/022073 A1).

Intermediates of general formula (**I-g**) could be reacted with a suitable halogenating reagent, such as, for example, copper(I) bromide and N-bromosuccinimide, preferably N-bromosuccinimide, in a suitable solvent system, such as, for example, acetonitrile, in a temperature range from 0℃ to the boiling point of the respective solvent, preferably the reaction is carried out at room temperature, to furnish general formula (**I-h**). Similar examples for the bromination of pyrroles have been previously published using lactams (Aiello, E. et al., J. Heterocyclic Chem., 1982, 19, 977 – 979; Duranti, A. et al., Bioorg. Med. Chem., 2003, 11, 3965 – 3973).

Intermediates of general formula (**I-h**) could be reacted with a suitable primary amines, such as, for example, primary aromatic amines and primary amines, preferably primary aromatic amines, such as, for example aniline or 3-aminothiophene, in the presence of a base, such as, for example, lithium bis(trimethylsilyl)amide (LHMDS), in the presence of a catalyst, such as, for example a suitable ligand, preferably 2-(di-tert-butylphosphino)-

2′,4′,6′- triisopropyl-3,6-dimethoxy-1,1′-biphenyl (tBuBrettPhos) and in the presence of a pre-catalyst, such as, for example a palladium pre-catalyst, preferably chloro[2-(dicyclohexylphosphino)-3,6-dimethoxy-2′,4′,6′-triisopropyl-1,1′-biphenyl][2-(2-aminoethyl)phenyl]palladium(II) (BrettPhos-PreCat MTBE ether adduct) in a suitable solvent system, such as, for example, tetrahydrofuran (THF), in a temperature range from 0℃ to the 200℃, preferably the reactio n is carried out at 80℃, to furnish compounds of general formula (**I**).

It is known to the person skilled in the art that, if there are a number of reactive centers on a starting or intermediate compound, it may be necessary to block one or more reactive centers temporarily by protective groups in order to allow a reaction to proceed specifically at the desired reaction center. A detailed description for the use of a large number of proven protective groups is found, for example, in T. W. Greene, Protective Groups in Organic Synthesis, John Wiley & Sons, 1999, 3rd Ed., or in P. Kocienski, Protecting Groups, Thieme Medical Publishers, 2000.

The compounds according to the invention are isolated and purified in a manner known per se, e.g. by distilling off the solvent *in vacuo* and recrystallizing the residue obtained from a suitable solvent or subjecting it to one of the customary purification methods, such as chromatography on a suitable support material. Furthermore, reverse phase preparative HPLC of compounds of the present invention which possess a sufficiently basic or acidic functionality, may result in the formation of a salt, such as, in the case of a compound of the present invention which is sufficiently basic, a trifluoroacetate or formate salt for example, or, in the case of a compound of the present invention which is sufficiently acidic, an ammonium salt for example. Salts of this type can either be transformed into its free base or free acid form, respectively, by various methods known to the person skilled in the art, or be used as salts in subsequent biological assays. Additionally, the drying process during the isolation of compounds of the present invention may not fully remove traces of cosolvents, especIlly such as formic acid or trifluoroacetic acid, to give solvates or inclusion complexes. The person skilled in the art will recognise which solvates or inclusion complexes are acceptable to be used in subsequent biological assays. It is to be understood that the specific form (e.g. salt, free base, solvate, inclusion complex) of a compound of the present invention as isolated as described herein is not necessarily the only form in which said compound can be applied to a biological assay in order to quantify the specific biological activity.

Salts of the compounds according to the invention can be obtained by dissolving the free compound in a suitable solvent (for example a ketone such as acetone, methylethylketone or methylisobutylketone, an ether such as diethyl ether, tetrahydrofuran or dioxane, a chlorinated hydrocarbon such as methylene chloride or chloroform, or a low molecular weight aliphatic alcohol such as methanol, ethanol or isopropanol) which contains the desired acid or base, or to which the desired acid or base is then added. The acid or base can be employed in salt preparation, depending on whether a mono- or polybasic acid or base is concerned and depending on which salt is desired, in an equimolar quantitative ratio or one differing therefrom. The salts are obtained by filtering, reprecipitating, precipitating with a non-solvent for the salt or by evaporating the solvent. Salts obtained can be converted into the free compounds which, in turn, can be converted into salts. In this manner, pharmaceutically unacceptable salts, which can be obtained, for example, as process products in the manufacturing on an industrial scale, can be converted into pharmaceutically acceptable salts by processes known to the person skilled in the art. Especially preferred are hydrochlorides and the process used in the example section.

Pure diastereomers and pure enantiomers of the compounds and salts according to the invention can be obtained e.g. by asymmetric synthesis, by using chiral starting compounds in synthesis and by splitting up enantiomeric and diasteriomeric mixtures obtained in synthesis.

Enantiomeric and diastereomeric mixtures can be split up into the pure enantiomers and pure diastereomers by methods known to a person skilled in the art. Preferably, diastereomeric mixtures are separated by crystallization, in particular fractional crystallization, or chromatography. Enantiomeric mixtures can be separated e.g. by forming dIstereomers with a chiral auxillry agent, resolving the dIstereomers obtained and removing the chiral auxilliary agent. As chiral auxilliary agents, for example, chiral acids can be used to separate enantiomeric bases such as e.g. mandelic acid and chiral bases can be used to separate enantiomeric acids vI formation of dIstereomeric salts. Furthermore, diastereomeric derivatives such as diastereomeric esters can be formed from enantiomeric mixtures of alcohols or enantiomeric mixtures of acids, respectively, using chiral acids or chiral alcohols, respectively, as chiral auxilliary agents. Additionally, diastereomeric complexes or diastereomeric clathrates may be used for separating enantiomeric mixtures. Alternatively, enantiomeric mixtures can be split up using chiral separating columns in chromatography. Another suitable method for the isolation of enantiomers is the enzymatic separation.

One preferred aspect of the invention is the process for the preparation of the compounds of the claims 1 to 5, according to the examples, as well as the intermediates used for their preparation.

Optionally, compounds of formula (I) according to the invention can be converted into their salts, or, optionally, salts of the compounds according to the invention can be converted into the free compounds. Corresponding processes are customary for the skilled person.

Commercial utility

As mentioned supra, the compounds of the present invention have surprisingly been found to effectively inhibit Bub1 finally resulting in cell death e.g. apoptosis and may therefore be used for the treatment or prophylaxis of diseases of uncontrolled cell growth, proliferation and/or survival, inappropriate cellular immune responses, or inappropriate cellular inflammatory responses, or diseases which are accompanied with uncontrolled cell growth, proliferation and/or survival, inappropriate cellular immune responses, or inappropriate cellular inflammatory responses, particularly in which the uncontrolled cell growth, proliferation and/or survival, inappropriate cellular immune responses, or inappropriate cellular inflammatory responses is mediated by Bub1, such as, for example, benign and malignant neoplasia, more specifically haematological tumours, solid tumours, and/or metastases thereof, e.g. leukaemias and myelodysplastic syndrome, malignant lymphomas, head and neck tumours including brain tumours and brain metastases, tumours of the thorax including non-small cell and small cell lung tumours, gastrointestinal tumours, endocrine tumours, mammary and other gynaecological tumours, urological tumours including renal, bladder and prostate tumours, skin tumours, and sarcomas, and/or metastases thereof,

especially haematological tumours, solid tumours, and/or metastases of breast, bladder, bone, brain, central and peripheral nervous system, cervix, colon, endocrine glands (e.g. thyroid and adrenal cortex), endocrine tumours, endometrium, esophagus, gastrointestinal tumours, germ cells, kidney, liver, lung, larynx and hypopharynx, mesothelioma, ovary, pancreas, prostate, rectum, renal, small intestine, soft tissue, stomach, skin, testis, ureter, vagina and vulva as well as malignant neoplasias including primary tumors in said organs and corresponding secondary tumors in distant organs ("tumor metastases"). Haematological tumors can e.g be exemplified by aggressive and indolent forms of leukemia and lymphoma, namely non-Hodgkins disease, chronic and acute myeloid

leukemia (CML / AML), acute lymphoblastic leukemia (ALL), Hodgkins disease, multiple myeloma and T-cell lymphoma. Also included are myelodysplastic syndrome, plasma cell neoplasia, paraneoplastic syndromes, and cancers of unknown primary site as well as AIDS related malignancies.

A further aspect of the invention is the use of the compounds of formula (I) according to the invention for the treatment of cervical -, breast -, non-small cell lung -, prostate -, colon - and melanoma tumors and/or metastases thereof, especially preferred for the treatment thereof as well as a method of treatment of cervical -, breast -, non-small cell lung -, prostate -, colon – and melanoma tumors and/or metastases thereof comprising administering an effective amount of a compound according to the invention.

One aspect of the invention is the use of the compounds of formula (I) according to the invention for the treatment of cervix tumors as well as a method of treatment of cervix tumors comprising administering an effective amount of a compound according to the invention.

In accordance with an aspect of the present invention therefore the invention relates to a compound of formula (I) according to the invention, or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer particularly a pharmaceutically acceptable salt thereof, or a mixture of same, as described and defined herein, for use in the treatment or prophylaxis of a disease, especially for use in the treatment of a disease.

Another particular aspect of the present invention is therefore the use of a compound of formula (I) according to the invention, described *supra*, or a stereoisomer, a tautomer, an N-oxide, a hydrate, a solvate, or a salt thereof, particularly a pharmaceutically acceptable salt thereof, or a mixture of same, for the prophylaxis or treatment of hyperproliferative disorders or disorders responsive to induction of cell death i.e apoptosis.

The term “inappropriate” within the context of the present invention, in particular in the context of “inappropriate cellular immune responses, or inappropriate cellular inflammatory responses”, as used herein, is to be understood as preferably meaning a response which is less than, or greater than normal, and which is associated with, responsible for, or results in, the pathology of said diseases.

Preferably, the use is in the treatment or prophylaxis of diseases, especially the treatment, wherein the diseases are haematological tumours, solid tumours and/or metastases thereof.

Another aspect is the use of a compound of formula (I) according to the invention for the treatment of cervical -, breast -, non-small cell lung -, prostate -, colon – and melanoma tumors and/or metastases thereof, especially preferred for the treatment thereof. A preferred aspect is the use of a compound of formula (I) according to the invention for the prophylaxis and/or treatment of cervical tumors especially preferred for the treatment thereof.

Another aspect of the present invention is the use of a compound according to the invention or a stereoisomer, a tautomer, an N-oxide, a hydrate, a solvate, or a salt thereof, particularly a pharmaceutically acceptable salt thereof, or a mixture of same, as described herein, in the manufacture of a medicament for the treatment or prophylaxis of a disease, wherein such disease is a hyperproliferative disorder or a disorder responsive to induction of cell death e.g.apoptosis. In an embodiment the disease is a haematological tumour, a solid tumour and/or metastases thereof. In another embodiment the disease is cervical -, breast -, non-small cell lung -, prostate -, colon – and melanoma tumor and/or metastases thereof, in a preferred aspect the disease is cervical tumor.

Method of treating hyper-proliferative disorders

The present invention relates to a method for using the compounds of the present invention and compositions thereof, to treat mammalian hyper-proliferative disorders. Compounds can be utilized to inhibit, block, reduce, decrease, etc., cell proliferation and/or cell division, and/or produce cell death e.g. apoptosis. This method comprises administering to a mammal in need thereof, including a human, an amount of a compound of this invention, or a pharmaceutically acceptable salt, isomer, polymorph, metabolite, hydrate, solvate or ester thereof ; etc. which is effective to treat the disorder. Hyper-proliferative disorders include but are not limited, e.g., psoriasis, keloids, and other hyperplasias affecting the skin, benign prostate hyperplasia (BPH), solid tumours, such as cancers of the breast, respiratory tract, brain, reproductive organs, digestive tract, urinary tract, eye, liver, skin, head and neck, thyroid, parathyroid and their distant metastases. Those disorders also include lymphomas, sarcomas, and leukaemias.

Examples of breast cancer include, but are not limited to invasive ductal carcinoma, invasive lobular carcinoma, ductal carcinoma in situ, and lobular carcinoma in situ.

Examples of cancers of the respiratory tract include, but are not limited to small-cell and non-small-cell lung carcinoma, as well as bronchial adenoma and pleuropulmonary blastoma.

Examples of brain cancers include, but are not limited to brain stem and hypophtalmic glioma, cerebellar and cerebral astrocytoma, medulloblastoma, ependymoma, as well as neuroectodermal and pineal tumour.

Tumours of the male reproductive organs include, but are not limited to prostate and testicular cancer. Tumours of the female reproductive organs include, but are not limited to endometrial, cervical, ovarian, vaginal, and vulvar cancer, as well as sarcoma of the uterus.

Tumours of the digestive tract include, but are not limited to anal, colon, colorectal, oesophageal, gallbladder, gastric, pancreatic, rectal, small-intestine, and salivary gland cancers.

Tumours of the urinary tract include, but are not limited to bladder, penile, kidney, renal pelvis, ureter, urethral and human papillary renal cancers.

Eye cancers include, but are not limited to intraocular melanoma and retinoblastoma.

Examples of liver cancers include, but are not limited to hepatocellular carcinoma (liver cell carcinomas with or without fibrolamellar variant), cholangiocarcinoma (intrahepatic bile duct carcinoma), and mixed hepatocellular cholangiocarcinoma.

Skin cancers include, but are not limited to squamous cell carcinoma, Kaposi's sarcoma, malignant melanoma, Merkel cell skin cancer, and non-melanoma skin cancer.

Head-and-neck cancers include, but are not limited to laryngeal, hypopharyngeal, nasopharyngeal, oropharyngeal cancer, lip and oral cavity cancer and squamous cell. Lymphomas include, but are not limited to AIDS-related lymphoma, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, Burkitt lymphoma, Hodgkin's disease, and lymphoma of the central nervous system.

Sarcomas include, but are not limited to sarcoma of the soft tissue, osteosarcoma, malignant fibrous histiocytoma, lymphosarcoma, and rhabdomyosarcoma.

Leukemias include, but are not limited to acute myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia, and hairy cell leukemia.

These disorders have been well characterized in humans, but also exist with a similar etiology in other mammals, and can be treated by administering pharmaceutical compositions of the present invention.

The term "treating" or "treatment" as stated throughout this document is used conventionally, *e.g.,* the management or care of a subject for the purpose of combating, alleviating, reducing, relieving, improving the condition of, *etc.*, of a disease or disorder, such as a carcinoma.

Methods of treating kinase disorders

The present invention also provides methods for the treatment of disorders associated with aberrant mitogen extracellular kinase activity, including, but not limited to stroke, heart failure, hepatomegaly, cardiomegaly, diabetes, Alzheimer's disease, cystic fibrosis, symptoms of xenograft rejections, septic shock or asthma.

Effective amounts of compounds of the present invention can be used to treat such disorders, including those diseases (*e.g.,* cancer) mentioned in the Background section above. Nonetheless, such cancers and other diseases can be treated with compounds of the present invention, regardless of the mechanism of action and/or the relationship between the kinase and the disorder.

The phrase "aberrant kinase activity" or "aberrant tyrosine kinase activity," includes any abnormal expression or activity of the gene encoding the kinase or of the polypeptide it encodes. Examples of such aberrant activity, include, but are not limited to, over-expression of the gene or polypeptide ; gene amplification ; mutations which produce constitutively-active or hyperactive kinase activity ; gene mutations, deletions, substitutions, additions, etc.

The present invention also provides for methods of inhibiting a kinase activity, especially of mitogen extracellular kinase, comprising administering an effective amount of a compound of the present invention, including salts, polymorphs, metabolites, hydrates, solvates, prodrugs (*e.g.*: esters) thereof, and diastereoisomeric forms thereof. Kinase activity can be inhibited in cells (*e.g., in vitro*), or in the cells of a mammalian subject, especially a human patient in need of treatment.

Methods of treating angiogenic disorders

The present invention also provides methods of treating disorders and diseases associated with excessive and/or abnormal angiogenesis.

Inappropriate and ectopic expression of angiogenesis can be deleterious to an organism. A number of pathological conditions are associated with the growth of extraneous blood vessels. These include, e.g., diabetic retinopathy, ischemic retinal-vein occlusion, and retinopathy of prematurity [Aiello et al. New Engl. J. Med. **1994**, 331, 1480 ; Peer et al. Lab. Invest. **1995**, 72, 638], age-related macular degeneration [AMD ; see, Lopez et al. Invest. Opththalmol. Vis. Sci. **1996**, 37, 855], neovascular glaucoma, psoriasis, retrolental fibroplasias, angiofibroma, inflammation, rheumatoid arthritis (RA), restenosis, in-stent restenosis, vascular graft restenosis, etc. In addition, the increased blood supply associated with cancerous and neoplastic tissue, encourages growth, leading to rapid tumour enlargement and metastasis. Moreover, the growth of new blood and lymph vessels in a tumour provides an escape route for renegade cells, encouraging metastasis and the consequence spread of the cancer. Thus, compounds of the present invention can be utilized to treat and/or prevent any of the aforementioned angiogenesis disorders, e.g., by inhibiting and/or reducing blood vessel formation ; by inhibiting, blocking, reducing, decreasing, etc. endothelial cell proliferation or other types involved in angiogenesis, as well as causing cell death e.g. apoptosis of such cell types.

Preferably, the diseases of said method are haematological tumours, solid tumour and/or metastases thereof.

The compounds of the present invention can be used in particular in therapy and prevention i.e. prophylaxis, especially in therapy of tumour growth and metastases, especially in solid tumours of all indications and stages with or without pre-treatment of the tumour growth.

Pharmaceutical compositions of the compounds of the invention

This invention also relates to pharmaceutical compositions containing one or more compounds of the present invention. These compositions can be utilised to achieve the desired pharmacological effect by administration to a patient in need thereof. A patient, for the purpose of this invention, is a mammal, including a human, in need of treatment for the particular condition or disease.

Therefore, the present invention includes pharmaceutical compositions that are comprised of a pharmaceutically acceptable carrier or auxiliary and a pharmaceutically effective amount of a compound, or salt thereof, of the present invention.

Another aspect of the invention is a pharmaceutical composition comprising a pharmaceutically effective amount of a compound of formula (I) according to the invention and a pharmaceutically acceptable auxiliary for the treatment of a disease mentioned supra, especially for the treatment of haematological tumours, solid tumours and/or metastases thereof.

A pharmaceutically acceptable carrier or auxiliary is preferably a carrier that is non-toxic and innocuous to a patient at concentrations consistent with effective activity of the active ingredient so that any side effects ascribable to the carrier do not vitiate the beneficial effects of the active ingredient. Carriers and auxiliaries are all kinds of additives assisting to the composition to be suitable for administration.

A pharmaceutically effective amount of compound is preferably that amount which produces a result or exerts the intended influence on the particular condition being treated.

The compounds of the present invention can be administered with pharmaceutically-acceptable carriers or auxiliaries well known in the art using any effective conventional dosage unit forms, including immediate, slow and timed release preparations, orally, parenterally, topically, nasally, ophthalmically, optically, sublingually, rectally, vaginally, and the like.

For oral administration, the compounds can be formulated into solid or liquid preparations such as capsules, pills, tablets, troches, lozenges, melts, powders, solutions, suspensions, or emulsions, and may be prepared according to methods known to the art for the manufacture of pharmaceutical compositions. The solid unit dosage forms can be a capsule that can be of the ordinary hard- or soft-shelled gelatine type containing auxiliaries, for example, surfactants, lubricants, and inert fillers such as lactose, sucrose, calcium phosphate, and corn starch.

In another embodiment, the compounds of this invention may be tableted with conventional tablet bases such as lactose, sucrose and cornstarch in combination with binders such as acacia, corn starch or gelatine, disintegrating agents intended to assist the break-up and dissolution of the tablet following administration such as potato starch,

alginic acid, corn starch, and guar gum, gum tragacanth, acacia, lubricants intended to improve the flow of tablet granulation and to prevent the adhesion of tablet material to the surfaces of the tablet dies and punches, for example talc, stearic acid, or magnesium, calcium or zinc stearate, dyes, colouring agents, and flavouring agents such as peppermint, oil of wintergreen, or cherry flavouring, intended to enhance the aesthetic qualities of the tablets and make them more acceptable to the patient. Suitable excipients for use in oral liquid dosage forms include dicalcium phosphate and diluents such as water and alcohols, for example, ethanol, benzyl alcohol, and polyethylene alcohols, either with or without the addition of a pharmaceutically acceptable surfactant, suspending agent or emulsifying agent. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance tablets, pills or capsules may be coated with shellac, sugar or both.

Dispersible powders and granules are suitable for the preparation of an aqueous suspension. They provide the active ingredient in admixture with a dispersing or wetting agent, a suspending agent and one or more preservatives. Suitable dispersing or wetting agents and suspending agents are exemplified by those already mentioned above. Additional excipients, for example those sweetening, flavouring and colouring agents described above, may also be present.

The pharmaceutical compositions of this invention may also be in the form of oil-in-water emulsions. The oily phase may be a vegetable oil such as liquid paraffin or a mixture of vegetable oils. Suitable emulsifying agents may be (1) naturally occurring gums such as gum acacia and gum tragacanth, (2) naturally occurring phosphatides such as soy bean and lecithin, (3) esters or partial esters derived form fatty acids and hexitol anhydrides, for example, sorbitan monooleate, (4) condensation products of said partial esters with ethylene oxide, for example, polyoxyethylene sorbitan monooleate. The emulsions may also contain sweetening and flavouring agents.

Oily suspensions may be formulated by suspending the active ingredient in a vegetable oil such as, for example, arachis oil, olive oil, sesame oil or coconut oil, or in a mineral oil such as liquid paraffin. The oily suspensions may contain a thickening agent such as, for example, beeswax, hard paraffin, or cetyl alcohol. The suspensions may also contain one or more preservatives, for example, ethyl or n-propyl p-hydroxybenzoate ; one or more colouring agents ; one or more flavouring agents ; and one or more sweetening agents such as sucrose or saccharin.

Syrups and elixirs may be formulated with sweetening agents such as, for example, glycerol, propylene glycol, sorbitol or sucrose. Such formulations may also contain a demulcent, and preservative, such as methyl and propyl parabens and flavouring and colouring agents.

The compounds of this invention may also be administered parenterally, that is, subcutaneously, intravenously, intraocularly, intrasynovially, intramuscularly, or interperitoneally, as injectable dosages of the compound in preferably a physiologically acceptable diluent with a pharmaceutical carrier which can be a sterile liquid or mixture of liquids such as water, saline, aqueous dextrose and related sugar solutions, an alcohol such as ethanol, isopropanol, or hexadecyl alcohol, glycols such as propylene glycol or polyethylene glycol, glycerol ketals such as 2,2-dimethyl-1,1-dioxolane-4-methanol, ethers such as poly(ethylene glycol) 400, an oil, a fatty acid, a fatty acid ester or, a fatty acid glyceride, or an acetylated fatty acid glyceride, with or without the addition of a pharmaceutically acceptable surfactant such as a soap or a detergent, suspending agent such as pectin, carbomers, methycellulose, hydroxypropylmethylcellulose, or carboxymethylcellulose, or emulsifying agent and other pharmaceutical adjuvants.

Illustrative of oils which can be used in the parenteral formulations of this invention are those of petroleum, animal, vegetable, or synthetic origin, for example, peanut oil, soybean oil, sesame oil, cottonseed oil, corn oil, olive oil, petrolatum and mineral oil. Suitable fatty acids include oleic acid, stearic acid, isostearic acid and myristic acid. Suitable fatty acid esters are, for example, ethyl oleate and isopropyl myristate. Suitable soaps include fatty acid alkali metal, ammonium, and triethanolamine salts and suitable detergents include cationic detergents, for example dimethyl dialkyl ammonium halides, alkyl pyridinium halides, and alkylamine acetates ; anionic detergents, for example, alkyl, aryl, and olefin sulfonates, alkyl, olefin, ether, and monoglyceride sulfates, and sulfosuccinates ; non-ionic detergents, for example, fatty amine oxides, fatty acid alkanolamides, and poly(oxyethylene-oxypropylene)s or ethylene oxide or propylene oxide copolymers ; and amphoteric detergents, for example, alkyl-beta-aminopropionates, and 2-alkylimidazoline quarternary ammonium salts, as well as mixtures.

The parenteral compositions of this invention will typically contain from about 0.5% to about 25% by weight of the active ingredient in solution. Preservatives and buffers may also be used advantageously. In order to minimise or eliminate irritation at the site of injection, such compositions may contain a non-ionic surfactant having a hydrophile-lipophile balance (HLB) preferably of from about 12 to about 17. The quantity of surfactant

in such formulation preferably ranges from about 5% to about 15% by weight. The surfactant can be a single component having the above HLB or can be a mixture of two or more components having the desired HLB.

Illustrative of surfactants used in parenteral formulations are the class of polyethylene sorbitan fatty acid esters, for example, sorbitan monooleate and the high molecular weight adducts of ethylene oxide with a hydrophobic base, formed by the condensation of propylene oxide with propylene glycol.

The pharmaceutical compositions may be in the form of sterile injectable aqueous suspensions. Such suspensions may be formulated according to known methods using suitable dispersing or wetting agents and suspending agents such as, for example, sodium carboxymethylcellulose, methylcellulose, hydroxypropylmethyl-cellulose, sodium alginate, polyvinylpyrrolidone, gum tragacanth and gum acacia ; dispersing or wetting agents which may be a naturally occurring phosphatide such as lecithin, a condensation product of an alkylene oxide with a fatty acid, for example, polyoxyethylene stearate, a condensation product of ethylene oxide with a long chain aliphatic alcohol, for example, heptadeca-ethyleneoxycetanol, a condensation product of ethylene oxide with a partial ester derived form a fatty acid and a hexitol such as polyoxyethylene sorbitol monooleate, or a condensation product of an ethylene oxide with a partial ester derived from a fatty acid and a hexitol anhydride, for example polyoxyethylene sorbitan monooleate.

The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally acceptable diluent or solvent. Diluents and solvents that may be employed are, for example, water, Ringer's solution, isotonic sodium chloride solutions and isotonic glucose solutions. In addition, sterile fixed oils are conventionally employed as solvents or suspending media. For this purpose, any bland, fixed oil may be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid can be used in the preparation of injectables.

A composition of the invention may also be administered in the form of suppositories for rectal administration of the drug. These compositions can be prepared by mixing the drug with a suitable non-irritation excipient which is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum to release the drug. Such materials are, for example, cocoa butter and polyethylene glycol.

Controlled release formulations for parenteral administration include liposomal, polymeric microsphere and polymeric gel formulations that are known in the art.

It may be desirable or necessary to introduce the pharmaceutical composition to the patient via a mechanical delivery device. The construction and use of mechanical delivery devices for the delivery of pharmaceutical agents is well known in the art. Direct techniques for administration, for example, administering a drug directly to the brain usually involve placement of a drug delivery catheter into the patient's ventricular system to bypass the blood-brain barrier. One such implantable delivery system, used for the transport of agents to specific anatomical regions of the body, is described in US Patent No. 5,011,472, issued April 30, 1991.

The compositions of the invention can also contain other conventional pharmaceutically acceptable compounding ingredients, generally referred to as carriers or diluents, as necessary or desired. Conventional procedures for preparing such compositions in appropriate dosage forms can be utilized.

Such ingredients and procedures include those described in the following references, each of which is incorporated herein by reference: Powell, M.F. *et al.*, "Compendium of Excipients for Parenteral Formulations" PDA Journal of Pharmaceutical Science & Technology **1998**, 52(5), 238-311 ; Strickley, R.G "Parenteral Formulations of Small Molecule Therapeutics Marketed in the United States (1999)-Part-1" PDA Journal of Pharmaceutical Science & Technology **1999**, 53(6), 324-349 ; and Nema, S. *et al.*, "Excipients and Their Use in Injectable Products" PDA Journal of Pharmaceutical Science & Technology **1997**, 51(4), 166-171.

Commonly used pharmaceutical ingredients that can be used as appropriate to formulate the composition for its intended route of administration include:

acidifying agents (examples include but are not limited to acetic acid, citric acid, fumaric acid, hydrochloric acid, nitric acid) ;

alkalinizing agents (examples include but are not limited to ammonia solution, ammonium carbonate, diethanolamine, monoethanolamine, potassium hydroxide, sodium borate, sodium carbonate, sodium hydroxide, triethanolamine, trolamine) ;

adsorbents (examples include but are not limited to powdered cellulose and activated charcoa)l ;

aerosol propellants (examples include but are not limited to carbon dioxide, CCl_2F_2, $F_2ClC\text{-}CClF_2$ and $CClF_3$)

air displacement agents - examples include but are not limited to nitrogen and argon ;

antifungal preservatives (examples include but are not limited to benzoic acid, butylparaben, ethylparaben, methylparaben, propylparaben, sodium benzoate) ;

antimicrobial preservatives (examples include but are not limited to benzalkonium chloride, benzethonium chloride, benzyl alcohol, cetylpyridinium chloride, chlorobutanol, phenol, phenylethyl alcohol, phenylmercuric nitrate and thimerosal) ;

antioxidants (examples include but are not limited to ascorbic acid, ascorbyl palmitate, butylated hydroxyanisole, butylated hydroxytoluene, hypophosphorus acid, monothioglycerol, propyl gallate, sodium ascorbate, sodium bisulfite, sodium formaldehyde sulfoxylate, sodium metabisulfite) ;

binding materials (examples include but are not limited to block polymers, natural and synthetic rubber, polyacrylates, polyurethanes, silicones, polysiloxanes and styrene-butadiene copolymers) ;

buffering agents (examples include but are not limited to potassium metaphosphate, dipotassium phosphate, sodium acetate, sodium citrate anhydrous and sodium citrate dihydrate);

carrying agents (examples include but are not limited to acacia syrup, aromatic syrup, aromatic elixir, cherry syrup, cocoa syrup, orange syrup, syrup, corn oil, mineral oil, peanut oil, sesame oil, bacteriostatic sodium chloride injection and bacteriostatic water for injection);

chelating agents (examples include but are not limited to edetate disodium and edetic acid);

colourants (examples include but are not limited to FD&C Red No. 3, FD&C Red No. 20, FD&C Yellow No. 6, FD&C Blue No. 2, D&C Green No. 5, D&C Orange No. 5, D&C Red No. 8, caramel and ferric oxide red) ;

clarifying agents (examples include but are not limited to bentonite) ;

emulsifying agents (examples include but are not limited to acacia, cetomacrogol, cetyl alcohol, glyceryl monostearate, lecithin, sorbitan monooleate, polyoxyethylene 50 monostearate) ;

encapsulating agents (examples include but are not limited to gelatin and cellulose acetate phthalate),

flavourants (examples include but are not limited to anise oil, cinnamon oil, cocoa, menthol, orange oil, peppermint oil and vanillin) ;

humectants (examples include but are not limited to glycerol, propylene glycol and sorbitol) ;

levigating agents (examples include but are not limited to mineral oil and glycerin) ;

oils (examples include but are not limited to arachis oil, mineral oil, olive oil, peanut oil, sesame oil and vegetable oil) ;

ointment bases (examples include but are not limited to lanolin, hydrophilic ointment, polyethylene glycol ointment, petrolatum, hydrophilic petrolatum, white ointment, yellow ointment, and rose water ointment) ;

penetration enhancers (transdermal delivery) (examples include but are not limited to monohydroxy or polyhydroxy alcohols, mono-or polyvalent alcohols, saturated or unsaturated fatty alcohols, saturated or unsaturated fatty esters, saturated or unsaturated dicarboxylic acids, essential oils, phosphatidyl derivatives, cephalin, terpenes, amides, ethers, ketones and ureas),

plasticizers (examples include but are not limited to diethyl phthalate and glycerol) ;

solvents (examples include but are not limited to ethanol, corn oil, cottonseed oil, glycerol, isopropanol, mineral oil, oleic acid, peanut oil, purified water, water for injection, sterile water for injection and sterile water for irrigation) ;

stiffening agents (examples include but are not limited to cetyl alcohol, cetyl esters wax, microcrystalline wax, paraffin, stearyl alcohol, white wax and yellow wax) ;

suppository bases (examples include but are not limited to cocoa butter and polyethylene glycols (mixtures)) ;

surfactants (examples include but are not limited to benzalkonium chloride, nonoxynol 10, oxtoxynol 9, polysorbate 80, sodium lauryl sulfate and sorbitan mono-palmitate) ;

suspending agents (examples include but are not limited to agar, bentonite, carbomers, carboxymethylcellulose sodium, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, kaolin, methylcellulose, tragacanth and veegum) ;

sweetening agents (examples include but are not limited to aspartame, dextrose, glycerol, mannitol, propylene glycol, saccharin sodium, sorbitol and sucrose) ;

tablet anti-adherents (examples include but are not limited to magnesium stearate and talc) ;

tablet binders (examples include but are not limited to acacia, alginic acid, carboxymethylcellulose sodium, compressible sugar, ethylcellulose, gelatin, liquid glucose, methylcellulose, non-crosslinked polyvinyl pyrrolidone, and pregelatinized starch) ;

tablet and capsule diluents (examples include but are not limited to dibasic calcium phosphate, kaolin, lactose, mannitol, microcrystalline cellulose, powdered cellulose, precipitated calcium carbonate, sodium carbonate, sodium phosphate, sorbitol and starch) ;

tablet coating agents (examples include but are not limited to liquid glucose, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, methylcellulose, ethylcellulose, cellulose acetate phthalate and shellac) ;

tablet direct compression excipients (examples include but are not limited to dibasic calcium phosphate) ;

tablet disintegrants (examples include but are not limited to alginic acid, carboxymethylcellulose calcium, microcrystalline cellulose, polacrillin potassium, cross-linked polyvinylpyrrolidone, sodium alginate, sodium starch glycollate and starch) ;

tablet glidants (examples include but are not limited to colloidal silica, corn starch and talc) ;

tablet lubricants (examples include but are not limited to calcium stearate, magnesium stearate, mineral oil, stearic acid and zinc stearate) ;

tablet/capsule opaquants (examples include but are not limited to titanium dioxide) ;

tablet polishing agents (examples include but are not limited to carnuba wax and white wax) ;

thickening agents (examples include but are not limited to beeswax, cetyl alcohol and paraffin) ;

tonicity agents (examples include but are not limited to dextrose and sodium chloride) ;

viscosity increasing agents (examples include but are not limited to alginic acid, bentonite, carbomers, carboxymethylcellulose sodium, methylcellulose, polyvinyl pyrrolidone, sodium alginate and tragacanth) ; and

wetting agents (examples include but are not limited to heptadecaethylene oxycetanol, lecithins, sorbitol monooleate, polyoxyethylene sorbitol monooleate, and polyoxyethylene stearate).

Pharmaceutical compositions according to the present invention can be illustrated as follows:

Sterile i.v. solution: A 5 mg/mL solution of the desired compound of this invention can be made using sterile, injectable water, and the pH is adjusted if necessary. The solution is diluted for administration to 1 – 2 mg/mL with sterile 5% dextrose and is administered as an i.v. infusion over about 60 minutes.

Lyophilised powder for i.v. administration: A sterile preparation can be prepared with (i) 100 - 1000 mg of the desired compound of this invention as a lyophilised powder, (ii) 32-327 mg/mL sodium citrate, and (iii) 300 – 3000 mg Dextran 40. The formulation is reconstituted with sterile, injectable saline or dextrose 5% to a concentration of 10 to 20 mg/mL, which is further diluted with saline or dextrose 5% to 0.2 – 0.4 mg/mL, and is administered either IV bolus or by IV infusion over 15 – 60 minutes.

Intramuscular suspension: The following solution or suspension can be prepared, for intramuscular injection:
50 mg/mL of the desired, water-insoluble compound of this invention
5 mg/mL sodium carboxymethylcellulose
4 mg/mL TWEEN 80
9 mg/mL sodium chloride
9 mg/mL benzyl alcohol

Hard Shell Capsules: A large number of unit capsules are prepared by filling standard two-piece hard galantine capsules each with 100 mg of powdered active ingredient, 150 mg of lactose, 50 mg of cellulose and 6 mg of magnesium stearate.

Soft Gelatin Capsules: A mixture of active ingredient in a digestible oil such as soybean oil, cottonseed oil or olive oil is prepared and injected by means of a positive displacement

pump into molten gelatin to form soft gelatin capsules containing 100 mg of the active ingredient. The capsules are washed and dried. The active ingredient can be dissolved in a mixture of polyethylene glycol, glycerin and sorbitol to prepare a water miscible medicine mix.

Tablets: A large number of tablets are prepared by conventional procedures so that the dosage unit is 100 mg of active ingredient, 0.2 mg. of colloidal silicon dioxide, 5 mg of magnesium stearate, 275 mg of microcrystalline cellulose, 11 mg. of starch, and 98.8 mg of lactose. Appropriate aqueous and non-aqueous coatings may be applied to increase palatability, improve elegance and stability or delay absorption.

Immediate Release Tablets/Capsules: These are solid oral dosage forms made by conventional and novel processes. These units are taken orally without water for immediate dissolution and delivery of the medication. The active ingredient is mixed in a liquid containing ingredient such as sugar, gelatin, pectin and sweeteners. These liquids are solidified into solid tablets or caplets by freeze drying and solid state extraction techniques. The drug compounds may be compressed with viscoelastic and thermoelastic sugars and polymers or effervescent components to produce porous matrices intended for immediate release, without the need of water.

Dose and administration

Based upon standard laboratory techniques known to evaluate compounds useful for the treatment of hyper-proliferative disorders and angiogenic disorders, by standard toxicity tests and by standard pharmacological assays for the determination of treatment of the conditions identified above in mammals, and by comparison of these results with the results of known medicaments that are used to treat these conditions, the effective dosage of the compounds of this invention can readily be determined for treatment of each desired indication. The amount of the active ingredient to be administered in the treatment of one of these conditions can vary widely according to such considerations as the particular compound and dosage unit employed, the mode of administration, the period of treatment, the age and sex of the patient treated, and the nature and extent of the condition treated.

The total amount of the active ingredient to be administered will generally range from about 0.001 mg/kg to about 200 mg/kg body weight per day, and preferably from about 0.01 mg/kg to about 20 mg/kg body weight per day. Clinically useful dosing schedules will range from one to three times a day dosing to once every four weeks dosing. In addition,

"drug holidays" in which a patient is not dosed with a drug for a certain period of time, may be beneficial to the overall balance between pharmacological effect and tolerability. A unit dosage may contain from about 0.5 mg to about 1500 mg of active ingredient, and can be administered one or more times per day or less than once a day. The average daily dosage for administration by injection, including intravenous, intramuscular, subcutaneous and parenteral injections, and use of infusion techniques will preferably be from 0.01 to 200 mg/kg of total body weight. The average daily rectal dosage regimen will preferably be from 0.01 to 200 mg/kg of total body weight. The average daily vaginal dosage regimen will preferably be from 0.01 to 200 mg/kg of total body weight. The average daily topical dosage regimen will preferably be from 0.1 to 200 mg administered between one to four times daily. The transdermal concentration will preferably be that required to maintain a daily dose of from 0.01 to 200 mg/kg. The average daily inhalation dosage regimen will preferably be from 0.01 to 100 mg/kg of total body weight.

Of course the specific initial and continuing dosage regimen for each patient will vary according to the nature and severity of the condition as determined by the attending diagnostician, the activity of the specific compound employed, the age and general condition of the patient, time of administration, route of administration, rate of excretion of the drug, drug combinations, and the like. The desired mode of treatment and number of doses of a compound of the present invention or a pharmaceutically acceptable salt or ester or composition thereof can be ascertained by those skilled in the art using conventional treatment tests.

Combination Therapies

The compounds of this invention can be administered as the sole pharmaceutical agent or in combination with one or more other pharmaceutical agents where the combination causes no unacceptable adverse effects. Those combined pharmaceutical agents can be other agents having antiproliferative effects such as for example for the treatment of haematological tumours, solid tumours and/or metastases thereof and/or agents for the treatment of undesired side effects.The present invention relates also to such combinations.

Other anti-hyper-proliferative agents suitable for use with the composition of the invention include but are not limited to those compounds acknowledged to be used in the treatment of neoplastic diseases in Goodman and Gilman's The Pharmacological Basis of Therapeutics (Ninth Edition), editor Molinoff *et al.*, publ. by McGraw-Hill, pages 1225-

1287, (1996), which is hereby incorporated by reference, especially (chemotherapeutic) anti-cancer agents as defined supra. The combination can be a non-fixed combination or a fixed-dose combination as the case may be.

Methods of testing for a particular pharmacological or pharmaceutical property are well known to persons skilled in the art.

The example testing experiments described herein serve to illustrate the present invention and the invention is not limited to the examples given.

As will be appreciated by persons skilled in the art, the invention is not limited to the particular embodiments described herein, but covers all modifications of said embodiments that are within the spirit and scope of the invention as defined by the appended claims.

The following examples illustrate the invention in greater detail, without restricting it. Further compounds according to the invention, of which the preparation is not explicitly described, can be prepared in an analogous way.

The compounds, which are mentioned in the examples and the salts thereof represent preferred embodiments of the invention as well as a claim covering all subcombinations of the residues of the compound of formula (I) according to the invention as disclosed by the specific examples.

The term “according to” within the experimental section is used in the sense that the procedure referred to is to be used “analogously to”.

EXPERIMENTAL PART

The following table lists the abbreviations used in this paragraph and in the Intermediate Examples and Examples section as far as they are not explained within the text body.

Abbreviation	**Meaning**
AcOH	acetic acid (ethanoic acid)
ACN	acetonitrile
aq.	aqueous
Boc	t-butoxycarbonyl
br	broad
CI	chemical ionisation
d	doublet
DAD	diode array detector
DBU	1, 8-Diazabicyclo(5.4.0)undec-7-ene
DCM	dichloromethane
dd	double-doublet
DIPEA	N-ethyl-N-isopropylpropan-2-amine
DMA	*N,N*-dimethylacetamide
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
dt	Double-triplet
ELSD	Evaporative Light Scattering Detector
EtOAc	ethyl acetate
EtOH	ethanol
eq.	equivalent
ESI	electrospray (ES) ionisation
h	hour
HATU	1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate
HCl	Hydrochloric acid
HPLC	high performance liquid chromatography
KO^{t}Bu	Potassium *tert*-butoxide
LC-MS	liquid chromatography mass spectrometry
m	multiplet
mCPBA	*meta*-chloroperbenzoic acid

min	minute
MeCN	acetonitrile
MeOH	methanol
MS	mass spectrometry
NaCl	Sodium chloride
$NaHCO_3$	Sodium hydrogen carbonate or sodium bicarbonate
NMR	nuclear magnetic resonance spectroscopy : chemical shifts (δ) are given in ppm. The chemical shifts were corrected by setting the DMSO signal to 2.50 ppm using unless otherwise stated.
PDA	Photo Diode Array
Pd/C	Palladium on activated charcoal
q	quartet
r.t. or rt or RT	room temperature
Rt	retention time (as measured either with HPLC or UPLC) in minutes
s	singlet
SIBX	Stabilized 2-iodoxybenzoic acid
SM	starting material
SQD	Single-Quadrupole-Detector
t	triplet
td	Triple-doublet
TEA	triethylamine
TFA	trifluoroacetic acid
THF	tetrahydrofuran
UPLC	ultra performance liquid chromatography

Other abbreviations have their meanings customary per se to the skilled person.

The various aspects of the invention described in this application are illustrated by the following examples which are not meant to limit the invention in any way.

Specific Experimental Descriptions

NMR peak forms in the following specific experimental descriptions are stated as they appear in the spectra, possible higher order effects have not been considered. Reactions

employing microwave irradiation may be run with a Biotage Initator® microwave oven optionally equipped with a robotic unit. The reported reaction times employing microwave heating are intended to be understood as fixed reaction times after reaching the indicated reaction temperature. The compounds and intermediates produced according to the methods of the invention may require purification. Purification of organic compounds is well known to the person skilled in the art and there may be several ways of purifying the same compound. In some cases, no purification may be necessary. In some cases, the compounds may be purified by crystallization. In some cases, impurities may be stirred out using a suitable solvent. In some cases, the compounds may be purified by chromatography, particularly flash column chromatography, using for example pre-packed silica gel cartridges, *e.g.* from Separtis such as Isolute® Flash silica gel or Isolute® Flash NH_2 silica gel in combination with a Isolera® autopurifier (Biotage) and eluents such as gradients of e.g. hexane/ethyl acetate or DCM/methanol. In some cases, the compounds may be purified by preparative HPLC using for example a Waters autopurifier equipped with a diode array detector and/or on-line electrospray ionization mass spectrometer in combination with a suitable prepacked reverse phase column and eluents such as gradients of water and acetonitrile which may contain additives such as trifluoroacetic acid, formic acid or aqueous ammonia. In some cases, purification methods as described above can provide those compounds of the present invention which possess a sufficiently basic or acidic functionality in the form of a salt, such as, in the case of a compound of the present invention which is sufficiently basic, a trifluoroacetate or formate salt for example, or, in the case of a compound of the present invention which is sufficiently acidic, an ammonium salt for example. A salt of this type can either be transformed into its free base or free acid form, respectively, by various methods known to the person skilled in the art, or be used as salts in subsequent biological assays. It is to be understood that the specific form (*e.g.* salt, free base etc) of a compound of the present invention as isolated as described herein is not necessarily the only form in which said compound can be applied to a biological assay in order to quantify the specific biological activity.

The percentage yields reported in the following examples are based on the starting component that was used in the lowest molar amount. Air and moisture sensitive liquids and solutions were transferred via syringe or cannula, and introduced into reaction vessels through rubber septa. Commercial grade reagents and solvents were used without further purification. The term “concentrated in vacuo” refers to use of a Buchi rotary evaporator at a minimum pressure of approximately 15 mm of Hg. All temperatures are reported uncorrected in degrees Celsius (℃).

In order that this invention may be better understood, the following examples are set forth. These examples are for the purpose of illustration only, and are not to be construed as limiting the scope of the invention in any manner. All publications mentioned herein are incorporated by reference in their entirety.

Analytical LC-MS conditions

LC-MS-data given in the subsequent specific experimental descriptions refer (unless otherwise noted) to the following conditions:

System:	Waters Acquity UPLC-MS: Binary Solvent Manager, Sample Manager/Organizer, Column Manager, PDA, ELSD, SQD 3001 or ZQ4000
Column:	Acquity UPLC BEH C18 1.7 50x2.1mm
Solvent:	A1 = water + 0.1% vol. formic acid (99%) A2 = water + 0.2% vol. ammonia (32%)
	B1 = acetonitrile
Gradient:	0-1.6 min 1-99% B, 1.6-2.0 min 99% B
Flow:	0.8 mL/min
Temperature:	60℃
Injection:	2.0 µl
Detection:	DAD scan range 210-400 nm -> Peaktable
	ELSD
Methods:	MS ESI+, ESI- Switch -> various scan ranges (Report Header) **Method 1:** A1 + B1 = C:\MassLynx**Mass_100_1000**.flp **Method 2:** A1 + B1 = C:\MassLynx**NH_3_Mass_100_1000**.flp

Preparative HPLC conditions

"Purification by preparative HPLC" in the subsequent specific experimental descriptions refers to (unless otherwise noted) the following conditions:

Analytics (pre- and post analytics: Method A):

System:	Waters Acquity UPLC-MS: Binary Solvent Manager, Sample Manager/Organizer, Column Manager, PDA, ELSD, SQD 3001
Column:	Acquity BEH C18 1.7 50x2.1mm
Solvent:	A = water + 0.1% vol. formic acid (99%)
	B = acetonitrile
Gradient:	0-1.6 min 1-99% B, 1.6-2.0 min 99% B
Flow:	0.8 mL/min
Temperature:	60℃
Injection:	2.0 µl
Detection:	DAD scan range 210-400 nm MS ESI+, ESI-, scan range 160-1000 m/z ELSD
Methods:	Purify_pre.flp Purify_post.flp

Analytics (pre- and post analytics: Method B):

System:	Waters Acquity UPLC-MS: Binary Solvent Manager, Sample Manager/Organizer, Column Manager, PDA, ELSD, SQD 3001
Column:	Acquity BEH C18 1.7 50x2.1mm
Solvent:	A = water + 0.2% vol. ammonia (32%)
	B = acetonitrile
Gradient:	0-1.6 min 1-99% B, 1.6-2.0 min 99% B
Flow:	0.8 mL/min
Temperature:	60℃
Injection:	2.0 µl
Detection:	DAD scan range 210-400 nm MS ESI+, ESI-, scan range 160-1000 m/z ELSD
Methods:	Purify_pre.flp Purify_post.flp

Preparative HPLC (Method acidic):

System:	Waters Autopurificationsystem: Pump 2545, Sample Manager 2767,

	CFO, DAD 2996, ELSD 2424, SQD 3001
Column:	XBridge C18 5µm 100x30 mm
Solvent:	A = water + 0.1% vol. formic acid (99%)
	B = acetonitrile
Gradient:	0–1 min 1% B, 1-8 min 1-99% B, 8-10 min 99% B
Flow:	50 mL/min
Temperature:	RT
Solution:	max. 250 mg / 2.5 mL dimethyl sufoxide or DMF
Injection:	1 x 2.5 mL
Detection:	DAD scan range 210–400 nm
	MS ESI+, ESI-, scan range 160-1000 m/z

Preparative HPLC (Method basic):

System:	Waters Autopurificationsystem: Pump 2545, Sample Manager 2767, CFO, DAD 2996, ELSD 2424, SQD 3001
Column:	XBridge C18 5µm 100x30 mm or Chromatorex RP C-18 10µm 125*30mm
Solvent:	A = water + 0.2% vol. ammonia (32%)
	B = acetonitrile
Gradient:	0–1 min 1% B, 1-8 min 1-99% B, 8-10 min 99% B
Flow:	50 mL/min
Temperature:	RT
Solution:	max. 250 mg / 2.5 mL dimethyl sufoxide or DMF
Injection:	1 x 2.5 mL
Detection:	DAD scan range 210–400 nm
	MS ESI+, ESI-, scan range 160-1000 m/z

Flash column chromatography conditions

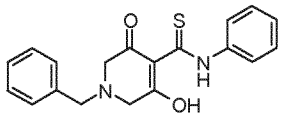
"Purification by (flash) column chromatography" as stated in the subsequent specific experimental descriptions refers to the use of a Biotage Isolera purification system. For technical specifications see "Biotage product catalogue" on www.biotage.com.

EXAMPLES

Example 1

6-Benzyl-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

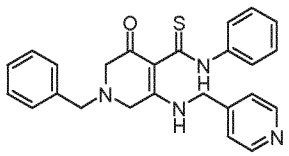
1-2: 1-Benzyl-5-hydroxy-3-oxo-N-phenyl-1,2,3,6-tetrahydropyridine-4-carbothioamide



To a solution of 1-benzylpiperidine-3, 5-dione (1129 mg, 5.6 mmol) and phenylisothiocyanate (751 mg, 5.6 mmol) in MeCN (25 mL) was added DBU (846 mg, 5.6 mmol) and the mixture was heated at 100℃ in sealed tube for 16 h. The mixture was concentrated and purified by Biotage (SNAP silica 100g, EtOAc:Hexane) to give the title compound (200 mg, 11%).

^{1}H NMR (600 MHz, DMSO-d_6) δ ppm 3.49 (br. s., 4 H) 3.79 (br. s., 2H) 7.30 (br. s., 1 H) 7.32 - 7.41 (m, 5 H) 7.43 (t, 2 H) 7.54 (d, 2 H) 13.33 (s, 1 H)

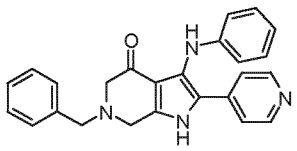
1-1: 1-Benzyl-3-oxo-N-phenyl-5-[(pyridin-4-ylmethyl)amino]-1,2,3,6-tetrahydropyridine-4-carbothioamide



A solution of 1-benzyl-5-hydroxy-3-oxo-N-phenyl-1,2,3,6-tetrahydropyridine-4-carbothioamide (1-2; 50 mg, 0.15 mmol) and 4-(methylamino)pyridine in EtOH (1 mL) and EtOAc (1 mL) was heated at reflux for 4 days. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (29 mg, 41%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.17 (s, 2 H) 3.58 - 3.69 (m, 3 H) 4.75 (d, 2 H) 7.20 - 7.48 (m, 14 H) 8.47 - 8.61 (m, 2 H) 13.82 (br. s., 1 H) 14.22 (s, 1 H)

6-Benzyl-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



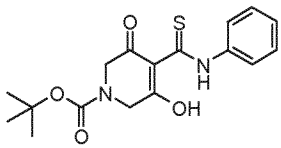
A mixture of 1-benzyl-3-oxo-N-phenyl-5-[(pyridin-4-ylmethyl)amino]-1,2,3,6-tetrahydropyridine-4-carbothioamide (1-1; 190 mg, 0.44 mmol), hydrogen peroxide (34% in water, 80 µL, 0.89 mmol) in MeOH (6 mL) was heated at 100℃ for 16h. The mixture was concentrated and the residue redissolved in MeOH (6 mL) and another portion of hydrogen peroxide (34% in water, 24 µL, 0.27 mmol) was added and heated at reflux for 4h. The mixture was concentrated and purified by preparative HPLC (Method: Waters XBridge C18 5µ 100x30mm; Solvent A: water + 0.1% Vol. formic acid (99%), Solvent B: Acetonitrile; Gradient: 0, 00–0, 50 min 17% B (25 to 70mL/min), 0, 51–5, 50 min 17-37% B; Flow: 70mL/min) to give the title compound (29 mg, 41%).

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 3.34 (s, 2 H) 3.78 (d, 4 H) 6.68 (d, 2 H) 6.80 (s, 1 H) 7.03 - 7.17 (m, 5 H) 7.28 - 7.41 (m, 5 H) 8.38 (br. s., 2 H) 8.68 (br. s., 1 H)

Example 2

2-(3-Chloropyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

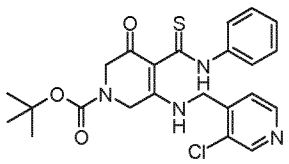
2-2: tert-Butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



To a solution of 1-*tert*-butoxycarbonylpiperidine-3, 5-dione (5 g, 23.4 mmol) and phenylisothiocyanate (3.17 g, 23.4 mmol) in MeCN (25 mL) cooled to 0℃ was slowly added DBU (7.65 g, 50.3 mmol) and stirred at RT for 16 h. The reaction was concentrated, the residue diluted with EtOAc and washed with 0.5M HCl (aq), water, sat. NaCl (aq), filtered thorugh a hydrophobic filter and concentrated. The residue was purified by Biotage (SNAP silica 100g, EtOAc:Hexane) to give the title compound (4.373 g, 54%).

^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 1.35 - 1.54 (m, 9 H) 4.30 (br. s., 4 H) 7.32 (d, 1 H) 7.45 (t, 2 H) 7.57 - 7.68 (m, 2 H) 12.74 (s, 1 H)

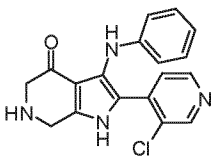
2-1: tert-Butyl 5-{[(3-chloropyridin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



To a solution of tert-butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 200 mg, 0.57 mmol) and 3-chloro-4-(methylamino)pyridine (98 mg, 0.70 mmol) in DMF (2 mL) in a sealed tube was added DBU (87 mg, 0.57 mmol) were heated at 90℃ for 16 h. The mixture was concentrat ed and purified by preparative HPLC (acidic method) to give the title compound (56 mg, 21%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.22 - 1.44 (br. m, 9 H) 4.00 - 4.13 (m, 2 H) 4.53 (br. s., 2 H) 4.88 (d, 2 H) 7.22 - 7.32 (m, 1 H) 7.41 (t, 2 H) 7.49 (br. s., 1 H) 7.56 (d, 2 H) 8.60 (br. s., 1 H) 8.69 (s, 1 H) 12.58 (br. s., 1 H) 13.52 (br. s., 1 H)

2-(3-Chloropyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



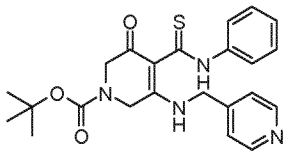
A mixture of tert-butyl 5-{[(3-chloropyridin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-1; 56 mg, 0.12 mmol), hydrogen peroxide (34% in water, 21 µL, 0.24 mmol) in DMSO (1 mL) was heated at 90℃ for 16h. The mixture was purified by preparative HPLC (basic method) to give the title compound (5 mg, 12%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.25 (s, 2 H) 3.96 (s, 2 H) 6.48 - 6.58 (m, 3 H) 6.93 (t, 2 H) 7.31 (d, 1 H) 7.41 (s, 1 H) 8.37 (d, 1 H) 8.57 (s, 1 H) 11.65 (s, 1 H)

Example 3

tert-Butyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

3-1: tert-Butyl 3-oxo-4-(phenylcarbamothioyl)-5-[(pyridin-4-ylmethyl)amino]-3,6-dihydropyridine-1(2H)-carboxylate

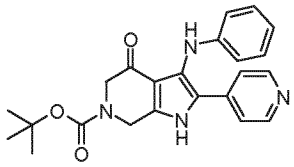


A solution of tert-butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 1.5 g, 4.3 mmol) and 4-(methylamino)pyridine (931 mg, 8.6 mmol)

in DMA (13 mL) was heated in a microwave tube in a microwave at 120℃ for 1.5h and then concentrated. The residue was purified by Biotage (SNAP silica 100g, EtOAc:Hexane) to give the title compound (1.06 g, 56%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.11 - 1.50 (br. m, 9 H) 3.98 - 4.11 (m, 2 H) 4.54 (s, 2 H) 4.85 (d, 2 H) 7.20 - 7.30 (m, 1 H) 7.36 - 7.45 (m, 4 H) 7.54 (d, 2 H) 8.60 (d, 2 H) 12.96 (br. s., 1 H) 13.69 (br. s., 1 H)

tert-Butyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



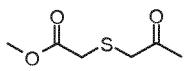
A mixture of tert-butyl 3-oxo-4-(phenylcarbamothioyl)-5-[(pyridin-4-ylmethyl)amino]-3,6-dihydropyridine-1(2H)-carboxylate (3-1; 1.05 g, 2.4 mmol), hydrogen peroxide (34% in water, 489 µL, 4.8 mmol) in MeOH (30 mL) was stirred for 3 days at RT. The mixture was concentrated and purified by Biotage (SNAP silica 50g, EtOAc:Hexane) to give the title compound (318 mg, 33%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.43 (br. s., 9 H) 3.91 - 4.13 (m, 2 H) 4.75 (br. s., 2 H) 6.50 - 6.68 (m, 3 H) 7.04 (t2 H) 7.40 - 7.60 (m, 3 H) 8.35 - 8.55 (m, 2 H) 12.20 (br. s., 1 H)

Example 4

3-(phenylamino)-2-(pyridin-4-yl)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one

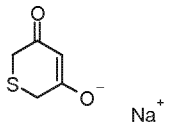
4-3: Methyl [(2-oxopropyl)sulfanyl]acetate



To a solution of methyl 2-mercaptoacetate (23.3 g, 219 mmol) and TEA (40.3 g, 398 mmol) in DCM (460 mL) cooled to 0℃ was slowly adde d 2-chloroacetone (18.4 g, 199 mmol). The reaction was stirred at 0℃ for 4h. The reaction was diluted with EtOAc and washed with sat. $NaHCO_3$ (aq) (2 x600 mL), sat. NaCl (aq), dried over Na_2SO_4, filtered and concentrated. The crude product was used without further purification (35.5 g, 100%).

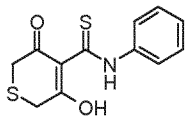
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 2.30 (s, 3 H) 3.27 (s, 2 H) 3.43 (s, 2 H) 3.74 (s, 3 H)

4-2: Sodium 5-oxo-5,6-dihydro-2H-thiopyran-3-olate



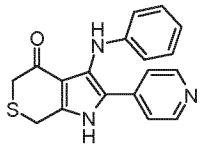
To a suspension of sodium hydride (60% dispersion on mineral oil, 9.2 g, 230 mmol) in dry THF (113 mL) and dry toluene (113 mL) was slowly added dropwise over 2h a solution of methyl [(2-oxopropyl)sulfanyl]acetate (4-3; 35, 5 g, 219 mmol) in dry THF (113 mL). The reaction was then stirred for 16h. The precipitate formed was collected by filtration and washed with diethyl ether, dried in and was used without further purification (31.4 g, 94%).
^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.82 (s., 4 H) 4.44 (s, 1 H).

4-1: 5-Hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide



To a suspension of sodium 5-oxo-5,6-dihydro-2H-thiopyran-3-olate (4-2; 0.5 g, 2.96 mmol) in dry MeCN (3.7 mL) was added 4M HCl in dioxane (0.74 mL, 2.96 mmol). The reaction was cooled to 0℃ and phenyl thioisocyanate (0.8 g, 5.92 mmol) was added. Then DBU (1.13g, 7.4 mmol) was added slowly dropwise over 15 mins and the reaction was stirred at RT for 1.5 h. The reaction was quenched by the addition of 4M HCl in dioxane (2 mL) and concentrated. The residue was purified by Biotage (SNAP silica, EtOAc:Hexane) to give the title compound (293 mg, 37%).
^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.45 - 3.63 (m, 4 H 3.66 (br. s., 1 H) 7.25 - 7.35 (m, 1 H) 7.38 - 7.47 (m, 2 H) 7.69 (d, 2 H) 12.44 (s, 1 H).

3-(phenylamino)-2-(pyridin-4-yl)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one

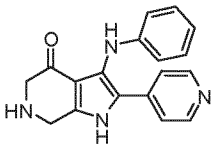


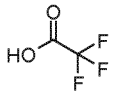
A solution of 5-hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide (4-1; 286 mg, 1.1 mmol) and 4-(methylamino)pyridine (140 mg, 1.3 mmol) in DMA (3 mL) was heated at 130℃ using a microwave. The mixture was concentrated and purified by Biotage (SNAP silica 50g, EtOAc:Hexane, followed by SNAP NH, EtOH:DCM) to give the title compound (56 mg, 16%).
^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.37 (s, 2 H) 3.97 (s, 2 H) 5.75 (s, 1 H) 6.55 - 6.70 (m, 3 H) 7.04 (t, 2 H) 7.41 - 7.55 (m, 3 H) 8.38 - 8.48 (m, 2 H) 12.10 (br. s., 1 H)

Example 5

6-(Cyclopropylcarbonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

5-1: 3-Anilino-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one trifluoroacetate

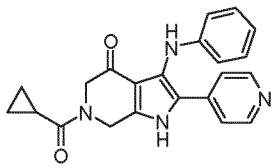




To a solution of tert-butyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (3; 290 mg, 0.72 mmol) in DCM (1 mL) was added TFA (0.1 mL) and stirred at RT for 1h and concentrated to give the title compound in quantitative yield.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.78 - 3.94 (m, 2 H) 4.63 (s, 2 H) 6.64 - 6.77 (m, 3 H) 7.11 (dd, 2 H) 7.86 - 7.94 (m, 2 H) 8.15 (s, 1 H) 8.71 (d, 2 H) 13.12 (s, 1 H)

6-(Cyclopropylcarbonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



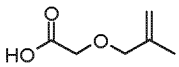
To a mixture of 3-anilino-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one trifluoroacetate (5-1; 67 mg, 0.13 mmol) in pyridine (1 mL) was added cyclopropanecarbonyl chloride(26 mg, 0.25 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative HPLC (acidic method) to give the title compound (19 mg, 47%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 0.75 (d, 4 H) 2.00 - 2.19 (m, 1 H) 4.17 (br. s., 1 H) 4.40 (br. s., 1 H) 4.89 (br. s., 1 H) 5.11 (br. s., 1 H) 6.56 - 6.67 (m, 3 H) 7.06 (t, 2 H) 7.53 - 7.63 (m, 3 H) 8.50 (d, 2 H) 12.31 (br. s., 1 H)

Example 6

3-(phenylamino)-2-(pyridin-4-yl)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

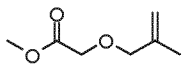
6-6: [(2-Methylprop-2-en-1-yl)oxy]acetic acid



To a solution of 2-chloroacetic acid (50 g, 529 mmol) and 2-methyl-2-propen-1-ol (45.4 g, 630 mmol) in THF (500 mL) cooled to 0℃ was slowly added a solution of KO^{t}Bu (118.7 g, 1058 mmol) in THF (630 mL) over 2.5h. The reaction was allowed to warm to RT and was stirred for 16h. The reaction was quenched by the addition of water (350 mL). The reaction mixture was extracted with EtOAc (x 2). The aqueous layer was acidified with 4M HCl to pH 1-2 and extracted with EtOAc (x 2). The organics layers were combined and washed with water, sat. NaCl (aq), dried over Na_2SO_4, filtered and concentrated. The crude product was used without further purification (57.9 g, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 1.77 (s, 3 H) 4.00 - 4.09 (m, 2 H) 4.09 - 4.14 (m, 2 H) 4.94 - 5.08 (m, 2 H)

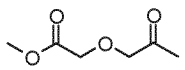
6-5: Methyl [(2-methylprop-2-en-1-yl)oxy]acetate



A suspension of [(2-methylprop-2-en-1-yl)oxy]acetic acid (6-6; 57.9 g, 445 mmol) and Amberlyst -15 resin (3.03 g) in MeOH 130 mL) was heated at 60℃ for 16 h. The reaction mixture was filtered and concentrated to give the title compound which was used without further purification (57.1 g, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 1.76 (s, 3 H) 3.71 - 3.80 (m, 3 H) 4.01 (s, 2 H) 4.06 - 4.10 (m, 2 H) 4.95 (s, 1 H) 4.99 (s, 1 H)

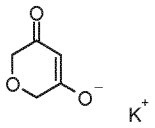
6-4: Methyl (2-oxopropoxy)acetate



To a solution of methyl [(2-methylprop-2-en-1-yl)oxy]acetate (6-5; 21.8 g, 151 mmol) in THF (72 mL) in water (720 mL) was added potassium osmate (21.8 mg, 0.07 mmol) followed by the addition of solution of sodium periodate (87.3 g, 408 mmol) in water over 30 min. The reaction was stirred at RT for 16h. Reaction was not complete, an additional portion of potassium osmate (21.8 mg, 0.07 mmol) was added and a precipitate observed, the reaction was stirred at RT for 16h. The reaction was filtered and the solid washed with DCM. The filtrate was extracted with DCM (x 3). The organics layers were combined and washed with water, sat. NaCl (aq), dried over Na_2SO_4, filtered and concentrated. The crude product was purified by Biotage (SNAP silica 340g, EtOAc:Hexane) to give the title compound (15.63 g, 64%).

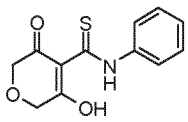
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 2.18 (s, 3 H) 3.77 (s, 3 H) 4.21 (d, 4 H)

6-3: Potassium 5-oxo-5,6-dihydro-2H-pyran-3-olate



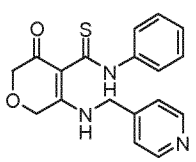
In a three-neck flask containinmg THF (159 mL) heated under reflux conditions was added simultaneously a solution of methyl (2-oxopropoxy)acetate (6-4; 13.18 g, 117.4 mmol) in THF (184 mL) and a solution of KO^{t}Bu (117.4 mmol) in THF (184 mL) over 15 mins and a yellow suspension was observed. The reaction was heated for a further 10 min and then water (1.97 mL) was added and allowed to cool with stirring. The solid was collected by filtration and the solid was washed with THF and diethyl ether. The hygroscopic solid was dried in vacuo at 60℃ and us ed directly (16.4 g, 91%).
^{1}H NMR (400 MHz, DEUTERIUM OXIDE)) δ ppm 4.10 (s, 4 H) 5.19 (s, 1 H)

6-2: 5-Hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide



To a suspension of potassium 5-oxo-5,6-dihydro-2H-pyran-3-olate (6-3; 3.0 g, 19.7 mmol) in dry MeCN (20 mL) was added 4M HCl in dioxane (4.93 mL, 19.7 mmol). The reaction was cooled to 0℃ and phenyl thioisocyanate (5.33 g , 39.4 mmol) was added. Then DBU (7.5 g, 49.3 mmol) was added slowly dropwise over 5 mins and the reaction was stirred at RT for 2 h. The reaction was acidified by the addition of 4M HCl in dioxane and concentrated. The residue was purified by Biotage (SNAP silica 100g, MeOH:DCM) to give the title compound (1.5 g, 31%).
^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.45 (br. s., 4 H) 7.29 - 7.40 (m, 1 H) 7.44 - 7.51 (m, 2 H) 7.51 - 7.58 (m, 2 H) 13.06 (s, 1 H)

6-1: 3-Oxo-N-phenyl-5-[(pyridin-4-ylmethyl)amino]-3,6-dihydro-2H-pyran-4-carbothioamide

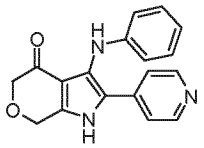


A solution of 5-hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (6-2; 90 mg, 0.36 mmol) and 4-(methylamino)pyridine (78 mg, 0.72 mmol) in DMA (1 mL) was

heated at 120℃ for 1 h. The mixture was concentrat ed and purified by Biotage (SNAP silica 10g, MeOH:DCM) to give the title compound (114 mg, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 4.18 - 4.28 (m, 2 H) 4.56 (s, 2 H) 4.62 - 4.72 (m, 2 H) 7.24 - 7.35 (m, 1 H) 7.37 - 7.55 (m, 6 H) 8.69 (d, 2 H) 13.99 (br. s., 1 H) 14.68 (br. s., 1 H)

3-(phenylamino)-2-(pyridin-4-yl)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one



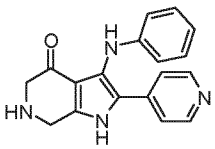
A solution of 3-oxo-N-phenyl-5-[(pyridin-4-ylmethyl)amino]-3,6-dihydro-2H-pyran-4-carbothioamide (6-1; 55 mg, 0.16 mmol) in EtOH (1 mL) and DCM (1 mL) was added SIBX (101 mg, 0.16 mmol) and stirred at RT for 1 h. The mixture was concentrated and purified by Biotage (SNAP NH 11g, MeOH:DCM) to give the title compound (20 mg, 39%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.94 - 4.13 (m, 2 H) 4.89 (s, 2 H) 6.54 - 6.65 (m, 3 H) 6.99 - 7.10 (m, 2 H) 7.46 - 7.56 (m, 3 H) 8.30 - 8.53 (m, 2 H) 12.16 (s, 1 H)

Example 7

6-Acetyl-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

7-2: 3-Anilino-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one hydrochloride

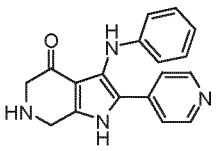


HCl

To tert-butyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (3; 48 mg, 0.12 mmol) was added 4M HCl in dioxane (1 mL) and stirred at RT for 1h and concentrated to give the title compound (45 mg, 100%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.84 (s, 2 H) 4.63 (s, 2 H) 6.68 - 6.78 (m, 3 H) 7.04 - 7.16 (m, 2 H) 8.06 - 8.14 (m, 2 H) 8.19 (br. s., 1 H) 8.66 - 8.75 (m, 2 H) 10.36 (br. s., 1 H) 14.06 (s, 1 H)

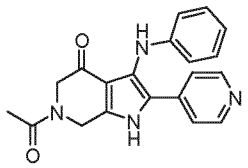
7-1: 3-Anilino-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



To a solution of 3-anilino-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one hydrochloride (7-2; 1.075 g, 2.85 mmol) in EtOH (50 mL) was added Amberlyst-21 (1.4 g) and stirred at RT for 1h. The reaction was filtered and concentrated to give the title compound (360 mg, 41%) which was used without further purification.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.75 (s, 2 H) 4.51 (s, 2 H) 6.54 - 6.67 (m, 3 H) 7.05 (t, 2 H) 7.53 - 7.65 (m, 3 H) 8.43 - 8.54 (m, 2 H) 12.80 (br. s., 1 H)

6-Acetyl-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

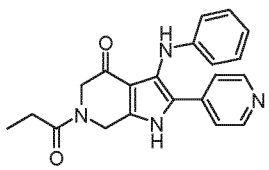


To a mixture of 3-anilino-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (7-1; 78 mg, 0.26 mmol) in pyridine (2 mL) was added acetyl chloride(20 mg, 0.51 mmol) and stirred for 60 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (22 mg, 23%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 2.05 - 2.17 (m, 3 H) 4.03 - 4.19 (m, 2 H) 4.84 (s, 2 H) 6.49 - 6.69 (m, 3 H) 7.04 (t, 2 H) 7.39 - 7.59 (m, 3 H) 8.46 (dd, 2 H) 12.14 - 12.29 (m, 1 H)

Example 8

3-(phenylamino)-6-propanoyl-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

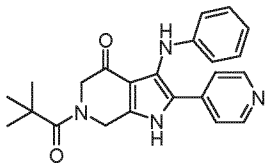


To a mixture of 3-anilino-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (7-1; 78 mg, 0.26 mmol) in pyridine (2 mL) was added propionyl chloride(47 mg, 0.51 mmol) and stirred for 60 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (22 mg, 25%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 0.90 - 1.10 (m, 3 H) 2.30 - 2.46 (m, 2 H) 4.14 (s, 2 H) 4.74 - 4.91 (m, 2 H) 6.46 - 6.66 (m, 3 H) 7.04 (t, 2 H) 7.41 - 7.55 (m, 3 H) 8.46 (d, 2 H) 12.21 (s, 1 H)

Example 9

6-(2,2-Dimethylpropanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

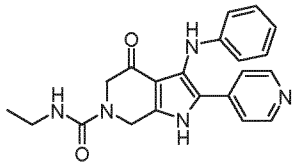


To a mixture of 3-anilino-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (7-1; 78 mg, 0.26 mmol) in pyridine (2 mL) was added propionyl chloride(47 mg, 0.51 mmol) and stirred for 60 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (29 mg, 29%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.22 (s, 9 H) 4.24 (s, 2 H) 4.95 (s, 2 H) 6.44 - 6.68 (m, 3 H) 7.03 (dd, 2 H) 7.39 - 7.55 (m, 3 H) 8.36 - 8.53 (m, 2 H) 12.21 (br. s., 1 H)

Example 10

N-Ethyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide



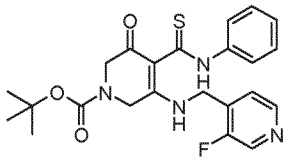
To a mixture of 3-anilino-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (7-1; 78 mg, 0.26 mmol) in pyridine (2 mL) was added ethyl isocyanate (36 mg, 0.51 mmol) and stirred for 60 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (29 mg, 29%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 0.97 - 1.05 (m, 3 H) 3.01 - 3.12 (m, 2 H) 4.00 (s, 2 H) 4.71 (s, 2 H) 6.53 - 6.64 (m, 3 H) 6.83 (t, 1 H) 7.03 (dd, 2 H) 7.46 (s, 1 H) 7.48 - 7.53 (m, 2 H) 8.42 - 8.48 (m, 2 H) 12.15 (s, 1 H)

Example 11

tert-Butyl 2-(3-fluoropyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

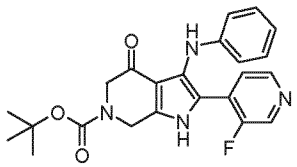
11-1: tert-Butyl 5-{[(3-fluoropyridin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 1.5 g, 4.3 mmol) and 3-fluoro-4-(methylamino)pyridine (1.086 g, 8.6 mmol) in DMA (13 mL) was heated in a microwave tube in a microwave at 120℃ for 1.5h and then concentrated. The residue was purified by Biotage (SNAP silica 100g, EtOAc:Hexane) to give the title compound (1.57 g, 80%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.29 - 1.62 (br.m., 9 H) 4.01 - 4.14 (m, 2 H) 4.57 (br. s., 2 H) 4.90 (d, 2 H) 7.21 - 7.32 (m, 1 H) 7.40 (t, 2 H) 7.47 - 7.60 (m, 3 H) 8.47 - 8.58 (m, 1 H) 8.62 (s, 1 H) 12.71 (br. s., 1 H) 12.86 (br. s., 1 H) 13.58 (br. s., 1 H)

tert-Butyl 2-(3-fluoropyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



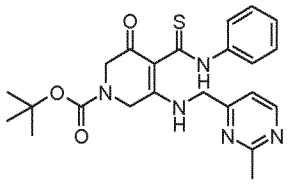
To a solution of tert-butyl 5-{[(3-fluoropyridin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (11-1; 1.05 g, 2.4 mmol) in DMA (60 mL) and TFA (315 mg, 2.76 mmol) was added 10% Pd/C (2.937 g, 2.76 mmol) and heated at 125℃ for 16h. To the reaction was ad ded TEA (0.4 mL) and filtered, the filter was washed with DCM:MeOH and the organics concentrated. The residue was purified by Biotage (SNAP silica 50g, EtOH:DCM) to give the title compound (107 mg, 9%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.40 - 1.57 (m, 9 H) 4.02 (br. s., 2 H) 4.75 (br. s., 2 H) 6.46 - 6.70 (m, 3 H) 7.00 (dd, 2 H) 7.41 - 7.58 (m, 2 H) 8.28 (dd, 1 H) 8.54 (d, 1 H) 11.91 (br. s., 1 H)

Example 12

tert-Butyl 2-(2-methylpyrimidin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

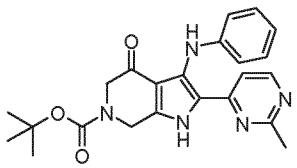
12-1: tert-Butyl 5-{[(2-methylpyrimidin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 1.5 g, 4.3 mmol) and 2-methylpyridmidin-4-yl)methanamine (1.06 g, 8.6 mmol) in DMA (13 mL) was heated in a microwave tube in a microwave at 120℃ for 1.5h and then concentrated. The residue was purified by Biotage (SNAP silica 100g, EtOAc:Hexane) to give the title compound (952 g, 49%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.40 (br. s., 9 H) 2.61 (s, 3 H) 4.09 (br. s., 2 H) 4.61 (br. s., 2 H) 4.91 (br. s., 2 H) 7.22 - 7.29 (m, 1 H) 7.34 - 7.47 (m, 3 H) 7.54 (d, 2 H) 8.72 (d, 1 H) 13.70 (br. s., 1 H)

tert-Butyl 2-(2-methylpyrimidin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



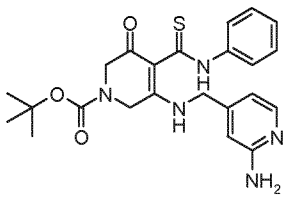
A solution of tert-butyl 5-{[(2-methylpyrimidin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (12-1; 550 mg, 1.2 mmol) in EtOH (22 mL) was added SIBX (755 mg, 1.2 mmol) and stirred at 40℃ for 16 h. The mixture was concentrated and purified by Biotage (SNAP NH, EtOH:DCM) to give the title compound (238 mg, 47%).

^{1}H NMR (400 MHz, DMSO-d$_6$) δ ppm 1.43 (br. s., 9 H) 2.62 (s, 3 H) 4.01 (s, 2 H) 4.77 (br. s., 2 H) 6.64 - 6.74 (m, 3 H) 7.10 (t, 2 H) 7.20 (d, 1 H) 8.19 (br. s., 1 H) 8.48 (d, 1 H) 12.24 (br. s., 1 H)

Example 13

tert-Butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

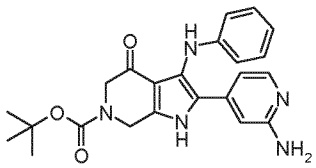
13-1: tert-Butyl 5-{[(2-aminopyridin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (3 g, 8.6 mmol) and 2-amino-4-(methylamino)pyridine (2-2; 2.121 g, 17.2 mmol) in DMA (26 mL) was heated in a microwave tube at 125℃ for 1.5h and then concentrated. The residue was purified by Biotage (SNAP silica 340 g, EtOH:DCM) to give the title compound (3.40 g, 87%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.29 (br. s., 9 H) 4.09 (br. s., 2 H) 4.56 (s, 2 H) 4.65 (d, 2 H) 6.03 (s, 2 H) 6.38 (br. s., 1 H) 6.46 (d, 1 H) 7.21 - 7.33 (m, 1 H) 7.41 (t, 2 H) 7.50 (d, 2 H) 7.85 - 7.93 (m, 1 H) 13.37 (br. s., 1 H) 13.88 (s, 1 H)

tert-Butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

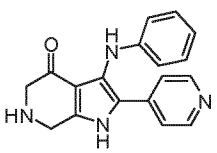


A solution of tert-butyl 5-{[(2-aminopyridin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (13-1; 3.3 g, 7.3 mmol) in EtOH (130 mL) was added SIBX (4.75 g, 7.6 mmol) and stirred at 40℃ for 16 h. Another portion of SIBX (905 mg, 1.46 mmol) was added and stirred at 40℃ for 2 h. The mixture was concentrated and purified by Biotage (SNAP NH, EtOH:DCM) to give the title compound (516 mg, 17%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.43 (br. s., 9 H) 3.97 (br. s., 2 H) 4.71 (br. s., 2 H) 5.75 - 5.84 (m, 2 H) 6.51 - 6.66 (m, 4 H) 6.71 (dd, 1 H) 6.97 - 7.09 (m, 2 H) 7.25 (s, 1 H) 7.79 (d, 1 H) 11.97 (br. s., 1 H)

Example 14

3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



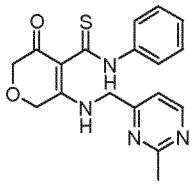
To tert-butyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (3; 314 mg, 0.78 mmol) was added 4M HCl in dioxane (0.39 mL, 1.55 mmol) and stirred at RT for 1h. The reaction was diluted with dioxane (1 mL) and another portion of 4M HCl in dioxane (0.39 mL, 1.55 mmol) was added and stirred at RT for 16 h. The mixture was concentrated and purified by Biotage (SNAP NH, EtOH:DCM) to give the title compound (99 mg, 40%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.20 (s, 3 H) 3.96 (s, 2 H) 6.55 - 6.67 (m, 3 H) 7.04 (dd, 2 H) 7.42 (s, 1 H) 7.45 - 7.52 (m, 2 H) 8.32 - 8.54 (m, 2 H) 11.92 (br. s., 1 H)

Example 15

2-(2-Methylpyrimidin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

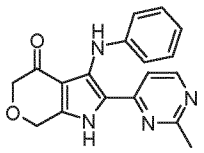
15-1: 5-{[(2-Methylpyrimidin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide



A solution of 5-hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (6-6; 113 mg, 0.45 mmol) and (2-methylpyrimidin-4-yl)methanamine (67 mg, 0.54 mmol) in DMA (1.2 mL) was heated at 80℃ in a microwave for 1 h. The mixture was concentrated and purified by Biotage (SNAP silica 25 g, EtOAc:Hexane) to give the title compound (127 mg, 75%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.62 (s, 3 H) 4.20 (s, 2 H) 4.83 (s, 2 H) 4.89 (d, 2 H) 7.21 - 7.28 (m, 1 H) 7.34 (d, 1 H) 7.38 - 7.47 (m, 2 H) 7.50 (d, 2 H) 8.71 (d, 1 H) 13.80 (t, 1 H) 14.04 (s, 1 H)

2-(2-Methylpyrimidin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

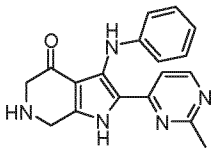


A solution of 5-{[(2-methylpyrimidin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (15-1; 123 mg, 0.35 mmol) in EtOH (10 mL) was added SIBX (216 mg, 0.35 mmol) and stirred at RT for 2 h. The mixture was concentrated and purified by Biotage (SNAP NH 28 g, MeOH:DCM) to give the title compound (36 mg, 32%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.61 (s, 3 H) 4.06 (s, 2 H) 4.89 (s, 2 H) 6.67 - 6.78 (m, 3 H) 7.11 (t, 2 H) 7.26 (d, 1 H) 8.39 (s, 1 H) 8.49 (d, 1 H) 12.17 (br. s., 1 H)

Example 16

2-(2-Methylpyrimidin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

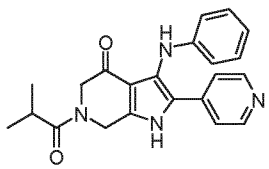


To a solution of tert-butyl 2-(2-methylpyrimidin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (12; 300 mg, 0.72 mmol) in DCM (20 mL) was added TFA (1.1 mL) and stirred at RT for 1h. The reaction was cooled to 0℃ and sat. $NaHCO_3$ (aq) was carefully added. The reaction mixture was extracted with DCM:MeOH (9:1). The organics were combined, washed with water, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by Biotage (SNAP silica, EtOH:DCM) to give the title compound (123 mg, 54%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.60 (s, 3 H) 3.22 (s, 3 H) 3.97 (s, 2 H) 6.66 - 6.78 (m, 3 H) 7.10 (t, 2 H) 7.17 (d, 1 H) 8.29 (s, 1 H) 8.44 (d, 1 H) 11.96 (br. s., 1 H)

Example 17

6-(2-Methylpropanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

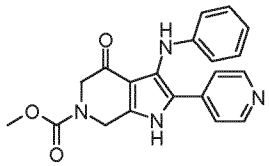


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 29 mg, 0.1 mmol) in pyridine (1 mL) was added isopropionyl chloride(20 mg, 0.19 mmol) and stirred for 2 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by preparative TLC (EtOH:DCM) to give the title compound (20 mg, 54%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.90 - 1.11 (m, 6 H) 2.86 - 3.09 (m, 1 H) 4.14 - 4.19 (m, 2 H) 4.83 - 4.95 (m, 2 H) 6.49 - 6.74 (m, 3 H) 7.03 (t, 2 H) 7.37 - 7.57 (m, 3 H) 8.45 (d, 2 H) 12.22 (br. s., 1 H)

Example 18

Methyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

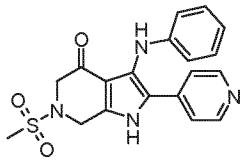


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.1 mmol) in pyridine (1 mL) was added methyl chloroformate(19 mg, 0.20 mmol) and stirred for 2 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by preparative TLC (EtOH:DCM) to give the title compound (25 mg, 66%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.00 (s, 3 H) 3.87 (s, 2 H) 4.63 (s, 2 H) 6.54 - 6.71 (m, 3 H) 6.99 - 7.10 (m, 2 H) 7.48 (s, 1 H) 7.50 - 7.56 (m, 2 H) 8.34 - 8.54 (m, 2 H)

Example 19

6-(Methylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

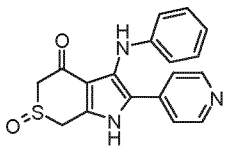


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.1 mmol) in pyridine (1 mL) was added methylsulfonyl chloride (23 mg, 0.20 mmol) and stirred for 2 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by preparative TLC (EtOH:DCM) to give the title compound (23 mg, 57%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.66 (s, 3 H) 4.04 (s, 2 H) 4.78 (s, 2 H) 6.51 - 6.70 (m, 3 H) 6.98 - 7.12 (m, 2 H) 7.45 (s, 1 H) 7.47 - 7.56 (m, 2 H) 8.37 - 8.53 (m, 2 H) 12.21 (br. s., 1 H)

Example 20

3-(phenylamino)-2-(pyridin-4-yl)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one 6-oxide

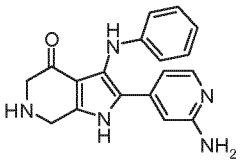


A solution of 3-(phenylamino)-2-(pyridin-4-yl)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one (4; 52 mg, 0.16 mmol) in DCM (3 mL) was added mCPBA (54 mg, 0.24 mmol) and was stirred at RT for 2.5 h. The reaction was diluted with DCM and washed with sat. $NaHCO_3$ (aq), dried over Na_2SO_4, filtered and concentrated. The crude product was suspended in diethyl ether and sonicated, the solid was collected by filtration to give the title compound (25 mg, 43%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.81 (dd, 1 H) 3.99 - 4.10 (m, 1 H) 4.32 (dd, 1.77 Hz, 1 H) 4.51 (d, 1 H) 6.52 - 6.72 (m, 3 H) 7.04 (dd, 2 H) 7.48 - 7.51 (m, 2 H) 7.52 (s, 1 H) 8.43 - 8.48 (m, 2 H) 12.29 (s, 1 H)

Example 21

2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



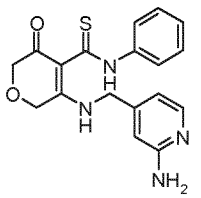
To a solution of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 75 mg, 0.18 mmol) in DCM (6 mL) was added TFA (407 mg) and stirred at RT for 1h. TEA added (0.6 mL) and concentrated. The crude product was purified by preparative HPLC (basic method) to give the title compound (18 mg, 29%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.17 (s, 2 H) 3.92 (s, 2 H) 5.67 - 5.79 (m, 2 H) 6.52 - 6.62 (m, 4 H) 6.70 (dd, 1 H) 6.98 - 7.06 (m, 2 H) 7.20 (s, 1 H) 7.76 (d, 1 H) 11.69 (s, 1 H)

Example 22

2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

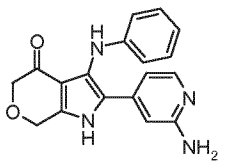
22-1: 5-{[(2-Aminopyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide



A solution of 5-hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (1.5 g, 6 mmol) and (2-aminopyridin-4-yl)methanamine (6-6; 1.04 g, 8.4 mmol) in DMA (16 mL) was heated at 80℃ in a microwave for 1.5 h. The mi xture was concentrated and the residue was suspended suspended in DCM and sonicated, the solid was collected by filtration to give the title compound (1.71 g, 80%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.20 (s, 2 H) 4.60 (d, 2 H) 4.75 (s, 2 H) 6.03 (s, 2 H) 6.35 - 6.42 (m, 1 H) 6.42 - 6.50 (m, 1 H) 7.22 - 7.30 (m, 1 H) 7.40 (t, 2 H) 7.48 (d, 2 H) 7.90 (d, 1 H) 13.72 (br. s., 1 H) 14.08 (s, 1 H)

2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

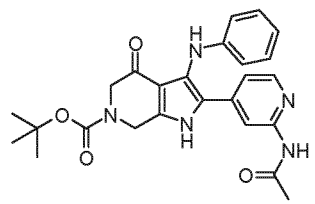


A solution of 5-{[(2-aminopyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (22-1; 1.604 g, 4.5 mmol) in MeOH (64 mL) and DCM (64 mL) was added SIBX (2.82 g, 4.5 mmol) and stirred at RT for 2 h. The mixture was concentrated and purified by Biotage (SNAP NH, MeOH:DCM) to give the title compound (535 mg, 37%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.01 (s, 2 H) 4.85 (s, 2 H) 5.80 (s, 2 H) 6.53 - 6.65 (m, 4 H) 6.70 - 6.76 (m, 1 H) 6.98 - 7.10 (m, 2 H) 7.29 (s, 1 H) 7.77 - 7.83 (m, 1 H) 11.92 (s, 1 H)

Example 23

tert-Butyl 2-[2-(acetylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

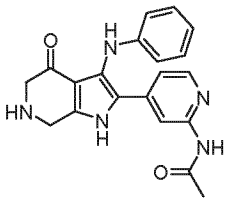


To a solution of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 305 mg, 0.73 mmol) in THF (20 mL) and pyridine (1 mL) was added acetyl chloride (286 mg, 3.64 mmol) and stirred for 1 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP silica, EtOH:DCM) to give the title compound (160 mg, 48%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.43 (br. s., 9 H) 2.02 - 2.12 (m, 4 H) 3.99 (br. s., 2 H) 4.74 (br. s., 2 H) 6.53 - 6.64 (m, 3 H) 6.97 - 7.08 (m, 2 H) 7.22 (dd, 1 H) 7.39 (s, 1 H) 8.12 (d, 1 H) 8.27 (s, 1 H) 10.39 (s, 1 H) 12.20 (br. s., 1 H)

Example 24

N-{4-[4-Oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

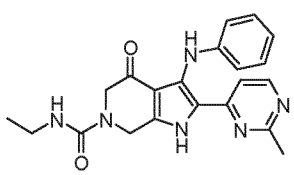


To a solution of tert-butyl 2-[2-(acetylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (23; 265 mg, 0.57 mmol) in DCM (16 mL) was added TFA (1.31 g) and stirred for 16 h at RT. The reaction was cooled to 0℃ and sat. $NaHCO_3$ (aq) was carefully added. The reaction mixture was extracted with DCM:MeOH (9:1). The organics were combined, washed with water, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by Biotage (SNAP silica, EtOH:DCM) to give the title compound (131 mg, 63%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.07 (s, 3 H) 3.19 (s, 2 H) 3.94 (s, 2 H) 6.53 - 6.66 (m, 3 H) 7.01 (t, 2 H) 7.18 (dd, 1 H) 7.33 (s, 1 H) 8.09 (d, 1 H) 8.23 (s, 1 H) 10.34 (s, 1 H) 11.90 (br. s., 1 H)

Example 25

N-Ethyl-2-(2-methylpyrimidin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

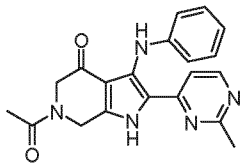


To a solution of 2-(2-methylpyrimidin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (16; 25 mg, 0.08 mmol) in pyridine (1 mL) was added ethyl isocyanate (11 mg, 0.16 mmol) and stirred for 2 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (22 mg, 69%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.93 - 1.06 (m, 3 H) 2.61 (s, 3 H) 2.99 - 3.13 (m, 2 H) 4.01 (s, 2 H) 4.71 (s, 2 H) 6.63 - 6.76 (m, 3 H) 6.84 (t, 1 H) 7.10 (dd, 2 H) 7.22 (d, 1 H) 8.37 (br. s., 1 H) 8.47 (d, 1 H) 12.23 (br. s., 1H)

Example 26

6-Acetyl-2-(2-methylpyrimidin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

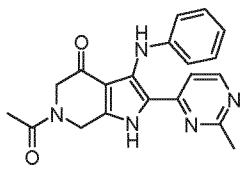


To a solution of 2-(2-methylpyrimidin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (16; 30 mg, 0.09 mmol) in pyridine (1.2 mL) was added acetyl chloride (15 mg, 0.19 mmol) and stirred for 2 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (19 mg, 54%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.09 - 2.15 (m, 2 H) 2.62 (s, 3 H) 4.08 - 4.19 (m, 2 H) 4.85 (d, 2 H) 6.65 - 6.75 (m, 3 H) 7.04 - 7.16 (m, 2 H) 7.19 - 7.26 (m, 1 H) 8.21 - 8.32 (m, 1 H) 8.48 (d, 1 H) 12.28 (br. s., 1 H)

Example 27

Methyl 2-(2-methylpyrimidin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



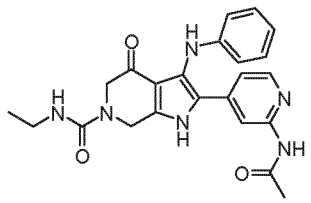
To a solution of 2-(2-methylpyrimidin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (16; 25 mg, 0.08 mmol) in pyridine (1 mL) was added methyl chloroformate (15 mg, 0.16 mmol) and stirred for 2 h at RT. MeOH was added, followed

by toluene and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (15 mg, 49%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.61 (s, 3 H) 3.67 (s, 3 H) 4.06 (s, 2 H) 4.80 (s, 2 H) 6.62 - 6.77 (m, 3 H) 7.05 - 7.16 (m, 2 H) 7.21 (d, 1 H) 8.23 (br. s., 1 H) 8.47 (d, 1 H) 12.29 (br. s., 1 H)

Example 28

2-[2-(Acetylamino)pyridin-4-yl]-N-ethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

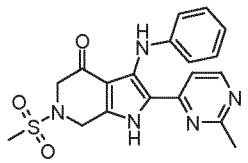


To a solution of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 30 mg, 0.08 mmol) in pyridine (1 mL) was added ethyl isocyanate (12 mg, 0.17 mmol) and stirred for 2 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude mixture was crystallized from DCM:MeOH to give the title compound (25 mg, 67%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.01 (t, 3 H) 2.07 (s, 3 H) 3.00 - 3.13 (m, 2 H) 3.98 (s, 2 H) 4.69 (s, 2 H) 6.50 - 6.66 (m, 3 H) 6.81 (t, 1 H) 7.01 (dd, 2 H) 7.21 (dd, 1 H) 7.37 (s, 1 H) 8.12 (d, 1 H) 8.26 (s, 1 H) 10.36 (s, 1 H) 12.16 (br. s., 1 H)

Example 29

2-(2-Methylpyrimidin-4-yl)-6-(methylsulfonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

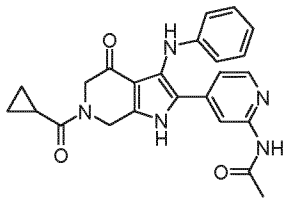


To a solution of 2-(2-methylpyrimidin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (16; 25 mg, 0.08 mmol) in pyridine (1 mL) was added methyl methanesulfonyl chloride (18 mg, 0.16 mmol) and stirred for 2 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (9 mg, 28%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.62 (s, 3 H) 3.00 (s, 3 H) 3.89 (s, 2 H) 4.66 (s, 2 H) 6.64 - 6.78 (m, 3 H) 7.03 - 7.18 (m, 2 H) 7.25 (d, 1 H) 8.28 (br. s., 1 H) 8.48 (d, 1 H) 12.34 (br. s., 1 H)

Example 30

N-{4-[6-(Cyclopropylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

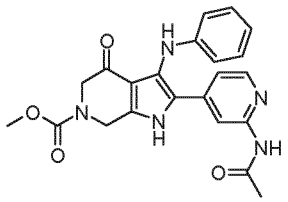


To a solution of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 30 mg, 0.08 mmol) in pyridine (1 mL) was added cyclopropanecarbonyl chloride (17 mg, 0.17 mmol) and stirred for 2 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (26 mg, 69%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.57 - 0.94 (m, 6 H) 2.00 - 2.13 (m, 4 H) 4.12 - 4.36 (m, 2 H) 4.85 - 5.06 (m, 2 H) 6.48 - 6.66 (m, 3 H) 6.94 - 7.10 (m, 2 H) 7.22 (d, 1 H) 7.30 - 7.45 (m, 1 H) 8.11 (d, 1 H) 8.23 - 8.37 (m, 1 H) 10.36 (br. s., 1 H)

Example 31

Methyl 2-[2-(acetylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

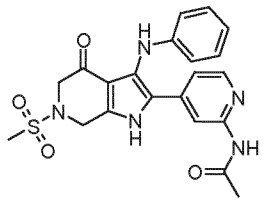


To a solution of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 30 mg, 0.08 mmol) in pyridine (1 mL) was added methyl chloroformate (16 mg, 0.17 mmol) and stirred for 2 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (21 mg, 56%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.99 - 2.20 (m, 3 H) 3.66 (br. s., 3 H) 4.03 (s, 2 H) 4.78 (s, 2 H) 6.49 - 6.65 (m, 3 H) 7.01 (dd, 2 H) 7.21 (dd, 1 H) 7.32 - 7.48 (m, 1 H) 8.12 (d, 1 H) 8.27 (s, 1 H) 10.38 (s, 1 H) 12.20 (br. s., 1 H)

Example 32

N-{4-[6-(Methylsulfonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

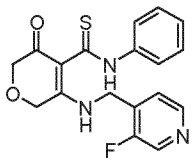


To a solution of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 30 mg, 0.08 mmol) in pyridine (1 mL) was added methanesulfonyl chloride (19 mg, 0.17 mmol) and stirred for 2 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (24 mg, 62%). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.08 (s, 3 H) 2.99 (s, 3 H) 3.86 (s, 2 H) 4.63 (s, 2 H) 6.48 - 6.66 (m, 3 H) 7.02 (dd, 2 H) 7.24 (dd, 1 H) 7.39 - 7.47 (m, 1 H) 8.13 (d, 1 H) 8.28 (s, 1 H) 10.39 (s, 1 H) 12.27 (br. s., 1 H)

Example 33

2-(3-Fluoropyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

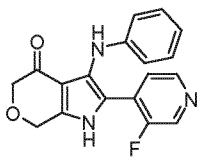
33-1: 5-{[(3-Fluoropyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide



A solution of 5-hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (6-6; 200 mg, 0.8 mmol) and (3-fluorpyridin-4-yl)methanamine (121 mg, 0.96 mmol) in DMA (2.1 mL) was heated at 80℃ in a microwave for 1 h. The mixture was concentrated and purified by Biotage (SNAP silica 25 g, EtOAc:Hexane) to give the title compound (251 mg, 83%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 4.20 (s, 2 H) 4.81 (s, 2 H) 4.85 - 4.92 (m, 2 H) 7.21 - 7.33 (m, 1 H) 7.40 (t, 2 H) 7.45 - 7.57 (m, 3 H) 8.49 (d, 1 H) 8.61 (s, 1 H) 13.60 (br. s., 1 H) 13.97 (br. s., 1 H)

2-(3-Fluoropyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

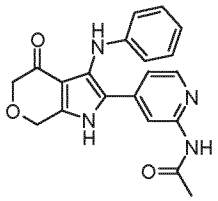


A solution of 5-{[(3-fluoropyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (33-1; 169 mg, 0.47 mmol) in DMA (8.4 mL) was added 10% Pd/C (502 mg, 0.47 mmol) and stirred at 120℃ for 7 h. Filter ed, concentrated and purified by Biotage (SNAP NH 11g, MeOH:DCM) to give the title compound (13 mg, 8%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 4.05 (s, 2 H) 4.88 (s, 2 H) 6.52 - 6.64 (m, 3 H) 6.94 - 7.10 (m, 2 H) 7.50 (dd, 1 H) 7.52 (s, 1 H) 8.29 (dd, 1 H) 8.55 (d, 1 H) 11.87 (br. s., 1 H)

Example 34

N-{4-[4-Oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}acetamide

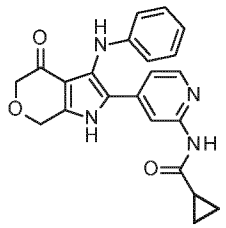


To a solution of 2-(2-aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 23.7 mg, 0.07 mmol) in THF (2 mL) was added pyridine (0.1 mL) and acetyl chloride (29 mg, 0.37 mmol) and stirred for 1h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (16.7 mg, 59%).

^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 2.00 - 2.14 (m, 3 H) 4.02 (s, 2 H) 4.86 (s, 2 H) 6.52 - 6.69 (m, 3 H) 7.02 (dd, 2 H) 7.24 (dd, 1 H) 7.38 (s, 1 H) 8.12 (d, 1 H) 8.27 (s, 1 H) 10.35 (s, 1 H) 12.12 (br. s., 1 H)

Example 35

N-{4-[4-Oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}cyclopropanecarboxamide

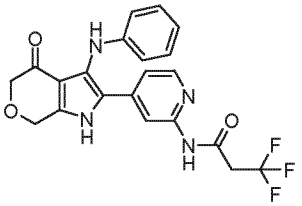


To a solution of 2-(2-aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.14 mmol) in THF (4 mL) was added pyridine (0.2 mL) and cyclopropanecarbonyl chloride (73 mg, 0.7 mmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (20 mg, 36%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.81 (d, 4 H) 1.95 - 2.07 (m, 1 H) 4.02 (s, 2 H) 4.86 (s, 2 H) 6.52 - 6.65 (m, 3 H) 7.02 (dd, 2 H) 7.24 (dd, 1 H) 7.42 (s, 1 H) 8.13 (d, 1 H) 8.25 - 8.29 (m, 1 H) 10.71 (s, 1 H) 12.11 (br. s., 1 H)

Example 36

3,3,3-Trifluoro-N-{4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}propanamide



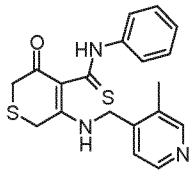
To a solution of 2-(2-aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.14 mmol) in THF (4 mL) was added pyridine (0.2 mL) and 3, 3, 3-trifluorpropionyl chloride (103 mg, 0.7 mmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP silica, EtOH:DCM) to give the title compound (18 mg, 26%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.53 - 3.72 (m, 2 H) 3.98 - 4.11 (m, 2 H) 4.88 (s, 2 H) 6.53 - 6.64 (m, 3 H) 7.02 (dd, 2 H) 7.31 (dd, 1 H) 7.46 (s, 1 H) 8.17 (d, 1 H) 8.27 (s, 1 H) 10.77 (s, 1 H) 12.18 (s, 1 H)

Example 37

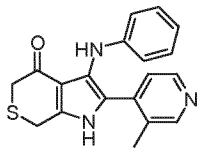
2-(3-Methylpyridin-4-yl)-3-(phenylamino)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one

37-1: 5-{[(3-Methylpyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide



A solution of 5-hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide (4-1; 526 mg, 1.98 mmol) and 1-(3-methylpyridin-4-yl)methanamine (339 mg, 2.77 mmol) in DMA (5.3 mL) was heated at 80℃ for 1.5 h. The mixt ure was concentrated and purified by Biotage (SNAP NH 50g, EtOAc:Hexane ; MeOH:DCM) to give the title compound (178 mg, 24%).

2-(3-Methylpyridin-4-yl)-3-(phenylamino)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one



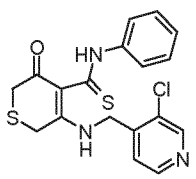
A solution of 5-{[(3-methylpyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide (37-1; 169 mg, 0.46 mmol) in EtOH (8.5 mL) was added SIBX (256 mg, 0.41 mmol) and stirred at RT for 2 days. The mixture was concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, EtOH:DCM) to give the title compound (29 mg, 17%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.18 (3H), 3.40 (2H), 3.94 (2H), 6.42-6.57 (3H), 6.90 (2H), 7.23 (1H), 7.50 (1H), 8.32 (2H), 11.78 (1H)

Example 38

2-(3-Chloropyridin-4-yl)-3-(phenylamino)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one

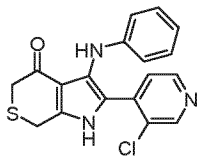
38-1: 5-{[(3-Chloropyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide



A solution of 5-hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide (4-1; 300 mg, 1.13 mmol), DIPEA (590 µL, 0.74 mmol) and (3-chloropyridin-4-

yl)methanaminium chloride (298 mg, 1.58 mmol) in DMA (3 mL) was heated at 80℃ for 1 h. The mixture was concentrated and purified by Biotage (SNAP NH 50g, EtOAc:Hexane) to give the title compound (117 mg, 25%).

2-(3-Chloropyridin-4-yl)-3-(phenylamino)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one



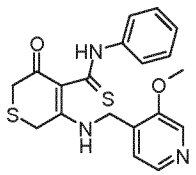
To a A solution of 5-{[(3-Chloropyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide (38-1; 112 mg, 0.29 mmol) in DMA (5.1 mL) was added 10% Pd/C (305 mg, 0.29 mmol) and heated at 120℃ for 3h . To the mixture was filtered and concentrated. The residue was purified by Biotage (SNAP NH 25g, MeOH:DCM) and preparative TLC (silica, MeOH:DCM) to give the title compound (5 mg, 4%).

^{1}H-NMR (400 MHz, CD_2Cl_2), δ [ppm]= 3.93 (2H), 5.26 (2H), 6.69 (2H), 6.76 (1H), 7.05 (2H), 7.24 (1H), 7.71 (1H), 8.12 (1H), 8.54 (1H), 9.17 (1H)

Example 39

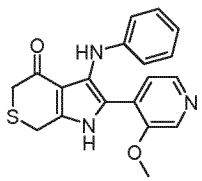
2-(3-Methoxypyridin-4-yl)-3-(phenylamino)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one

39-1: 5-{[(3-Methoxypyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide



A solution of 5-hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide (4-1; 260 mg, 0.98 mmol) and 1-(3-methoxypyridin-4-yl)methanamine (190 mg, 1.37 mmol) in DMA (2.6 mL) was heated at 100℃ for 1.5 h. The mix ture was concentrated and purified by Biotage (SNAP NH 50g, EtOAc:Hexane ; MeOH:DCM) to give the title compound (86 mg, 20%).

2-(3-Methoxypyridin-4-yl)-3-(phenylamino)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one



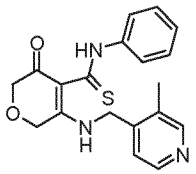
A solution of 5-{[(3-methoxypyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide (39-1; 71 mg, 0.18 mmol) in EtOH (5.3 mL) was added SIBX (114 mg, 0.18 mmol) and stirred at RT for 2.5 days. The mixture was concentrated and purified by Biotage (SNAP NH 10g, EtOAc:Hexane; MeOH:DCM) and preparative TLC (silica, EtOAc) to give the title compound (8 mg, 11%).

^{1}H-NMR (500 MHz, CD_2Cl_2), δ [ppm]= 3.91 (2H), 4.11 (3H), 5.34 (2H), 6.69 (2H), 6.79 (1H), 7.10 (2H), 7.34 (1H), 7.50 (1H), 7.96 (1H), 8.34 (1H), 9.92 (1H)

Example 40

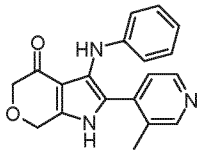
2-(3-Methylpyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

40-1: 5-{[(3-methylpyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide



A solution of 5-Hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (6-2; 250 mg, 1.00 mmol) DIPEA (699 µL, 0.74 mmol) and 1-(3-methylpyridin-4-yl)methanamine dihydrochloride (391 mg, 2.00 mmol) in DMA (3 mL) was heated at 120℃ for 2 h. The mixture was concentrated and purified by Biotage (SNAP NH 25g, EtOAc:Hexane; MeOH:DCM) to give the title compound (260 mg, 73%).

2-(3-Methylpyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one



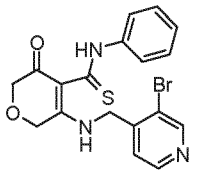
A solution of 5-{[(3-methylpyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide (40-1; 255 mg, 0.72 mmol) in EtOH (10 mL) and DCM (5 mL) was added SIBX (404 mg, 0.65 mmol) and stirred at RT for 16 h. The mixture was concentrated and purified by Biotage (SNAP NH 25g, EtOH:DCM) and preparative TLC (silica, EtOH:DCM) to give the title compound (45 mg, 19%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.20 (3H), 4.05 (2H), 4.87 (2H), 6.49-6.55 (3H), 6.94 (2H), 7.24 (1H), 7.36 (1H), 8.35 (1H), 8.38 (1H), 11.76 (1H)

Example 41

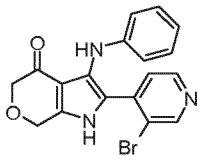
2-(3-Bromopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

41-1: 5-{[(3-Bromopyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide



A solution of 5-Hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (6-2; 500 mg, 2.01 mmol) and 1-(3-bromopyridin-4-yl)methanamine (750 mg, 4.01 mmol) in DMA (6 mL) was heated at 85℃ for 2 h. The mixture was con centrated and purified by Biotage (SNAP NH 50g, EtOAc:Hexane) to give the title compound (767 mg, 91%).

2-(3-Bromopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one



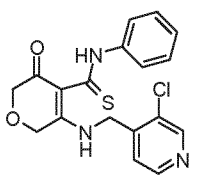
A solution of 5-{[(3-bromopyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (41-1; 660 mg, 1.58 mmol) in DMA (32 mL) and TFA (121 µL) was added 10% Pd/C (1.68 g, 1.58 mmol) and heated at 125℃ for 16h. TEA was added (60 µL), the mixture was filtered and concentrated. The residue was purified by Biotage (SNAP NH 55g, EtOH:DCM), recrystallization from EtOH and preparative TLC (silica, EtOH:DCM) to give the title compound (72 mg, 11%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.07 (2H), 4.87 (2H), 6.51-6.60 (3H), 6.95 (2H), 7.32 (1H), 7.41 (1H), 8.44 (1H), 8.74 (1H), 11.89 (1H)

Example 42

2-(3-Chloropyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

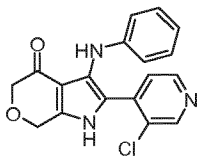
42-1: 5-{[(3-Chloropyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide



A solution of 5-Hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (6-2; 250 mg, 1.00 mmol), DIPEA (524 µL, 3.01 mmol) and 1-(3-chloropyridin-4-yl)methanamine

hydrochloride (359 mg, 2.06 mmol) in DMA (3 mL) was heated at 85℃ for 2 h. The mixture was concentrated and purified by Biotage (SNAP NH 10g, EtOAc:Hexane) to give the title compound (321 mg, 86%).

2-(3-Chloropyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

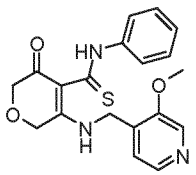


A solution of 5-{[(3-chloropyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (42-1; 217 mg, 0.58 mmol) in DMA (11 mL) and TFA (45 µL) was added 10% Pd/C (618 mg, 0.58 mmol) and heated at 125℃ for 16h. TEA was added (100 µL), the mixture was filtered and concentrated. The residue was purified by Biotage (SNAP NH 25g, MeOH:DCM) to give the title compound (40 mg, 20%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.07 (2H), 4.88 (2H), 6.51-6.57 (3H), 6.96 (2H), 7.35 (1H), 7.46 (1H), 8.41 (1H), 8.62 (1H), 11.90 (1H)

Example 43

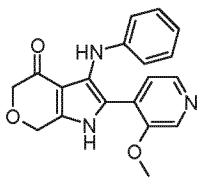
2-(3-Methoxypyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

43-1: 5-{[(3-Methoxypyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide



A solution of 5-Hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (6-2; 280 mg, 1.12 mmol), DIPEA (174 µL, 1.57 mmol) and (3-methoxypyridin-4-yl)methanaminium chloride (550 mg, 3.14 mmol) in DMA (3 mL) was heated at 80℃ for 3.5 h. The mixture was concentrated and purified by Biotage (SNAP NH 55g, EtOAc:Hexane; MeOH:DCM) to give the title compound (96 mg, 21%).

2-(3-Methoxypyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

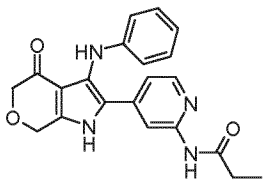


A solution of 5-{[(3-methoxypyridin-4-yl)methyl]amino}-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (43-1; 92 mg, 0.22 mmol) in EtOH (6.5 mL) was added SIBX (139 mg, 0.224 mmol) and stirred at RT for 16 h. TEA was added (100 µL) and the mixture concentrated and purified by Biotage (SNAP NH 11g, MeOH:DCM) and preparative HPLC (basic method) to give the title compound (7 mg, 8%).

^{1}H-NMR (500 MHz, DMSO-d6), δ [ppm]= 3.92 (3H), 4.02 (2H), 4.87 (2H), 6.51-6.59 (3H), 6.99 (2H), 7.34 (1H), 7.40 (1H), 8.05 (1H), 8.38 (1H), 11.53 (1H)

Example 44

N-{4-[4-Oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}propanamide

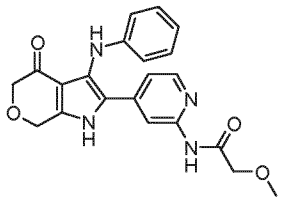


To a mixture of 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.14 mmol) in pyridine (176 µL) and THF (3.8 mL) was added propanoyl chloride (61 µL, 0.70 mmol) and stirred for 60 h at RT. Methanol was added and the mixture concentrated and purified by Biotage (SNAP NH 25g, MeOH:DCM) and preparative TLC (NH_2-Phase, EtOH:DCM) to give the title compound (10 mg, 20%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.07 (3H), 2.38 (2H), 4.00 (2H), 4.84 (2H), 6.55-6.62 (3H), 7.02 (2H), 7.23 (1H), 7.36 (1H), 8.08 (1H), 8.33 (1H), 10.27 (1H), 12.14 (1H)

Example 45

2-Methoxy-N-{4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}acetamide

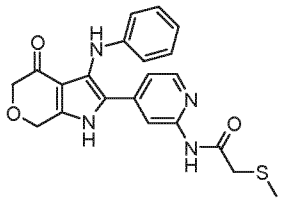


To a mixture of 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.14 mmol) in pyridine (196 µL) and THF (3.8 mL) was added methoxyacetyl chloride (64 µL, 0.70 mmol) and stirred for 16 h at RT. Methanol was added and the mixture concentrated and purified by Biotage (SNAP NH 25g, MeOH:DCM) and preparative TLC (silica, MeOH:DCM) to give the title compound (15 mg, 26%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.37 (3H), 4.04 (2H), 4.05 (2H), 4.89 (2H), 6.56-6.62 (3H), 7.03 (2H), 7.30 (1H), 7.46 (1H), 8.16 (1H), 8.29 (1H), 9.89 (1H), 12.18 (1H)

Example 46

2-(Methylsulfanyl)-N-{4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}acetamide

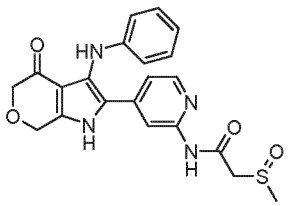


To a mixture of 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.16 mmol) in pyridine (217 µL) and THF (4.2 mL) was added (methylsulfanyl)acetyl chloride (85 µL, 0.78 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by Biotage (SNAP NH 25g, EtOAc:Hexane; MeOH:DCM) to give the title compound (7 mg, 10%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.16 (3H), 2.54-2.58 (2H), 4.04 (2H), 4.89 (2H), 6.51-6.66 (3H), 7.03 (2H), 7.28 (1H), 7.47 (1H), 8.16 (1H), 8.29 (1H), 10.48 (1H), 12.19 (1H)

Example 47

2-(Methylsulfinyl)-N-{4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}acetamide

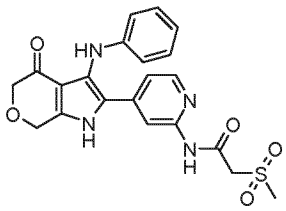


To a mixture of 2-(Methylsulfanyl)-N-{4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}acetamide (46; 40 mg, 0.09 mmol) in DCM (2 mL) was added 3-chlorobenzenecarboperoxoic acid (79 mg, 0.35 mmol) and stirred for 4 h at RT. The mixture was concentrated and purified by Biotage (SNAP NH 11g, EtOAc:Hexane; MeOH:DCM) and preparative TLC (silica, MeOH:DCM) to give the title compound (1 mg, 2%).

^{1}H-NMR (400 MHz, CD_3OD), δ [ppm]= 2.80 (3H), 3.33 (2H), 4.14 (2H), 4.94 (2H), 6.64-6.73 (3H), 7.06 (2H), 7.26 (1H), 8.09 (1H), 8.26 (1H)

Example 48

2-(Methylsulfonyl)-N-{4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}acetamide

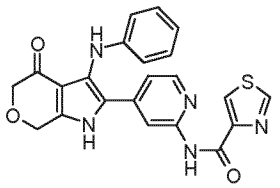


To a mixture of 2-(Methylsulfanyl)-N-{4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}acetamide (46; 40 mg, 0.09 mmol) in DCM (2 mL) was added 3-chlorobenzenecarboperoxoic acid (79 mg, 0.35 mmol) and stirred for 4 h at RT. The mixture was concentrated and purified by (SNAP NH 11g, EtOAc:Hexane; MeOH:DCM) and preparative TLC (silica, MeOH:DCM) to give the title compound (3 mg, 6%).

^{1}H-NMR (400 MHz, CD_3OD), δ [ppm]= 3.19 (3H), 3.34 (2H), 4.14 (2H), 4.93 (2H), 6.64-6.73 (3H), 7.07 (2H), 7.26 (1H), 8.10 (1H), 8.27 (1H)

Example 49

N-{4-[4-Oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}-1,3-thiazole-4-carboxamide

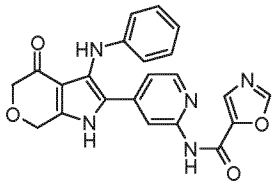


A solution of 1,3-thiazole-4-carboxylic acid (24 mg, 0.19 mmol) and HATU (71 mg, 0,19 mmol) in DMA (1 mL) was added to a mixture of 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.16 mmol) and DIPEA (236 µL, 1.36 mmol) in DMA (1 mL) and stirred for 2.5 days at RT. The mixture concentrated and purified by preparative HPLC (basic method) to give the title compound (5 mg, 7%).

^{1}H-NMR (400 MHz, CD_3OD), δ [ppm]= 4.15 (2H), 4.95 (2H), 6.65-6.77 (3H), 7.07 (2H), 7.28 (1H), 8.11 (1H), 8.43 (1H), 8.48 (1H), 9.10 (1H)

Example 50

N-{4-[4-Oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}-1,3-oxazole-5-carboxamide

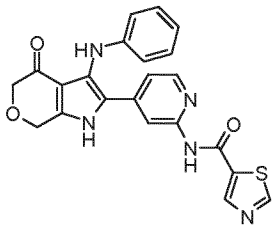


A solution of 1,3-oxazole-5-carboxylic acid (21 mg, 0.19 mmol) and HATU (71 mg, 0,19 mmol) in DMA (1 mL) was added to a mixture of 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.16 mmol) and DIPEA (236 µL, 1.36 mmol) in DMA (1 mL) and stirred for 18 h at RT. The mixture was concentrated and purified by Biotage (SNAP NH 25g, EtOAc:Hexane; MeOH:DCM) to give the title compound (2 mg, 3%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.05 (2H), 4.90 (2H), 6.60 (3H), 7.04 (2H), 7.36 (1H), 7.50 (1H), 8.22 (1H), 8.25 (1H), 8.35 (1H), 8.66 (1H), 10.95 (1H), 12.22 (1H)

Example 51

N-{4-[4-Oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}-1,3-thiazole-5-carboxamide

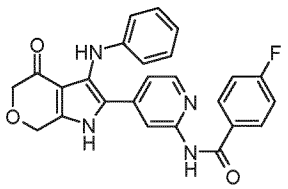


A solution of 1,3-thiazole-5-carboxylic acid (24 mg, 0.19 mmol) and HATU (71 mg, 0,19 mmol) in DMA (1 mL) was added to a mixture of 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.16 mmol) and DIPEA (236 µL, 1.36 mmol) in DMA (1 mL) and stirred for 2.5 days at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (6 mg, 8%).

^{1}H-NMR (400 MHz, CD_2Cl_2), δ [ppm]= 4.19 (2H), 4.92 (2H), 6.72 (2H), 6.80 (2H), 7.07 (1H), 7.13 (2H), 8.02 (1H), 8.25 (1H), 8.50 (1H), 9.03 (2H), 10.14 (1H)

Example 52

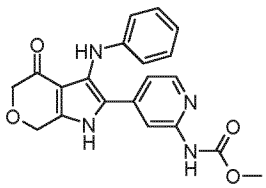
4-Fluoro-N-{4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}benzamide



A solution of 4-fluorobenzoic acid (52 mg, 0.31 mmol) and HATU (142 mg, 0,38 mmol) in DMA (2 mL) was added to a mixture of 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 100 mg, 0.31 mmol) and DIPEA (472 µL, 2.71 mmol) in DMA (2 mL) and stirred for 2.5 days at RT. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (6 mg, 4%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.04 (2H), 4.89 (2H), 6.58-6.63 (3H), 7.04 (2H), 7.32-7.39 (3H), 7.48 (1H), 8.02-8.14 (2H), 8.23 (1H), 8.39 (1H), 10.78 (1H), 12.23 (1H)

Example 53

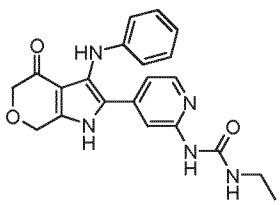
Methyl {4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}carbamate



To a mixture of 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.14 mmol) in pyridine (196 µL) and THF (3.8 mL) was added methyl carbonochloridate (54 µL, 1.41 mmol) and stirred for 16 h at 40℃. Methanol was added and the mixture concentrated and purified by Biotage (SNAP NH 25g, MeOH:DCM) and preparative TLC (silica, MeOH:DCM) to give the title compound (11 mg, 19%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.66 (3H), 4.03 (2H), 4.88 (2H), 6.56-6.62 (3H), 7.03 (2H), 7.23 (1H), 7.42 (1H), 8.04 (1H), 8.10 (1H), 10.05 (1H), 12.14 (1H)

Example 54

1-Ethyl-3-{4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}urea

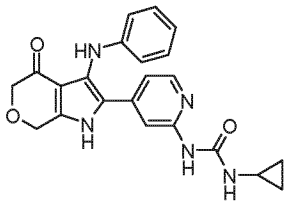


To a mixture of 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.14 mmol) in pyridine (1 mL) was added isocyanatoethane (55 µL, 0.70 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by Biotage (SNAP NH 25g, MeOH:DCM) and preparative TLC (silica, MeOH:DCM) to give the title compound (22 mg, 38%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.07 (3H), 3.16 (2H), 4.02 (2H), 4.86 (2H), 6.54-6.61 (3H), 7.01 (2H), 7.08 (1H), 7.35 (1H), 7.57 (1H), 7.88 (1H), 8.01 (1H), 9.07 (1H), 12.04 (1H)

Example 55

1-Cyclopropyl-3-{4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl}urea

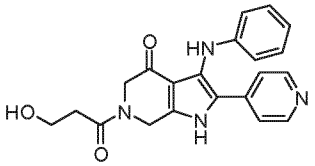


To a mixture of 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.14 mmol) in pyridine (1 mL) was added isocyanatocyclopropane (33 µL, 0.42 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by Biotage (SNAP NH 25g, MeOH:DCM) and preparative TLC (silica, EtOH:DCM) to give the title compound (20 mg, 33%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.43 (2H), 0.66 (2H), 2.58 (1H), 4.01 (2H), 4.84 (2H), 6.55-6.61 (3H), 7.02 (2H), 7.10 (1H), 7.34 (1H), 7.65 (1H), 7.99 (1H), 8.07 (1H), 9.01 (1H), 12.12 (1H)

Example 56

6-(3-Hydroxypropanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



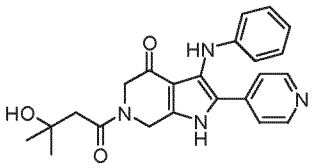
A solution of 3-[(2RS)-tetrahydro-2H-pyran-2-yloxy]propanoic acid (86 mg, 0.49 mmol) and HATU (187 mg, 0.49 mmol) in DMA (1 mL) was added to a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50

mg, 0.16 mmol) and DIPEA (85 µL, 0.49 mmol) in DMA (1 mL) and stirred for 16h at 50℃. The mixture was concentrated, THF (5mL), Methanol (2mL) and hydrochloric acid (1 mL, 4M in dioxane) were added and stirred for 1h at RT. Ammonia (25% in water) was added, the mixture was concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (7 mg, 11%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.55+2.64 (2H), 3.60-3.71 (2H), 4.14+4.10 (2H), 4.56+4.63 (1H), 4.85-4.91 (2H), 6.56-6.64 (3H), 7.05 (2H), 7.48-7.55 (3H), 8.46 (2H), 12.25 (1H)

Example 57

6-(3-Hydroxy-3-methylbutanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

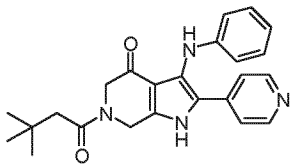


A solution of 3-hydroxy-3-methylbutanoic acid (39 mg, 0.33 mmol) and HATU (125 mg, 0,33 mmol) in DMA (1 mL) was added to a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) and DIPEA (57 µL, 0.33 mmol) in DMA (1 mL) and stirred for 16 h at RT. The mixture was concentrated and purified by Biotage (SNAP NH 25g, MeOH:DCM) and digestion with DCM to give the title compound (48 mg, 68%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.17+1.21 (6H), 2.52+2.60 (2H), 4.17+4.25 (2H), 4.67+4.76 (1H), 4.90+4.97 (2H), 6.55-6.65 (3H), 7.04 (2H), 7.48-7.54 (3H), 8.46 (2H), 12.24 (1H)

Example 58

6-(3,3-Dimethylbutanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



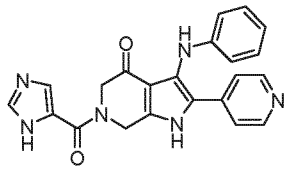
To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) in pyridine (2 mL) was added 3,3-dimethylbutanoyl chloride (46 µL, 0.33 mmol) and stirred for 2 h at RT. Methanol was added and the

mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (36 mg, 52%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.96+1.00 (9H), 2.32+2.39 (2H), 4.15+4.19 (2H), 4.87+4.89 (2H), 6.55-6.63 (3H), 7.00-7.06 (2H), 7.46-7.54 (3H), 8.42-8.47 (2H), 12.24 (1H)

Example 59

6-(1H-Imidazol-5-ylcarbonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

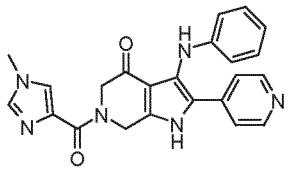


A solution of 1H-imidazole-5-carboxylic acid (37 mg, 0.33 mmol) and HATU (125 mg, 0,33 mmol) in DMA (1 mL) was added to a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) and DIPEA (57 µL, 0.33 mmol) in DMA (1 mL) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and recrystallization from methanol to give the title compound (21 mg, 31%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.29 (1H), 5.04 (2H), 5.61 (1H), 6.55-6.64 (3H), 7.04 (2H), 7.46-7.55 (3H), 7.72 (1H), 7.84 (1H), 8.45 (2H), 12.33 (1H), 12.60 (1H)

Example 60

6-[(1-Methyl-1H-imidazol-4-yl)carbonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

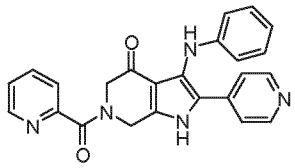


A solution of 1-methyl-1H-imidazole-4-carboxylic acid (41 mg, 0.33 mmol) and HATU (125 mg, 0,33 mmol) in DMA (1 mL) was added to a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) and DIPEA (57 µL, 0.33 mmol) in DMA (1 mL) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (24 mg, 34%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.70 (3H), 4.26 (1H), 5.01 (2H), 5.77 (1H), 6.55-6.68 (3H), 7.04 (2H), 7.46-7.59 (3H), 7.74 (2H), 8.44 (2H), 12.29 (1H)

Example 61

3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-2-ylcarbonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

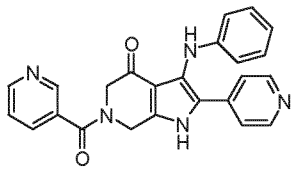


A solution of pyridine-2-carboxylic acid (40 mg, 0.33 mmol) and HATU (125 mg, 0,33 mmol) in DMA (1 mL) was added to a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) and DIPEA (57 µL, 0.33 mmol) in DMA (1 mL) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (26 mg, 36%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.15+4.37 (2H), 4.95+5.09 (2H), 6.57-6.65 (3H), 7.05 (2H), 7.46 (1H), 7.49-7.60 (3H), 7.64+7.71 (1H), 7.97+8.01 (1H), 8.42+8.47 (2H), 8.61+8.70 (1H), 12.22 (1H)

Example 62

3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-3-ylcarbonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

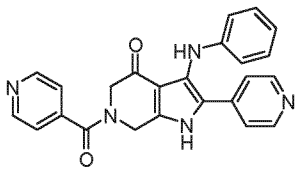


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) in pyridine (2 mL) was added nicotinoyl chloride hydrochloride (58 mg, 0.33 mmol) and stirred for 16 h at RT an 4h at 100℃. Methanol was added and the mixture concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (10 mg, 14%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.03+4.35 (2H), 4.80+5.08 (2H), 6.57-6.65 (3H), 7.05 (2H), 7.45 (1H), 7.48-7.58 (3H), 7.85+7.96 (1H), 8.38-8.50 (2H), 8.59-8.76 (2H), 12.21 (1H)

Example 63

3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-4-ylcarbonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

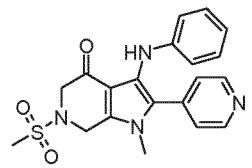


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) in pyridine (2 mL) was added isonicotinoyl chloride hydrochloride (58 mg, 0.33 mmol) and stirred for 16 h at RT. Methanol was added and the mixture concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (36 mg, 51%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.97+4.35 (2H), 4.73+5.08 (2H), 6.56-6.66 (3H), 7.01-7.09 (2H), 7.40+7.44 (2H), 7.48-7.55 (3H), 8.43+8.48 (2H), 8.70+8.76 (2H), 12.19 (1H)

Example 64

1-Methyl-6-(methylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

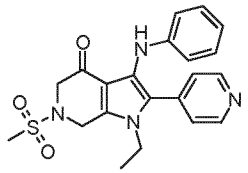


To a mixture of 6-(methylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (19; 50 mg, 0.13 mmol) in DMA (2 mL) was added cesium carbonate (170 mg, 0.52 mmol), iodomethane (28 mg, 0.20 mmol) and stirred for 16 h at RT. The mixture was filtered, concentrated and purified by preparative HPLC (Method: PrepCon Chromatorex RP C-18 10_m; 125*30mm Solvent A: water + 0.2% Vol. NH_3 (30%), Solvent B: Acetonitrile) and preparative TLC (NH_2-Phase, MeOH:DCM) to give the title compound (10 mg, 18%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.89 (3H), 3.75 (2H), 3.91 (3H), 4.34 (2H), 6.65-6.73 (3H), 7.11 (2H), 7.67 (2H), 7.82 (1H), 8.16 (2H)

Example 65

1-Ethyl-6-(methylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

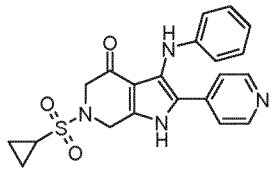


To a mixture of 6-(methylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (19; 50 mg, 0.13 mmol) in DMA (1.5 mL) was added cesium carbonate (170 mg, 0.52 mmol), iodoethane (31 mg, 0.20 mmol) and stirred for 16 h at RT. The mixture was filtered, concentrated and purified by preparative HPLC (Method: PrepCon Chromatorex RP C-18 10_m; 125*30mm Solvent A: water + 0.2% Vol. NH_3 (30%), Solvent B: Acetonitrile) and preparative TLC (NH_2-Phase, MeOH:DCM) to give the title compound (11 mg, 20%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.38 (3H), 2.89 (3H), 3.75 (2H), 4.18 (2H), 4.35 (2H), 6.60-6.73 (3H), 7.11 (2H), 7.67 (2H), 7.82 (1H), 8.26 (2H)

Example 66

6-(Cyclopropylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

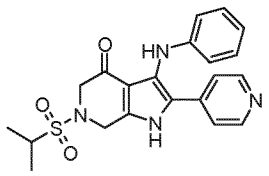


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added cyclopropanesulfonyl chloride (28 mg, 0.20 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (28 mg, 67%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.87-0.94 (4H), 2.48 (1H), 3.93 (2H), 4.74 (2H), 6.56-6.64 (3H), 7.04 (2H), 7.49-7.55 (3H), 8.46 (2H), 12.28 (1H)

Example 67

3-(phenylamino)-6-(propan-2-ylsulfonyl)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

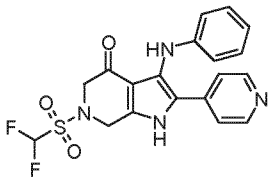


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added propane-2-sulfonyl chloride (28 mg, 0.20 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (25 mg, 59%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.22 (6H), 3.42 (1H), 3.95 (2H), 4.73 (2H), 6.55-6.64 (3H), 7.04 (2H), 7.49-7.55 (3H), 8.46 (2H), 12.25 (1H)

Example 68

6-[(Difluoromethyl)sulfonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

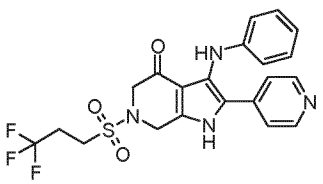


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added difluoromethanesulfonyl chloride (30 mg, 0.20 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (12 mg, 27%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.08 (2H), 4.87 (2H), 6.55-6.65 (3H), 7.04 (2H), 7.23 (1H), 7.52 (2H), -7.55 (1H), 8.48 (2H), 12.28 (1H)

Example 69

3-(phenylamino)-2-(pyridin-4-yl)-6-[(3,3,3-trifluoropropyl)sulfonyl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

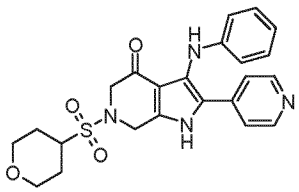


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 40 mg, 0.13 mmol) in pyridine (1.4 mL) was added 3,3,3-trifluoropropane-1-sulfonyl chloride (52 mg, 0.26 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) and digestion with methanol to give the title compound (16 mg, 25%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.74 (2H), 3.50 (2H), 3.98 (2H), 4.74 (2H), 6.58 (2H), 6.62 (1H), 7.04 (2H), 7.50-7.57 (3H), 8.47 (2H), 12.30 (1H)

Example 70

3-(phenylamino)-2-(pyridin-4-yl)-6-(tetrahydro-2H-pyran-4-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

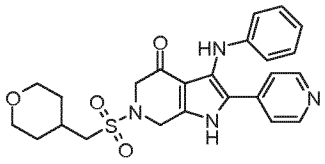


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added tetrahydro-2H-pyran-4-sulfonyl chloride (36 mg, 0.20 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (20 mg, 43%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.61 (2H), 1.84 (2H), 3.29 (2H), 3.56 (1H), 3.91 (2H), 3.95 (2H), 4.73 (2H), 6.57 (2H), 6.62 (1H), 7.04 (2H), 7.46-7.55 (3H), 8.46 (2H), 12.26 (1H)

Example 71

3-(phenylamino)-2-(pyridin-4-yl)-6-[(tetrahydro-2H-pyran-4-ylmethyl)sulfonyl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



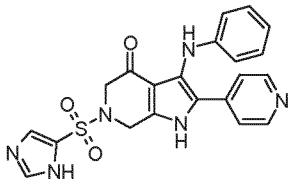
To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added tetrahydro-2H-pyran-4-ylmethanesulfonyl chloride (39 mg, 0.20 mmol) and stirred for 2 h at RT. Methanol was

added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (27 mg, 53%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.31 (2H), 1.71 (2H), 2.03 (1H), 3.09 (2H), 3.20-3.30 (2H), 3.80 (2H), 3.92 (2H), 4.68 (2H), 6.58 (2H), 6.62 (1H), 7.04 (2H), 7.46-7.58 (3H), 8.47 (2H), 12.28 (1H)

Example 72

6-(1H-Imidazol-5-ylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

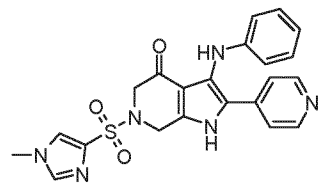


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added 1H-imidazole-5-sulfonyl chloride (149 mg, 0.89 mmol) and stirred for 4 days at RT. Methanol was added and the mixture concentrated and purified by preparative HPLC (Method: PrepCon Chromatorex RP C-18 10_m; 125*30mm Solvent A: water + 0.2% Vol. NH_3 (30%), Solvent B: Acetonitrile) to give the title compound (12 mg, 27%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.83 (2H), 4.69 (2H), 6.47 (2H), 6.61 (1H), 7.05 (2H), 7.40 (1H), 7.47 (2H), 7.75 (1H), 7.82 (1H), 8.46 (2H), 12.44 (2H)

Example 73

6-[(1-Methyl-1H-imidazol-4-yl)sulfonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

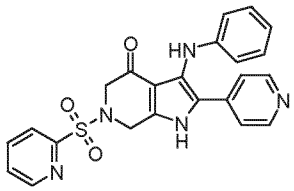


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added 1-methyl-1H-imidazole-4-sulfonyl chloride (36 mg, 0.20 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (16 mg, 33%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.57 (3H), 3.80 (2H), 4.65 (2H), 6.51 (2H), 6.62 (1H), 7.06 (2H), 7.38 (1H), 7.47 (2H), 7.71 (1H), 7.83 (1H), 8.44 (2H), 12.17 (1H)

Example 74

3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-2-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

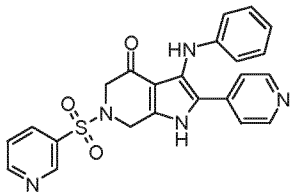


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 40 mg, 0.13 mmol) in pyridine (1 mL) was added pyridine-2-sulfonyl chloride (47 mg, 0.26 mmol) and stirred for 16 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (40 mg, 66%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.02 (2H), 4.88 (2H), 6.36 (2H), 6.61 (1H), 7.03 (2H), 7.33 (1H), 7.43 (2H), 7.59 (1H), 7.89 (1H), 8.02 (1H), 8.45 (2H), 8.50 (1H), 12.16 (1H)

Example 75

3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-3-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

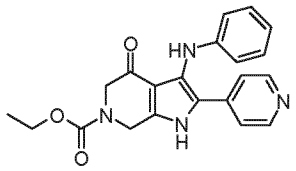


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added pyridine-3-sulfonyl chloride hydrochloride (42 mg, 0.20 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (20 mg, 44%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.97 (2H), 4.78 (2H), 6.34 (2H), 6.61 (1H), 7.03 (2H), 7.32 (1H), 7.43 (2H), 7.55 (1H), 8.11 (1H), 8.44 (2H), 8.78 (1H), 8.87 (1H), 12.18 (1H)

Example 76

Ethyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

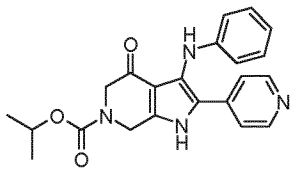


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added ethyl carbonochloridate (21 mg, 0.20 mmol) and stirred for 2 h at RT. Methanol was added, the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (25 mg, 63%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.22 (3H), 4.06 (2H), 4.11 (2H), 4.80 (2H), 6.58 (2H), 6.62 (1H), 7.05 (2H), 7.46-7.57 (3H), 8.46 (2H), 12.25 (1H)

Example 77

Propan-2-yl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

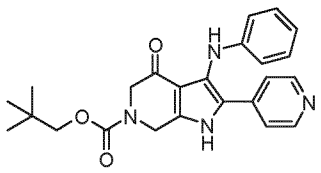


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added isopropyl carbonochloridate (24 mg, 0.20 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (12 mg, 28%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.22 (6H), 4.04 (2H), 4.79 (2H), 4.83 (1H), 6.58 (2H), 6.62 (1H), 7.04 (2H), 7.47-7.54 (3H), 8.46 (2H), 12.23 (1H)

Example 78

2,2-Dimethylpropyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

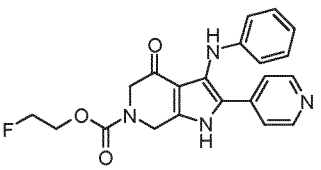


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added 2,2-dimethylpropyl carbonochloridate (30 mg, 0.20 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (23 mg, 53%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.90+0.94 (9H), 3.78 (2H), 4.04+4.10 (2H), 4.80+4.86 (2H), 6.57 (2H), 6.62 (1H), 7.04 (2H), 7.45-7.55 (3H), 8.46 (2H), 12.24 (1H)

Example 79

2-Fluoroethyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

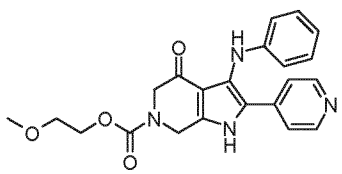


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added 2-fluoroethyl carbonochloridate (25 mg, 0.20 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (12 mg, 30%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.07+4.10 (2H), 4.28+4.36 (2H), 4.58+4.70 (2H), 4.81+4.86 (2H), 6.58 (2H), 6.62 (1H), 7.05 (2H), 7.46-7.55 (3H), 8.46 (2H), 12.25 (1H)

Example 80

2-Methoxyethyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



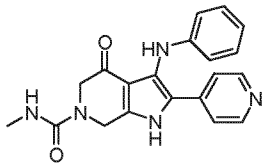
To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added 2-methoxyethyl

carbonochloridate (27 mg, 0.20 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (19 mg, 46%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.28 (3H), 3.55 (2H), 4.07 (2H), 4.19 (2H), 4.82 (2H), 6.58 (2H), 6.62 (1H), 7.05 (2H), 7.46-7.55 (3H), 8.47 (2H), 12.24 (1H)

Example 81

N-Methyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

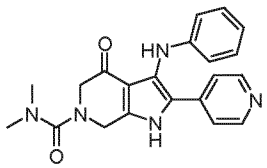


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) in pyridine (1.8 mL) was added methylcarbamic chloride (31 mg, 0.33 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and digestion with EtOH and diethylether to give the title compound (28 mg, 44%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.58 (3H), 3.99 (2H), 4.72 (2H), 6.57 (2H), 6.62 (1H), 6.81 (1H), 7.04 (2H), 7.47-7.53 (3H), 8.46 (2H), 12.18 (1H)

Example 82

N,N-Dimethyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

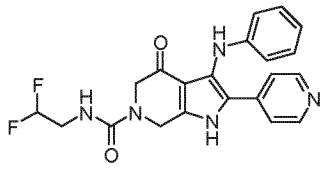


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) in pyridine (1.8 mL) was added dimethylcarbamic chloride (35 mg, 0.33 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and digestion with EtOH and diethylether to give the title compound (33 mg, 51%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.79 (6H), 3.79 (2H), 4.59 (2H), 6.57 (2H), 6.62 (1H), 7.04 (2H), 7.46-7.51 (3H), 8.45 (2H), 12.13 (1H)

Example 83

N-(2,2-Difluoroethyl)-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

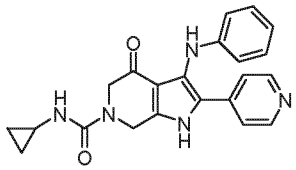


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added 1,1-difluoro-2-isocyanatoethane (21 mg, 0.20 mmol) and stirred for 2 days at RT. The mixture was concentrated and purified by crystallization from EtOH/DCM to give the title compound (37 mg, 87%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.43 (2H), 4.06 (2H), 4.76 (2H), 5.98 (1H), 6.58 (2H), 6.62 (1H), 7.04 (2H), 7.31 (1H), 7.48-7.54 (3H), 8.46 (2H), 12.20 (1H)

Example 84

N-Cyclopropyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

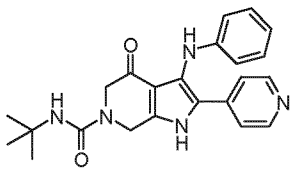


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added isocyanatocyclopropane (16 mg, 0.20 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by crystallization from EtOH/DCM to give the title compound (28 mg, 70%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.38 (2H), 0.55 (2H), 2.54 (1H), 3.98 (2H), 4.70 (2H), 6.57 (2H), 6.62 (1H), 6.95 (1H), 7.04 (2H), 7.48 (1H), 7.51 (2H), 8.45 (2H), 12.17 (1H)

Example 85

N-tert-Butyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

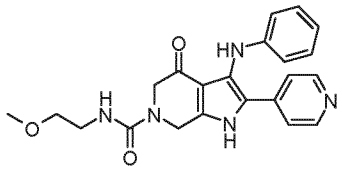


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added 2-isocyanato-2-methylpropane (20 mg, 0.20 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by crystallization from EtOH/DCM to give the title compound (37 mg, 87%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.25 (9H), 4.00 (2H), 4.68 (2H), 6.21 (1H), 6.58 (2H), 6.62 (1H), 7.04 (2H), 7.48 (1H), 7.52 (2H), 8.45 (2H), 12.17 (1H)

Example 86

N-(2-Methoxyethyl)-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

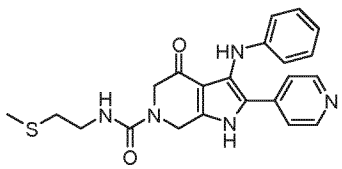


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added 2-isocyanatoethyl methyl ether (20 mg, 0.20 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by crystallization from EtOH/DCM to give the title compound (36 mg, 86%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.19 (2H), 3.22 (3H), 3.33 (2H), 4.01 (2H), 4.72 (2H), 6.58 (2H), 6.62 (1H), 6.94 (1H), 7.04 (2H), 7.49 (1H), 7.52 (2H), 8.46 (2H), 12.18 (1H)

Example 87

N-[2-(Methylsulfanyl)ethyl]-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide



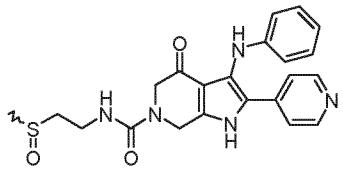
To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) in pyridine (1.7 mL) was added 2-isocyanatoethyl

methyl sulfide (38 mg, 0.33 mmol) and stirred for 2.5 days at RT. The mixture was concentrated and purified by crystallization from MeOH/DCM to give the title compound (69 mg, 90%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.05 (3H), 2.53 (2H), 3.22 (2H), 4.01 (2H), 4.73 (2H), 6.58 (2H), 6.62 (1H), 7.01-7.08 (3H), 7.48 (1H), 7.52 (2H), 8.46 (2H), 12.18 (1H)

Example 88

N-{2-[(RS)-Methylsulfinyl]ethyl}-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

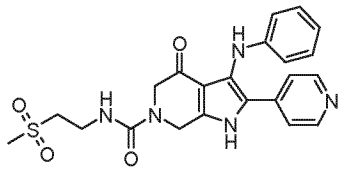


To a mixture of N-[2-(methylsulfanyl)ethyl]-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide (87; 25 mg, 0.06 mmol) in DCM (2 mL) was added mCPBA (19 mg, 0.18 mmol) and stirred for 16 h at RT. TEA (0.2 mL) was added, the mixture concentrated and purified by preparative HPLC (basic method)and preparative TLC (silica, MeOH:DCM) to give the title compound (3 mg, 8%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.54 (3H), 2.77 (1H), 2.93 (1H), 3.38-3.47 (2H), 3.99 (2H), 4.71 (2H), 6.57 (2H), 6.61 (1H), 7.04 (2H), 7.17 (1H), 7.45 (1H), 7.52 (2H), 8.42 (2H), 12.38 (1H)

Example 89

N-[2-(Methylsulfonyl)ethyl]-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

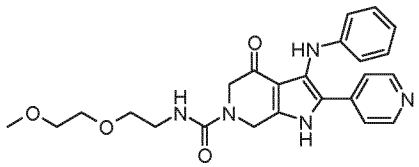


To a mixture of N-[2-(methylsulfanyl)ethyl]-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide (87; 25 mg, 0.06 mmol) in DMA (2 mL) was added mCPBA (19 mg, 0.18 mmol) and stirred for 4 h at RT. TEA (0.2 mL) was added, the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) and preparative TLC (NH_2-Phase, MeOH:DCM) to give the title compound (10 mg, 35%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.97 (3H), 3.25 (2H), 3.45 (2H), 3.99 (2H), 4.71 (2H), 6.57 (2H), 6.61 (1H), 7.04 (2H), 7.14 (1H), 7.45 (1H), 7.53 (2H), 8.43 (2H), 12.27 (1H)

Example 90

N-[2-(2-Methoxyethoxy)ethyl]-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

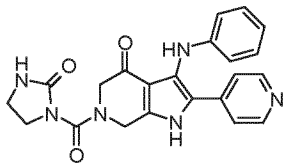


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added 1-isocyanato-2-(2-methoxyethoxy)ethane (29 mg, 0.20 mmol) and stirred for 2.5 days at RT. The mixture was concentrated and purified by crystallization from MeOH/DCM to give the title compound (34 mg, 74%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.18 (2H), 3.22 (3H), 3.38-3.43 (4H), 3.47-3.50 (2H), 4.01 (2H), 4.72 (2H), 6.58 (2H), 6.62 (1H), 6.93 (1H), 7.04 (2H), 7.48 (1H), 7.51 (2H), 8.46 (2H), 12.18 (1H)

Example 91

6-[(2-Oxoimidazolidin-1-yl)carbonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

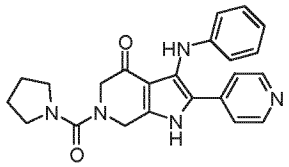


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) in pyridine (1.8 mL) was added 2-oxoimidazolidine-1-carbonyl chloride (49 mg, 0.33 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and digestion with ethanol/diethylether to give the title compound (32 mg, 44%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.32 (2H), 3.66 (2H), 4.10 (2H), 4.86 (2H), 6.59 (2H), 6.62 (1H), 7.05 (2H), 7.44 (1H), 7.49 (2H), 7.51 (1H), 8.46 (2H), 12.18 (1H)

Example 92

3-(phenylamino)-2-(pyridin-4-yl)-6-(pyrrolidin-1-ylcarbonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

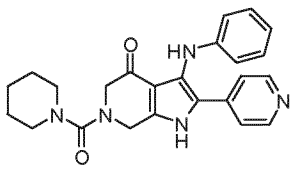


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) in pyridine (1.8 mL) was added pyrrolidine-1-carbonyl chloride (44 mg, 0.33 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (25 mg, 36%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.78 (4H), 3.30 (4H), 3.84 (2H), 4.63 (2H), 6.57 (2H), 6.62 (1H), 7.04 (2H), 7.44-7.53 (3H), 8.45 (2H), 12.13 (1H)

Example 93

3-(phenylamino)-6-(piperidin-1-ylcarbonyl)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

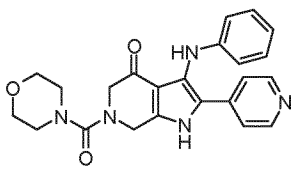


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) in pyridine (1.8 mL) was added piperidine-1-carbonyl chloride (48 mg, 0.33 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and digestion with ethanol/diethylether to give the title compound (20 mg, 28%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.45-1.61 (6H), 3.13-3.21 (4H), 3.80 (2H), 4.60 (2H), 6.57 (2H), 6.62 (1H), 7.04 (2H), 7.45-7.53 (3H), 8.45 (2H), 12.13 (1H)

Example 94

6-(Morpholin-4-ylcarbonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

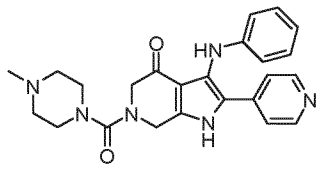


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) in pyridine (1.8 mL) was added morpholine-4-carbonyl chloride (49 mg, 0.33 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and digestion with ethanol/diethylether to give the title compound (38 mg, 52%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.20 (4H), 3.60 (4H), 3.85 (2H), 4.64 (2H), 6.57 (2H), 6.62 (1H), 7.04 (2H), 7.47-7.52 (3H), 8.46 (2H), 12.16 (1H)

Example 95

6-[(4-Methylpiperazin-1-yl)carbonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

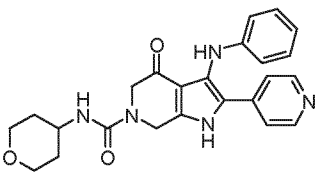


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) in pyridine (1.8 mL) was added 4-methylpiperazine-1-carbonyl chloride (53 mg, 0.33 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (29 mg, 38%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.19 (3H), 2.31 (4H), 3.20 (4H), 3.82 (2H), 4.62 (2H), 6.57 (2H), 6.62 (1H), 7.04 (2H), 7.46-7.52 (3H), 8.45 (2H), 12.15 (1H)

Example 96

4-Oxo-3-(phenylamino)-2-(pyridin-4-yl)-N-(tetrahydro-2H-pyran-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

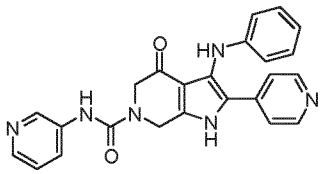


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added 4-isocyanatotetrahydro-2H-pyran (127 µL, 0.20 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by crystallization from MeOH/DCM to give the title compound (38 mg, 84%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.45 (2H), 1.67 (2H), 3.30 (2H), 3.64 (1H), 3.82 (2H), 4.04 (2H), 4.72 (2H), 6.58 (2H), 6.61 (1H), 6.68 (1H), 7.04 (2H), 7.49 (1H), 7.51 (2H), 8.46 (2H), 12.17 (1H)

Example 97

4-Oxo-3-(phenylamino)-N-(pyridin-3-yl)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

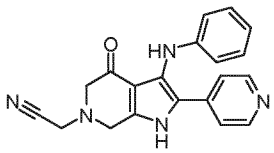


To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 30 mg, 0.10 mmol) in pyridine (1 mL) was added 3-isocyanatopyridine (24 mg, 0.20 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by crystallization from MeOH/DCM to give the title compound (38 mg, 84%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.24 (2H), 4.88 (2H), 6.60 (2H), 6.62 (1H), 7.05 (2H), 7.29 (1H), 7.51 (1H), 7.53 (2H), 7.87 (1H), 8.19 (1H), 8.47 (2H), 8.64 (1H), 9.09 (1H), 12.27 (1H)

Example 98

[4-Oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridin-6-yl]acetonitrile



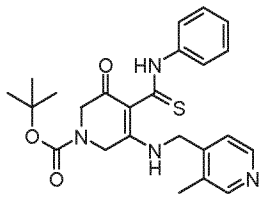
To a solution of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 150 mg, 0.49 mmol) in ACN (12 mL) were added potassium iodide (245 mg, 1.48 mmol), potassium carbonate (204 mg, 1.48 mmol) chloroacetonitrile (93 µL, 1.48 mmol) and the mixture was stirred for 1.5 h at 100℃. The mixture was filtered, concentrated and purified by Biotage (SNAP NH 25g, MeOH:DCM) to give the title compound (124 mg, 73%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.21 (2H), 3.90 (2H), 4.03 (2H), 6.58 (2H), 6.61 (1H), 7.04 (2H), 7.49 (1H), 7.52 (2H), 8.46 (2H), 12.20 (1H)

Example 99

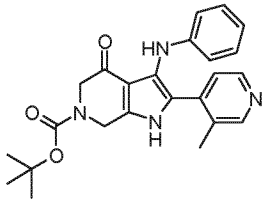
tert-Butyl 2-(3-methylpyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

99-1: tert-Butyl 5-{[(3-methylpyridin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 250 mg, 0.72 mmol), DIPEA (0.5 mL, 2.87 mmol) and 1-(3-methylpyridin-4-yl)methanamine dihydrochloride (280 mg, 1.44 mmol) in DMA (2.2 mL) was heated at 120℃ for 2h. The mixture was concent rated and purified by Biotage (SNAP NH 25g, EtOAc:Hexane) to give the title compound (180 mg, 55%).

tert-Butyl 2-(3-methylpyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



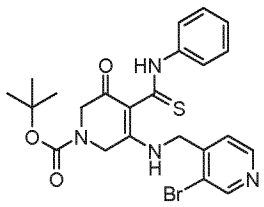
A solution of tert-butyl 5-{[(3-methylpyridin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (99-1; 175 mg, 0.39 mmol) in EtOH (7 mL) was added SIBX (241 mg, 0.39 mmol) and stirred at RT for 16 h. The mixture was concentrated and purified by Biotage (SNAP NH 28g, EtOH:DCM) and preparative TLC (silica, MeOH:DCM) to give the title compound (21 mg, 12%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.44 (9H), 2.19 (3H), 4.02 (2H), 4.72 (2H), 6.48-6.54 (3H), 6.92 (2H), 7.24 (1H), 7.36 (1H), 8.34 (1H), 8.37 (1H), 11.82 (1H)

Example 100

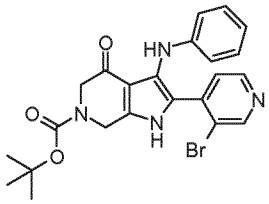
tert-Butyl 2-(3-bromopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

100-1: tert-Butyl 5-{[(3-bromopyridin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-Butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 300 mg, 0.86 mmol) and 1-(3-bromopyridin-4-yl)methanamine (322 mg, 1.72 mmol) in DMA (2.6 mL) was heated at 120℃ for 1.5 h. The mixture was concentrated and purified by Biotage (SNAP NH 25g, EtOAc:Hexane) to give the title compound (386 mg, 87%).

tert-Butyl 2-(3-bromopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

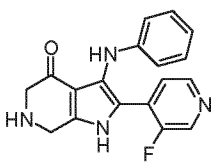


A solution of tert-butyl 5-{[(3-bromopyridin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (100-1; 330 mg, 0.64 mmol) in DMA (13 mL) and TFA (49 µL) was added 10% Pd/C (679 mg, 0.64 mmol) and heated at 120℃ for 16h. TEA was added (100 µL), the mixtu re was filtered and concentrated. The residue was purified by Biotage (SNAP NH 28g, EtOH:DCM) and preparative TLC (silica, EtOH:DCM) to give the title compound (11 mg, 3%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.44 (9H), 4.03 (2H), 4.71 (2H), 6.50-6.56 (3H), 6.93 (2H), 7.31 (1H), 7.40 (1H), 8.42 (1H), 8.72 (1H), 11.95 (1H)

Example 101

2-(3-Fluoropyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



To a solution of tert-Butyl 2-(3-fluoropyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (11; 105 mg, 0.25 mmol) in DCM (7

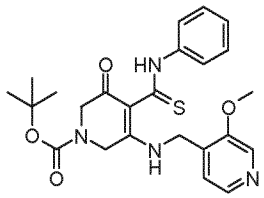
mL) was added TFA (383 µL) and the mixture was stirred at RT for 16h. TEA was added (800 µL) at 0℃, the mixture was concentrated and p urified by Biotage (SNAP NH 28g, EtOH:DCM) and preparative TLC (silica, MeOH:DCM) to give the title compound (9 mg, 11%).

^{1}H-NMR (400 MHz, CD_2Cl_2), δ [ppm]= 3.49 (2H), 4.14 (2H), 6.74 (2H), 6.84 (1H), 7.14 (2H), 7.20 (1H), 7.33 (1H), 8.11 (1H), 8.46 (1H), 9.08 (1H)

Example 102

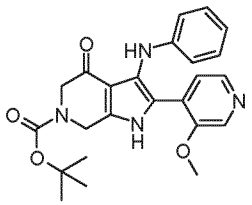
tert-Butyl 2-(3-methoxypyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

102-1: tert-Butyl 5-{[(3-methoxypyridin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-Butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 2.00 g, 5.74 mmol) and (3-methoxypyridin-4-yl)methanaminium chloride (2.01 g, 11.5 mmol) in DMA (15 mL) was heated at 85℃ for 2 h. The mixture was concentrated and purified by Biotage (SNAP NH 100g, EtOAc:Hexane) to give the title compound (2.10 g, 78%).

tert-Butyl 2-(3-methoxypyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

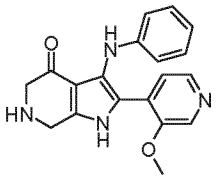


To a solution of tert-butyl 5-{[(3-methoxypyridin-4-yl)methyl]amino}-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (100-1; 2.10 g, 4.48 mmol) in EtOH (125 mL) was added SIBX (2.79 g, 0.4.48 mmol) and the mixture was stirred at RT for 40 h. The mixture was concentrated and purified by Biotage (SNAP NH 110g, EtOH:DCM) to give the title compound (532 mg, 27%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 3.93 (3H), 4.00 (2H), 4.75 (2H), 6.53 (2H), 6.58 (1H), 7.00 (2H), 7.38 (2H), 8.04 (1H), 8.38 (1H), 11.63 (1H)

Example 103

2-(3-Methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

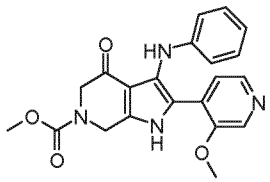


To a solution of tert-butyl 2-(3-methoxypyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (102; 528 mg, 1.22 mmol) in DCM (35 mL) was added TFA (1.87 mL) and the mixture was stirred at RT for 16h. The mixture was poured into saturated sodium hydrogenate solution, extracted with DCM/methanol and dried over sodium sulfate. After filtration and concentration the residue was purified by Biotage (SNAP NH 10g, MeOH:DCM), digestion with methanol and preparative TLC (silica, MeOH:DCM) to give the title compound (267 mg, 63%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.20 (3H), 3.91 (3H), 3.95 (2H), 6.55 (2H), 6.57 (1H), 6.99 (2H), 7.34 (2H), 8.02 (1H), 8.36 (1H), 11.34 (1H)

Example 104

Methyl 2-(3-methoxypyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

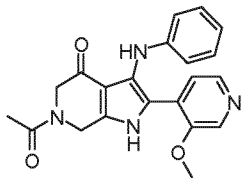


To a mixture of 2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (103; 30 mg, 0.09 mmol) in pyridine (1 mL) was added methyl carbonochloridate (14 µL, 0.18 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (22 mg, 60%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.67 (3H), 3.94 (3H), 4.05 (2H), 4.81 (2H), 6.54 (2H), 6.58 (1H), 7.00 (2H), 7.36-7.43 (2H), 8.05 (1H), 8.40 (1H), 11.63 (1H)

Example 105

6-Acetyl-2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

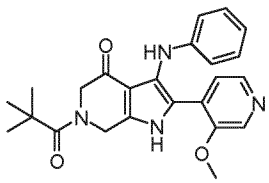


To a mixture of 2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (103; 30 mg, 0.09 mmol) in pyridine (1 mL) was added methyl acetyl chloride (13 µL, 0.18 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (13 mg, 37%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.09+2.16 (3H), 3.93+3.95 (3H), 4.12+4.14 (2H), 4.85+4.86 (2H), 6.55 (2H), 6.58 (1H), 7.00 (2H), 7.35-7.46 (2H), 8.05 (1H), 8.39 (1H), 11.64 (1H)

Example 106

6-(2,2-Dimethylpropanoyl)-2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

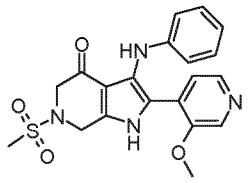


To a mixture of 2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (103; 30 mg, 0.09 mmol) in pyridine (1 mL) was added 2,2-dimethylpropanoyl chloride (22 µL, 0.18 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (22 mg, 55%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.23 (9H), 3.95 (3H), 4.23 (2H), 4.98 (2H), 6.53 (2H), 6.57 (1H), 6.99 (2H), 7.38-7.41 (2H), 8.05 (1H), 8.40 (1H), 11.62 (1H)

Example 107

2-(3-Methoxypyridin-4-yl)-6-(methylsulfonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

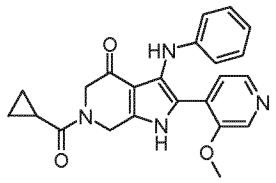


To a mixture of 2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (103; 30 mg, 0.09 mmol) in pyridine (1 mL) was added methanesulfonyl chloride (14 µL, 0.18 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative HPLC (basic method) and digestion with ethanol to give the title compound (15 mg, 38%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.01 (3H), 3.87 (2H), 3.94 (3H), 4.66 (2H), 6.54 (2H), 6.59 (1H), 7.01 (2H), 7.42 (2H), 8.07 (1H), 8.41 (1H), 11.70 (1H)

Example 108

6-(Cyclopropylcarbonyl)-2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

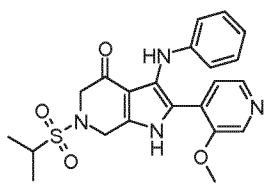


To a mixture of 2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (103; 30 mg, 0.09 mmol) in pyridine (1 mL) was added cyclopropanecarbonyl chloride (16 µL, 0.18 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (20 mg, 43%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.72-0.86 (4H), 1.97-2.12 (1H), 3.93+3.95 (3H), 4.16+4.39 (2H), 4.89+5.12 (2H), 6.55 (2H), 6.58 (1H), 7.00 (2H), 7.39 (2H), 8.05 (1H), 8.39 (1H), 11.67 (1H)

Example 109

2-(3-Methoxypyridin-4-yl)-3-(phenylamino)-6-(propan-2-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

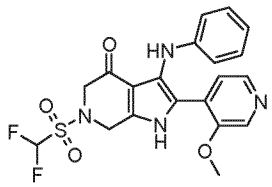


To a mixture of 2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (103; 30 mg, 0.09 mmol) in pyridine (1 mL) was added propane-2-sulfonyl chloride (20 µL, 0.18 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (24 mg, 57%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.23 (6H), 3.40 (1H), 3.91-4.00 (5H), 4.76 (2H), 6.55 (2H), 6.59 (1H), 7.01 (2H), 7.41-7.45 (2H), 8.05 (1H), 8.40 (1H), 11.63 (1H)

Example 110

6-[(Difluoromethyl)sulfonyl]-2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

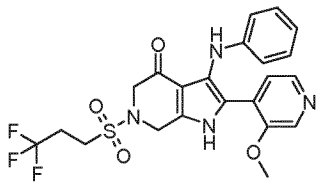


To a mixture of 2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (103; 30 mg, 0.09 mmol) in pyridine (1 mL) was added difluoromethanesulfonyl chloride (17 µL, 0.18 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (20 mg, 48%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.95 (3H), 4.08 (2H), 4.90 (2H), 6.55 (2H), 6.59 (1H), 7.01 (2H), 7.23 (1H), 7.42-7.47 (2H), 8.06 (1H), 8.41 (1H), 11.69 (1H)

Example 111

2-(3-Methoxypyridin-4-yl)-3-(phenylamino)-6-[(3,3,3-trifluoropropyl)sulfonyl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

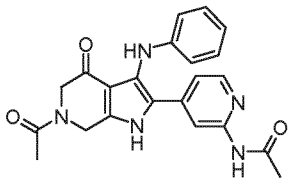


To a mixture of 2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (103; 30 mg, 0.09 mmol) in pyridine (1 mL) was added 3,3,3-trifluoropropane-1-sulfonyl chloride (24 µL, 0.18 mmol) and stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (30 mg, 65%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.74 (2H), 3.48 (2H), 3.94 (3H), 3.98 (2H), 4.76 (2H), 6.54 (2H), 6.59 (1H), 7.00 (2H), 7.39-7.45 (2H), 8.07 (1H), 8.41 (1H), 11.69 (1H)

Example 112

N-{4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

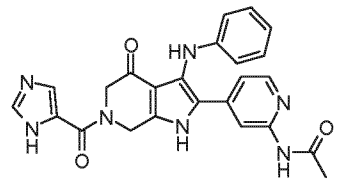


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 30 mg, 0.08 mmol) in pyridine (1 mL) was added methyl acetyl chloride (12 µL, 0.17 mmol) and stirred for 1 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (23 mg, 65%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08+2.16 (6H), 4.11+4.13 (2H), 4.83 (2H), 6.55-6.62 (3H), 7.02 (2H), 7.23 (1H), 7.41 (1H), 8.13 (1H), 8.29 (1H), 10.41 (1H), 12.24 (1H)

Example 113

N-{4-[6-(1H-Imidazol-5-ylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

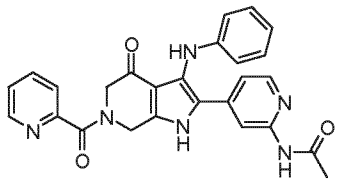


A solution of 1H-imidazole-5-carboxylic acid (29 mg, 0.26 mmol) and HATU (97 mg, 0,26 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 46 mg, 0.13 mmol) and DIPEA (44 µL, 0.26 mmol) in DMA (1 mL) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (19 mg, 32%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 4.26+5.00+5.77 (4H), 6.56 (2H), 6.59 (1H), 7.02 (2H), 7.22 (1H), 7.39 (1H), 7.70 (1H), 7.82 (1H), 8.11 (1H), 8.29 (1H), 10.37 (1H), 12.35 (1H), 12.63 (1H)

Example 114

N-{4-[4-Oxo-3-(phenylamino)-6-(pyridin-2-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

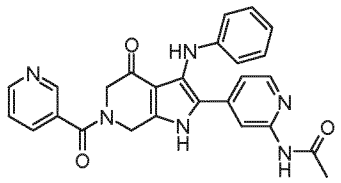


A solution of pyridine-2-carboxylic acid (31 mg, 0.26 mmol) and HATU (97 mg, 0,26 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 46 mg, 0.13 mmol) and DIPEA (44 µL, 0.26 mmol) in DMA (1 mL) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (24 mg, 38%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.06+2.09 (3H), 4.14+4.36 (2H), 4.93+5.09 (2H), 6.55-6.63 (3H), 7.03 (2H), 7.20+7.23 (1H), 7.42+7.45 (1H), 7.53+7.58 (1H), 7.64+7.69 (1H), 7.97+8.01 (1H), 8.10+8.14 (1H), 8.23+8.32 (1H), 8.61+8.70 (1H), 10.38+10.42 (1H), 12.10+12.33 (1H)

Example 115

N-{4-[4-Oxo-3-(phenylamino)-6-(pyridin-3-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

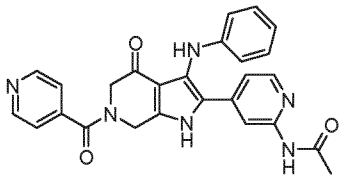


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 46 mg, 0.13 mmol) in pyridine (1.55 mL) was added nicotinoyl chloride hydrochloride (45 mg, 0.26 mmol) and stirred for 5 h at 100℃. Methanol was added and the mixture concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (9 mg, 14%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.06+2.08 (3H), 4.02+4.34 (2H), 4.80+5.07 (2H), 6.54-6.64 (3H), 7.03 (2H), 7.20 (1H), 7.42 (1H), 7.54 (1H), 7.85+7.96 (1H), 8.10+8.12 (1H), 8.22+8.32 (1H), 8.59-8.76 (2H), 10.37+10.40 (1H), 12.09+12.29 (1H)

Example 116

N-{4-[4-Oxo-3-(phenylamino)-6-(pyridin-4-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

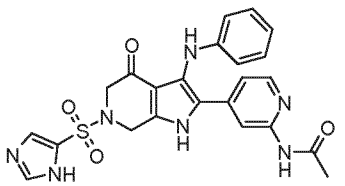


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 46 mg, 0.13 mmol) in pyridine (1.6 mL) was added isonicotinoyl chloride hydrochloride (45 mg, 0.26 mmol) and stirred for 16 h at RT. Methanol was added and the mixture concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (30 mg, 47%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.06+2.09 (3H), 3.95+4.33 (2H), 4.72+5.07 (2H), 6.55-6.63 (3H), 7.03 (2H), 7.19+7.23 (1H), 7.38-7.47 (2H), 7.50+7.51 (1H), 8.10+8.14 (1H), 8.21+8.31 (1H), 8.70+8.76 (2H), 10.38+10.42 (1H), 12.05+12.34 (1H)

Example 117

N-{4-[6-(1H-Imidazol-5-ylsulfonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

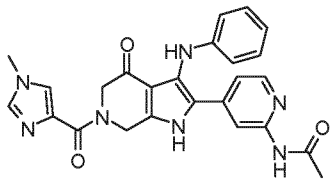


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) in pyridine (4 mL) was added 1H-imidazole-5-sulfonyl chloride (115 mg, 0.69 mmol) and stirred for 16 h at 60℃. Methanol was added and the mixture concentrated and purified by preparative HPLC (Method: PrepCon Chromatorex RP C-18 10_m; 125*30mm Solvent A: water + 0.2% Vol. NH3 (30%), Solvent B: Acetonitrile) and preparative TLC (silica, MeOH:DCM) to give the title compound (30 mg, 41%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 3.81 (2H), 4.67 (2H), 6.46 (2H), 6.59 (1H), 7.03 (2H), 7.19 (1H), 7.32 (1H), 7.75 (1H), 7.80 (1H), 8.12 (1H), 8.24 (1H), 10.40 (1H), 12.39 (2H)

Example 118

N-(4-{6-[(1-Methyl-1H-imidazol-4-yl)carbonyl]-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide

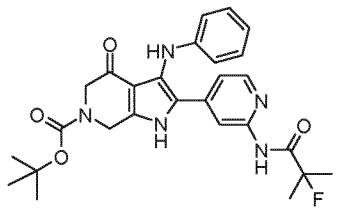


A solution of 1-methyl-1H-imidazole-4-carboxylic acid (32 mg, 0.26 mmol) and HATU (97 mg, 0,26 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 46 mg, 0.13 mmol) and DIPEA (44 µL, 0.26 mmol) in DMA (1 mL) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and digestion with methanol to give the title compound (35 mg, 55%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 3.70 (3H), 4.25+5.00+5.76 (4H), 6.55 (2H), 6.59 (1H), 7.01 (2H), 7.22 (1H), 7.39 (1H), 7.67-7.81 (2H), 8.11 (1H), 8.28 (1H), 10.38 (1H), 12.28 (1H)

Example 119

tert-Butyl 2-{2-[(2-fluoro-2-methylpropanoyl)amino]pyridin-4-yl}-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

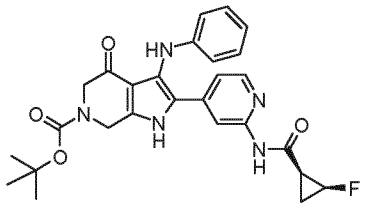


A solution of 2-fluoro-2-methylpropanoic acid (139 µL, 1.91 mmol) and HATU (725 mg, 1.91 mmol) in DMA (8 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 400 mg, 0.95 mmol) and DIPEA (332 µL, 1.91 mmol) in DMA (8 mL) and stirred for 16 h at 50℃. The mixture was concentrated and purified by Biotage (SNAP NH 25g, EtOAc:Hexane) and preparative TLC (silica, EtOH:DCM) to give the title compound (172 mg, 34%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 1.59 (6H), 4.01 (2H), 4.75 (2H), 6.57 (2H), 6.61 (1H), 7.03 (2H), 7.31 (1H), 7.47 (1H), 8.19 (1H), 8.21 (1H), 9.78 (1H), 12.28 (1H)

Example 120

tert-Butyl 2-[2-({[rel-(1S,2S)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



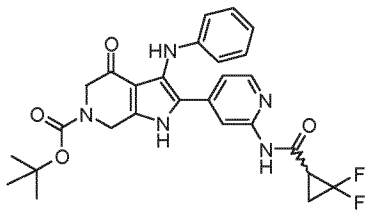
racemate

A solution of rel-(1R,2R)-2-fluorocyclopropanecarboxylic acid (298 mg, 2.86 mmol) and HATU (1.09 g, 2.86 mmol) in DMA (11 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 600 mg, 1.43 mmol) and DIPEA (498 µL, 2.86 mmol) in DMA (11 mL) and stirred for 40 h at 50℃. The mixture was conce ntrated and purified by Biotage (SNAP NH50, EtOAc:Hexane; EtOH: EtOAc) and preparative TLC (silica, EtOH:DCM) to give the title compound (215 mg, 28%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.19 (1H), 1.43 (9H), 1.65 (1H), 2.21 (1H), 4.00 (2H), 4.74 (2H), 4.86+5.02 (1H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.24 (1H), 7.43 (1H), 8.13 (1H), 8.31 (1H), 10.78 (1H), 12.25 (1H)

Example 121

tert-Butyl 2-[2-({[(1RS)-2,2-difluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

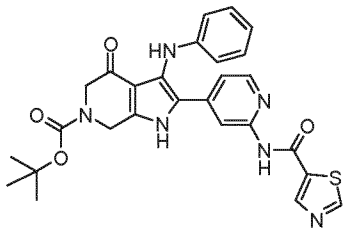


A solution of (1RS)-2,2-difluorocyclopropanecarboxylic acid (349 mg, 2.86 mmol) and HATU (1.09 g, 2.86 mmol) in DMA (11 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 600 mg, 1.43 mmol) and DIPEA (498 µL, 2.86 mmol) in DMA (11 mL) and stirred for 16 h at 50℃. The mixture was conce ntrated and purified by Biotage (SNAP NH 50g, EtOAc:Hexane)and preparative TLC (silica, EtOH:DCM) to give the title compound (261 mg, 33%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 2.02 (2H), 2.99 (1H), 4.00 (2H), 4.74 (2H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.27 (1H), 7.44 (1H), 8.16 (1H), 8.27 (1H), 10.94 (1H), 12.26 (1H)

Example 122

tert-Butyl 4-oxo-3-(phenylamino)-2-{2-[(1,3-thiazol-5-ylcarbonyl)amino]pyridin-4-yl}-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



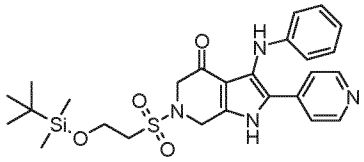
A solution of 1,3-thiazole-5-carboxylic acid (332 µL, 1.91 mmol) and HATU (725 mg, 1.91 mmol) in DMA (8 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 400 mg, 0.95 mmol) and DIPEA (332 µL, 1.91 mmol) in DMA (8 mL) and stirred for 16 h at 50°C. The mixture was concentrated and purified by Biotage (SNAP NH 25g, EtOH:DCM)and preparative TLC (silica, EtOH:DCM) to give the title compound (193 mg, 32%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 4.01 (2H), 4.76 (2H), 6.58 (2H), 6.61 (1H), 7.03 (2H), 7.33 (1H), 7.48 (1H), 8.24 (1H), 8.35 (1H), 8.89 (1H), 9.34 (1H), 11.16 (1H), 12.30 (1H)

Example 123

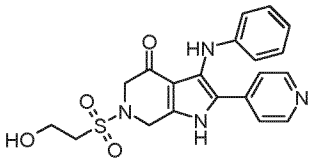
3-Anilino-6-[(2-hydroxyethyl)sulfonyl]-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

123-1: 3-Anilino-6-[(2-{[tert-butyl(dimethyl)silyl]oxy}ethyl)sulfonyl]-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



To a mixture of 3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (14; 50 mg, 0.16 mmol) in pyridine (3 mL) was added 2-{[tert-butyl(dimethyl)silyl]oxy}ethanesulfonyl chloride (723 µL, 3.26 mmol) and stirred for 16 h at RT. Methanol was added and the mixture concentrated to give the crude title compound that already contains some silylether cleavage product.

3-Anilino-6-[(2-hydroxyethyl)sulfonyl]-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

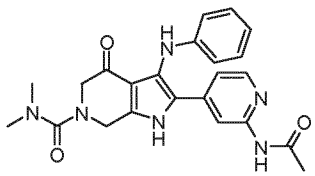


A solution of crude 3-anilino-6-[(2-{[tert-butyl(dimethyl)silyl]oxy}ethyl)sulfonyl]-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (123-1; max. 0.16 mmol) in THF (5 mL) and methanol (2 mL) was added hydrochloric acid (1 mL, 4M in dioxane) and the mixture was stirred for 1h at RT. Ammonia (25% in water) was added, the mixture was concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (7 mg, 10%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.32(2H), 3.76 (2H), 3.91 (2H), 4.68 (2H), 5.13 (1H), 6.58 (2H), 6.62 (1H), 7.05 (2H), 7.50-7.55 (3H), 8.48 (2H), 12.27 (1H)

Example 124

2-(2-Acetamidopyridin-4-yl)-3-anilino-N,N-dimethyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

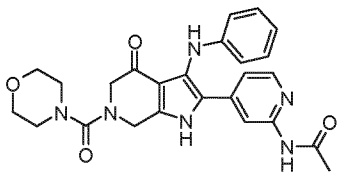


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) in pyridine (1.54 mL) was added dimethylcarbamic chloride (25 µL, 0.28 mmol) and the reaction was stirred for 4 h at 50℃. Methanol was added and the mixture was concentrated and purified by preparative HPLC (basic method) and digestion with diethylether to give the title compound (23 mg, 37%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 2.79 (6H), 3.78 (2H), 4.59 (2H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.20 (1H), 7.40 (1H), 8.11 (1H), 8.26 (1H), 10.40 (1H), 12.09 (1H)

Example 125

N-{4-[3-Anilino-6-(morpholin-4-ylcarbonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

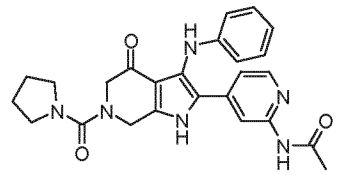


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) in pyridine (1.54 mL) was added morpholine-4-carbonyl chloride (32 µL, 0.28 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative HPLC (basic method) and digestion with diethylether to give the title compound (41 mg, 59%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 3.19 (4H), 3.60 (4H), 3.83 (2H), 4.64 (2H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.20 (1H), 7.40 (1H), 8.12 (1H), 8.26 (1H), 10.41 (1H), 12.12 (1H)

Example 126

N-{4-[3-Anilino-4-oxo-6-(pyrrolidin-1-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

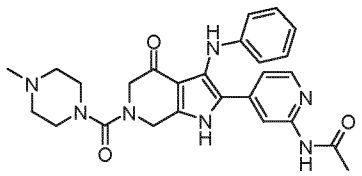


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) in pyridine (1.54 mL) was added pyrrolidine-1-carbonyl chloride (31 µL, 0.28 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative HPLC (basic method) and digestion with diethylether to give the title compound (43 mg, 64%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.78 (4H), 2.08 (3H), 3.30 (4H), 3.82 (2H), 4.63 (2H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.20 (1H), 7.40 (1H), 8.11 (1H), 8.26 (1H), 10.40 (1H), 12.08 (1H)

Example 127

N-(4-{3-Anilino-6-[(4-methylpiperazin-1-yl)carbonyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide

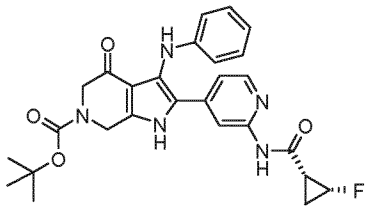


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) in pyridine (1.54 mL) was added 4-methylpiperazine-1-carbonyl chloride (37 µL, 0.28 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative HPLC (basic method) and digestion with diethylether to give the title compound (41 mg, 57%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 2.19 (3H), 2.31 (4H), 3.19 (4H), 3.81 (2H), 4.62 (2H), 6.55 (2H), 6.59 (1H), 7.02 (2H), 7.20 (1H), 7.40 (1H), 8.12 (1H), 8.26 (1H), 10.41 (1H), 12.10 (1H)

Example 128

tert-Butyl 3-anilino-2-[2-({[(1R,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

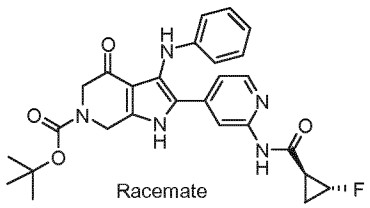


A solution of (1R,2R)-2-fluorocyclopropanecarboxylic acid (127 mg, 1.22 mmol) and HATU (462 mg, 1.22 mmol) in DMA (5.4 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 300 mg, 0.72 mmol) and DIPEA (249 µL, 1.43 mmol) in DMA (5.4 mL) and stirred for 16 h at 50℃. The mixture was conce ntrated and purified by Biotage (SNAP NH 50g, EtOAc:Hexane; EtOH: EtOAc) and preparative TLC (silica, EtOH:DCM) to give the title compound (261 mg, 72%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.19 (1H), 1.44 (9H), 1.65 (1H), 2.22 (1H), 4.00 (2H), 4.74 (2H), 4.86+5.03 (1H), 6.56 (2H), 6.60 (1H), 7.03 (2H), 7.24 (1H), 7.43 (1H), 8.13 (1H), 8.31 (1H), 10.79 (1H), 12.26 (1H)

Example 129

tert-Butyl 3-anilino-2-[2-({[(rel-1S,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

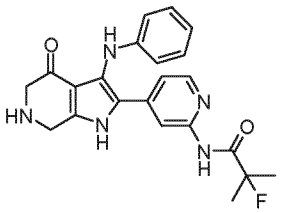


A solution of rel-(1S,2R)-2-fluorocyclopropanecarboxylic acid (133 mg, 1.29 mmol) and HATU (489 mg, 1.29 mmol) in DMA (5.4 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 300 mg, 0.72 mmol) and DIPEA (249 µL, 1.43 mmol) in DMA (5.4 mL) and stirred for 16 h at 50℃. The mixture was conce ntrated and purified by Biotage (SNAP NH 50g, EtOAc:Hexane; EtOH: EtOAc) and preparative TLC (silica, EtOH:DCM) to give the title compound (229 mg, 63%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.23 (1H), 1.43 (9H), 1.54 (1H), 2.56 (1H), 4.00 (2H), 4.74 (2H), 4.78+4.94 (1H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.25 (1H), 7.43 (1H), 8.15 (1H), 8.23 (1H), 10.89 (1H), 12.22 (1H)

Example 130

N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluoro-2-methylpropanamide

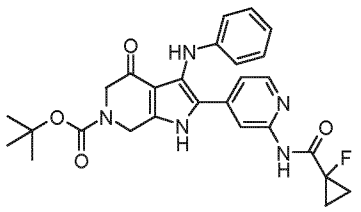


To a solution of tert-butyl 2-{2-[(2-fluoro-2-methylpropanoyl)amino]pyridin-4-yl}-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (119; 310 mg, 0.55 mmol) in DCM (16 mL) was added TFA (847 µL) and the mixture was stirred at RT for 16h. The mixture was poured into saturated sodium hydrogenate solution, extracted with DCM/methanol and dried over sodium sulfate. After filtration and concentration the residue was digested with methanol to give the title compound (142 mg, 60%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.55 (3H), 1.61 (3H), 3.21 (3H), 3.96 (2H), 6.59 (2H), 6.61 (1H), 7.03 (2H), 7.28 (1H), 7.42 (1H), 8.13-8.19 (2H), 9.74 (1H), 11.97 (1H)

Example 131

tert-Butyl 3-anilino-2-(2-{[(1-fluorocyclopropyl)carbonyl]amino}pyridin-4-yl)-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

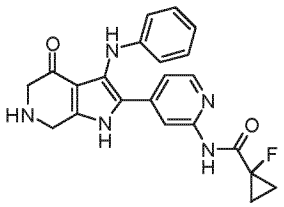


A solution of 1-fluorocyclopropanecarboxylic acid (298 mg, 2.86 mmol) and HATU (1.09 g, 2.86 mmol) in DMA (11 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 600 mg, 1.43 mmol) and DIPEA (498 µL, 2.86 mmol) in DMA (11 mL) and the mixture was stirred for 16 h at 50℃. The mixture was concentra ted and purified by Biotage (SNAP NH 50g, EtOAc:Hexane) and preparative TLC (silica, EtOH:DCM) to give the title compound (312 mg, 41%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.33 (2H), 1.43 (9H), 1.46 (2H), 4.01 (2H), 4.75 (2H), 6.57 (2H), 6.61 (1H), 7.03 (2H), 7.32 (1H), 7.47 (1H), 8.18 (1H), 8.21 (1H), 10.18 (1H), 12.26 (1H)

Example 132

N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-1-fluorocyclopropanecarboxamide

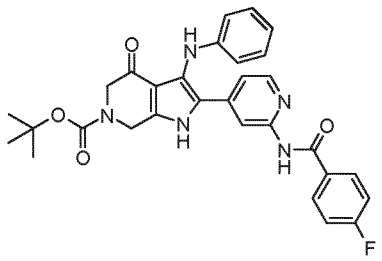


To a solution of tert-butyl 3-anilino-2-(2-{[(1-fluorocyclopropyl)carbonyl]amino}pyridin-4-yl)-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (131; 545 mg, 1.08 mmol) in DCM (30 mL) was added TFA (1.66 mL) and the mixture was stirred at RT for 16h. The mixture was poured into saturated sodium hydrogenate solution, extracted with DCM/methanol and dried over sodium sulfate. After filtration and concentration the residue was digested with methanol to give the title compound (52 mg, 11%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.31 (2H), 1.45 (2H), 3.20 (3H), 3.95 (2H), 6.56-6.65 (3H), 7.03 (2H), 7.29 (1H), 7.41 (1H), 8.14 (1H), 8.18 (1H), 10.13 (1H), 11.96 (1H)

Example 133

tert-Butyl 3-anilino-2-{2-[(4-fluorobenzoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

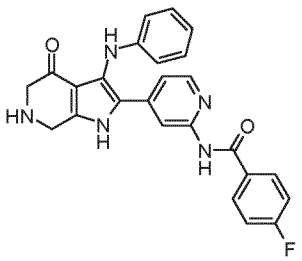


A solution of 4-fluorobenzoic acid (100 mg, 0.72 mmol) and HATU (272 mg, 0.72 mmol) in DMA (3 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 150 mg, 0.36 mmol) and DIPEA (125 µL, 0.72 mmol) in DMA (3 mL) and stirred for 40 h at 50°C. The mixture was concentrated and purified by Biotage (SNAP NH 25g, EtOAc:Hexane) and preparative TLC (silica, EtOH:DCM) to give the title compound (77 mg, 40%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 4.01 (2H), 4.75 (2H), 6.56-6.64 (3H), 7.03 (2H), 7.32 (1H), 7.36 (2H), 7.46 (1H), 8.11 (2H), 8.22 (1H), 8.39 (1H), 10.79 (1H), 12.30 (1H)

Example 134

N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-4-fluorobenzamide

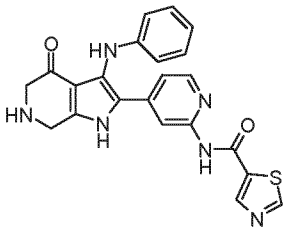


To a solution of tert-butyl 3-anilino-2-{2-[(4-fluorobenzoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (133; 132 mg, 0.24 mmol) in DCM (7 mL) was added TFA (375 µL) and the mixture was stirred at RT for 16h. The mixture was poured into saturated $NaHCO_3$ solution and extracted with DCM/methanol. The organic layer was washed with water and dried over sodium sulphate. After filtration and concentration, the residue was purified by preparative TLC (silica, MeOH:DCM) to give the title compound (24 mg, 21%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.21 (3H), 3.97 (2H), 6.58-6.64 (3H), 7.03 (2H), 7.29 (1H), 7.36 (2H), 7.42 (1H), 8.08-8.13 (2H), 8.19 (1H), 8.35 (1H), 10.76 (1H), 11.99 (1H)

Example 135

N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-1,3-thiazole-5-carboxamide

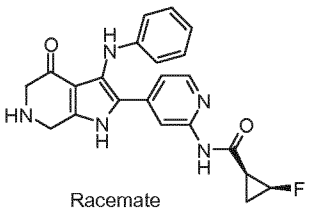


To a solution of tert-butyl 4-oxo-3-(phenylamino)-2-{2-[(1,3-thiazol-5-ylcarbonyl)amino]pyridin-4-yl}-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (122; 459 mg, 0.87 mmol) in DCM (25 mL) was added TFA (1.33 mL) and the mixture was stirred at RT for 16h. The mixture was poured into saturated $NaHCO_3$ solution and extracted with DCM/methanol. The organic layer was washed with water and dried over sodium sulphate. After filtration and concentration, the residue was purified by Biotage (SNAP NH 10g, MeOH:DCM) and preparative TLC (silica, MeOH:DCM) to give the title compound (184 mg, 49%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.21 (3H), 3.96 (2H), 6.57-6.64 (3H), 7.03 (2H), 7.30 (1H), 7.42 (1H), 8.21 (1H), 8.31 (1H), 8.88 (1H), 9.33 (1H), 11.12 (1H), 11.99 (1H)

Example 136

rel-(1S,2S)-N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide



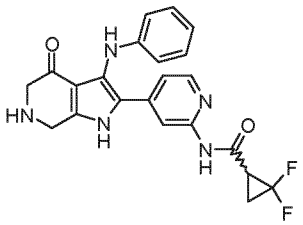
Racemate

To a solution of tert-butyl 2-[2-({[rel-(1S,2S)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (120; 653 mg, 1.29 mmol) in DCM (35 mL) was added TFA (1.99 mL) and the mixture was stirred at RT for 16h. The mixture was poured into saturated $NaHCO_3$ solution and extracted with DCM/methanol. The organic layer was washed with water and dried over sodium sulphate. After filtration and concentration, the residue was purified by Biotage (SNAP NH 25g, MeOH:DCM) and preparative TLC (silica, MeOH:DCM) to give the title compound (199 mg, 38%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.18 (1H), 1.64 (1H), 2.20 (1H), 3.19 (3H), 3.94 (2H), 4.93 (1H), 6.56-6.62 (3H), 7.02 (2H), 7.20 (1H), 7.37 (1H), 8.10 (1H), 8.27 (1H), 10.74 (1H), 11.95 (1H)

Example 137

(1RS)-N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2,2-difluorocyclopropanecarboxamide

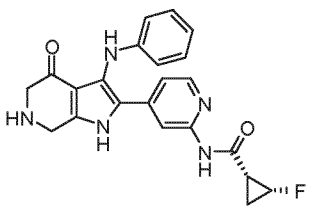


To a solution of tert-Butyl 2-[2-({[(1RS)-2,2-difluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (121; 545 mg, 1.04 mmol) in DCM (28 mL) was added TFA (1.60 mL) and the mixture was stirred at RT for 16h. The mixture was poured into saturated $NaHCO_3$ solution and extracted with DCM/methanol. The organic layer was washed with water and dried over sodium sulphate. After filtration and concentration, the residue was purified by Biotage (SNAP NH 25g, MeOH:DCM) and preparative TLC (silica, MeOH:DCM) to give the title compound (187 mg, 42%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.01 (2H), 2.98 (1H), 3.20 (3H), 3.95 (2H), 6.55-6.63 (3H), 7.02 (2H), 7.23 (1H), 7.38 (1H), 8.13 (1H), 8.23 (1H), 10.90 (1H), 11.95 (1H)

Example 138

(1R,2R)-N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide



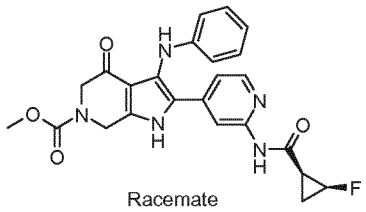
To a solution of tert-Butyl 3-anilino-2-[2-({[(1R,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (128; 240 mg, 0.48 mmol) in DCM (12 mL) was added TFA (0.73 mL) and the mixture was stirred at RT for 16h. The mixture was poured into saturated $NaHCO_3$ solution and extracted with DCM/methanol. The organic layer was washed with

water and dried over sodium sulphate. After filtration and concentration, the residue was purified by Biotage (SNAP NH 10g, MeOH:DCM) and preparative TLC (silica, MeOH:DCM) to give the title compound (64 mg, 33%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.18 (1H), 1.64 (1H), 2.20 (1H), 3.19 (3H), 3.94 (2H), 4.93 (1H), 6.56-6.62 (3H), 7.02 (2H), 7.20 (1H), 7.36 (1H), 8.10 (1H), 8.27 (1H), 10.73 (1H), 11.95 (1H)

Example 139

Methyl 3-anilino-2-[2-({[rel-(1S,2S)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



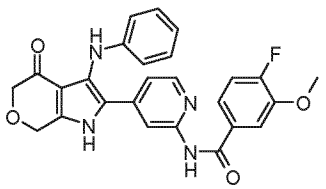
Racemate

To a mixture of rel-(1S,2S)-N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (136; 30 mg, 0.07 mmol) in pyridine (1 mL) was added methyl carbonochloridate (17.1 µL, 0.22 mmol) and the reaction was stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (25 mg, 70%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.18 (1H), 1.65 (1H), 2.21 (1H), 3.66 (3H), 4.04 (2H), 4.79 (2H), 4.94 (1H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.24 (1H), 7.43 (1H), 8.14 (1H), 8.30 (1H), 10.79 (1H), 12.25 (1H)

Example 140

N-[4-(3-Anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-4-fluoro-3-methoxybenzamide

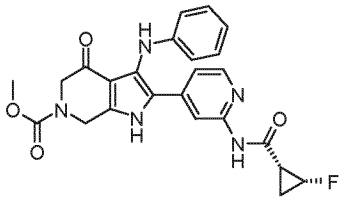


A mixture of 4-fluoro-3-methoxybenzoic acid (40 mg, 0.23 mmol), 1,1-carbonyldiimidazole (76 mg, 0.47 mmol) and THF (3 mL) was stirred for 1 h at 50℃. 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.16 mmol) was

added and the mixture stirred for 5 h at 120℃. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (18.3 mg, 24%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.95 (3H), 4.05 (2H), 4.90 (2H), 6.58-6.63 (3H), 7.04 (2H), 7.33-7.40 (2H), 7.49 (1H), 7.65 (1H), 7.87 (1H), 8.24 (1H), 8.40 (1H), 10.84 (1H), 12.22 (1H)

Example 141

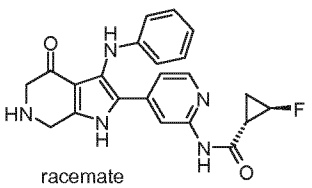
Methyl 3-anilino-2-[2-({[(1R,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



To a mixture of (1R,2R)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (138; 36 mg, 0.089 mmol) in pyridine (1.2 mL) was added methyl carbonochloridate (20.6 µL, 0.27 mmol) and the reaction was stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (15 mg, 36%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.19 (1H), 1.65 (1H), 2.21 (1H), 3.66 (3H), 4.04 (2H), 4.79 (2H), 4.94 (1H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.24 (1H), 7.43 (1H), 8.13 (1H), 8.30 (1H), 10.79 (1H), 12.25 (1H)

Example 142

rel-(1S,2R)-N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide



racemate

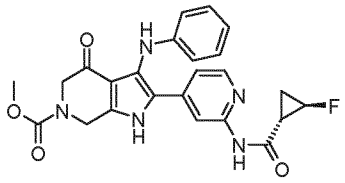
To a solution of tert-butyl 3-anilino-2-[2-({[rel-(1S,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (129; 207 mg, 0.41 mmol) in DCM (10 mL) was added TFA (0.63 mL) and stirred at RT for 16h. The reaction was cooled to 0℃ and added to sat. $NaHCO_3$ (aq). The reaction mixture was extracted with DCM:MeOH (9:1). The organics were combined, washed with water, dried over Na_2SO_4, filtered and concentrated. The crude

product was purified by Biotage (SNAP 10g silica, MeOH:DCM) to give the title compound (109 mg, 65%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.21 (1H), 1.53(1H), 2.56 (1H), 3.19 (3H), 3.94 (2H), 4.84 (1H), 6.57 (2H), 6.60 (1H), 7.02 (2H), 7.21 (1H), 7.36 (1H), 8.11 (1H), 8.19 (1H), 10.84 (1H), 11.91 (1H)

Example 143

Methyl 3-anilino-2-[2-({[(1S,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

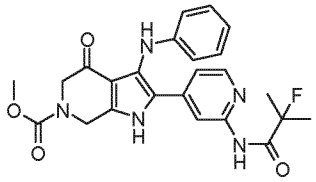


To a mixture of (1S,2R)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (142; 36 mg, 0.089 mmol) in pyridine (1.2 mL) was added methyl carbonochloridate (20.6 µL, 0.27 mmol) and the reaction was stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (22 mg, 50%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.22 (1H), 1.54 (1H), 2.56 (1H), 3.66 (3H), 4.04 (2H), 4.78 (2H), 4.86 (1H), 6.55 (2H), 6.60 (1H), 7.02 (2H), 7.24 (1H), 7.42 (1H), 8.15 (1H), 8.22 (1H), 10.89 (1H), 12.22 (1H)

Example 144

Methyl 3-anilino-2-{2-[(2-fluoro-2-methylpropanoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

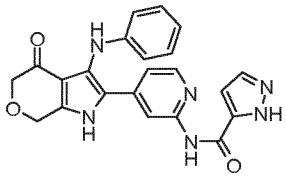


To a mixture of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluoro-2-methylpropanamide (130; 30 mg, 0.074 mmol) in pyridine (1 mL) was added methyl carbonochloridate (17.1 µL, 0.22 mmol) and the reaction was stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (17 mg, 48%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.59 (6H), 3.67 (3H), 4.05 (2H), 4.80 (2H), 6.57 (2H), 6.61 (1H), 7.03 (2H), 7.30 (1H), 7.47 (1H), 8.17-8.22 (2H), 9.80 (1H), 12.28 (1H)

Example 145

N-[4-(3-Anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-1H-pyrazole-5-carboxamide

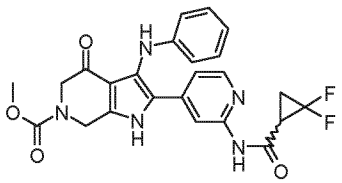


A mixture of 1H-pyrazole-5-carboxylic acid (31 mg, 0.28 mmol), 1,1-carbonyldiimidazole (91 mg, 0.56 mmol) and THF (2.7 mL) was stirred for 1 h at 50℃. 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 60 mg, 0.187 mmol) was added and the mixture stirred for 1 h at 140℃. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (16.2 mg, 20%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.05 (2H), 4.90 (2H), 6.57-6.64 (3H), 6.87 (1H), 7.04 (2H), 7.33 (1H), 7.50 (1H), 7.94 (1H), 8.21 (1H), 8.42 (1H), 9.55 (1H), 12.25 (1H), 13.56 (1H)

Example 146

Methyl 3-anilino-2-[2-({[(1RS)-2,2-difluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

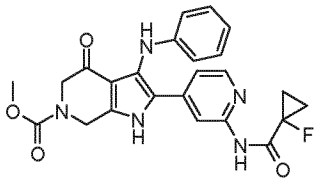


To a mixture of (1RS)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2,2-difluorocyclopropanecarboxamide (137; 30 mg, 0.07 mmol) in pyridine (1 mL) was added methyl carbonochloridate (16.4 µL, 0.21 mmol) and the reaction was stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (8 mg, 21%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.02 (2H), 2.99 (1H), 3.67 (3H), 4.05 (2H), 4.79 (2H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.26 (1H), 7.44 (1H), 8.16 (1H), 8.27 (1H), 10.95 (1H), 12.25 (1H)

Example 147

Methyl 3-anilino-2-(2-{[(1-fluorocyclopropyl)carbonyl]amino}pyridin-4-yl)-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

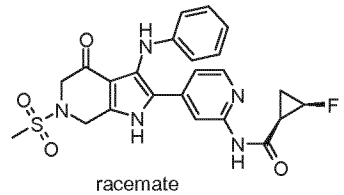


To a mixture of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-1-fluorocyclopropanecarboxamide (132; 34 mg, 0.084 mmol) in pyridine (1 mL) was added methyl carbonochloridate (19.4 µL, 0.24 mmol) and the reaction was stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (14 mg, 34%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.32 (2H), 1.46 (2H), 3.67 (3H), 4.05 (2H), 4.79 (2H), 6.57 (2H), 6.61 (1H), 7.03 (2H), 7.32 (1H), 7.47 (1H), 8.17 (1H), 8.21 (1H), 10.19 (1H), 12.26 (1H)

Example 148

rel-(1R,2R)-N-{4-[3-Anilino-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2-fluorocyclopropanecarboxamide



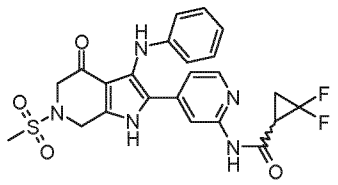
racemate

To a mixture of rel-(1S,2S)-N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (136; 30 mg, 0.074 mmol) in pyridine (1 mL) was added methanesulfonyl chloride (11.5 µL, 0.15 mmol) and the reaction was stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (28 mg, 75%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.19 (1H), 1.65 (1H), 2.22 (1H), 3.00 (3H), 3.88 (2H), 4.64 (2H), 4.94 (1H), 6.57 (2H), 6.60 (1H), 7.03 (2H), 7.27 (1H), 7.47 (1H), 8.15 (1H), 8.31 (1H), 10.81 (1H), 12.32 (1H)

Example 149

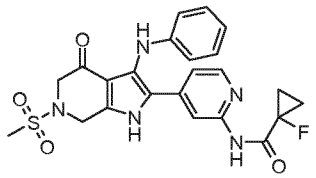
(1RS)-N-{4-[3-Anilino-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2,2-difluorocyclopropanecarboxamide



To a mixture of (1RS)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2,2-difluorocyclopropanecarboxamide (137; 30 mg, 0.071 mmol) in pyridine (1 mL) was added methanesulfonyl chloride (11.0 µL, 0.14 mmol) and the reaction was stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (21 mg, 56%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.02 (2H), 3.00 (4H), 3.88 (2H), 4.64 (2H), 6.57 (2H), 6.60 (1H), 7.03 (2H), 7.29 (1H), 7.48 (1H), 8.18 (1H), 8.28 (1H), 10.96 (1H), 12.32 (1H)

Example 150

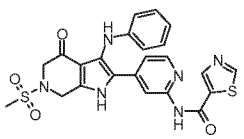
N-{4-[3-Anilino-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-1-fluorocyclopropanecarboxamide



To a mixture of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-1-fluorocyclopropanecarboxamide (132; 30 mg, 0.074 mmol) in pyridine (1 mL) was added methanesulfonyl chloride (11.5 µL, 0.15 mmol) and the reaction was stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (19 mg, 52%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.32 (2H), 1.46 (2H), 3.01 (3H), 3.88 (2H), 4.64 (2H), 6.57 (2H), 6.61 (1H), 7.03 (2H), 7.34 (1H), 7.50 (1H), 8.19 (1H), 8.23 (1H), 10.20 (1H), 12.32 (1H)

Example 151

N-{4-[3-Anilino-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-1,3-thiazole-5-carboxamide

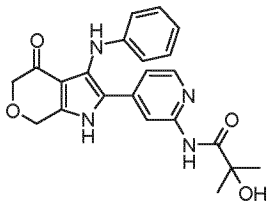


To a mixture of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-1,3-thiazole-5-carboxamide (135; 30 mg, 0.07 mmol) in pyridine (1 mL) was added methanesulfonyl chloride (10.8 µL, 0.14 mmol) and the reaction was stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (6 mg, 15%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.02 (3H), 3.89 (2H), 4.65 (2H), 6.56-6.64 (3H), 7.04 (2H), 7.36 (1H), 7.52 (1H), 8.26 (1H), 8.36 (1H), 8.89 (1H), 9.34 (1H), 11.18 (1H), 12.36 (1H)

Example 152

N-[4-(3-Anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-2-hydroxy-2-methylpropanamide

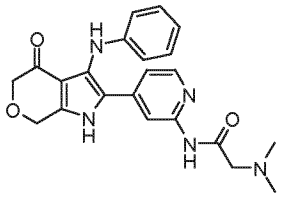


A mixture of 2-hydroxy-2-methylpropanoic acid (22 mg, 0.21 mmol), 1,1-carbonyldiimidazole (68 mg, 0.42 mmol) and THF (2.7 mL) was stirred for 1 h at 50℃. 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 45 mg, 0.14 mmol) was added and the mixture stirred for 1 h at 140℃. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (13.1 mg, 22%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.37 (6H), 4.04 (2H), 4.88 (2H), 6.04 (1H), 6.56-6.62 (3H), 7.03 (2H), 7.30 (1H), 7.48 (1H), 8.15 (1H), 8.32 (1H), 9.34 (1H), 12.20 (1H)

Example 153

N-[4-(3-Anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-N^2,N^2-dimethylglycinamide

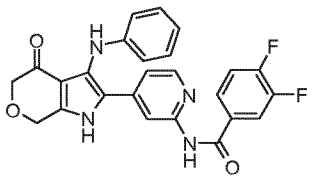


A mixture of N,N-dimethylglycine (21.7 mg, 0.21 mmol), 1,1-carbonyldiimidazole (68 mg, 0.42 mmol) and THF (2.7 mL) was stirred for 1 h at 50℃. 2-(2-Aminopyridin-4-yl)-3-

(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 45 mg, 0.14 mmol) was added and the mixture stirred for 1 h at 140℃. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (17 mg, 28%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.29 (6H), 3.11 (2H), 4.04 (2H), 4.89 (2H), 6.56-6.62 (3H), 7.03 (2H), 7.29 (1H), 7.47 (1H), 8.15 (1H), 8.30 (1H), 9.81 (1H), 12.18 (1H)

Example 154

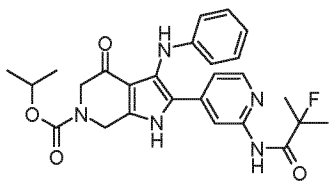
N-[4-(3-Anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-3,4-difluorobenzamide



A mixture of 3,4-difluorobenzoic acid (37 mg, 0.23 mmol), 1,1-carbonyldiimidazole (76 mg, 0.47 mmol) and THF (3 mL) was stirred for 1 h at 50℃. 2-(2-Aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one (22; 50 mg, 0.16 mmol) was added and the mixture stirred for 1 h at 140℃. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (20 mg, 26%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.05 (2H), 4.90 (2H), 6.58-6.63 (3H), 7.04 (2H), 7.36 (1H), 7.50 (1H), 7.61 (1H), 7.93 (1H), 8.12 (1H), 8.25 (1H), 8.38 (1H), 10.89 (1H), 12.22 (1H)

Example 155

Isopropyl 3-anilino-2-{2-[(2-fluoro-2-methylpropanoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

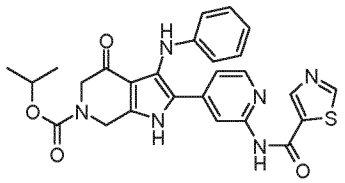


To a mixture of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluoro-2-methylpropanamide (130; 30 mg, 0.074 mmol) in pyridine (1 mL) was added isopropyl carbonochloridate (196 µL, 1M in toluene, 0.20 mmol) and the reaction was stirred for 1 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (28.7 mg, 56%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.22 (6H), 1.56 (3H), 1.62 (3H), 4.05 (2H), 4.79 (2H), 4.83 (1H), 6.57 (2H), 6.61 (1H), 7.03 (2H), 7.31 (1H), 7.48 (1H), 8.17-8.22 (2H), 9.80 (1H), 12.28 (1H)

Example 156

Isopropyl 3-anilino-4-oxo-2-{2-[(1,3-thiazol-5-ylcarbonyl)amino]pyridin-4-yl}-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

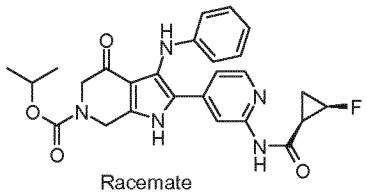


To a mixture of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-1,3-thiazole-5-carboxamide (135; 40 mg, 0.093 mmol) in pyridine (1.4 mL) was added isopropyl carbonochloridate (186 µL, 1M in toluene, 0.19 mmol) and the reaction was stirred for 1 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (24.6 mg, 49%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.22 (6H), 4.05 (2H), 4.79 (2H), 4.83 (1H), 6.55-6.63 (3H), 7.03 (2H), 7.33 (1H), 7.48 (1H), 8.24 (1H), 8.35 (1H), 8.89 (1H), 9.34 (1H), 11.16 (1H), 12.30 (1H)

Example 157

Isopropyl 3-anilino-2-[2-({[rel-(1R,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



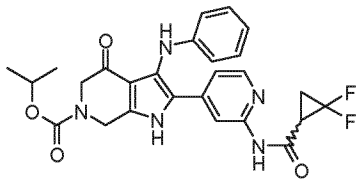
Racemate

To a mixture of rel-(1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (136; 40 mg, 0.099 mmol) in pyridine (1.5 mL) was added isopropyl carbonochloridate (197 µL, 1M in toluene, 0.20 mmol) and the reaction was stirred for 1 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (29.1 mg, 57%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.12-1.30 (7H), 1.65 (1H), 2.21 (1H), 4.03 (2H), 4.78 (2H), 4.83 (1H), 4.94 (1H), 6.56 (2H), 6.60 (1H), 7.03 (2H), 7.24 (1H), 7.44 (1H), 8.13 (1H), 8.31 (1H), 10.79 (1H), 12.26 (1H)

Example 158

Isopropyl 3-anilino-2-[2-({[(1RS)-2,2-difluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

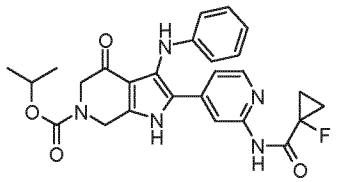


To a mixture of (1RS)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2,2-difluorocyclopropanecarboxamide (137; 40 mg, 0.094 mmol) in pyridine (1.4 mL) was added isopropyl carbonochloridate (189 µL, 1M in toluene, 0.19 mmol) and the reaction was stirred for 1 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (30.5 mg, 60%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.22 (6H), 2.02 (2H), 3.00 (1H), 4.04 (2H), 4.78 (2H), 4.82 (1H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.27 (1H), 7.45 (1H), 8.16 (1H), 8.27 (1H), 10.95 (1H), 12.26 (1H)

Example 159

Isopropyl 3-anilino-2-(2-{[(1-fluorocyclopropyl)carbonyl]amino}pyridin-4-yl)-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

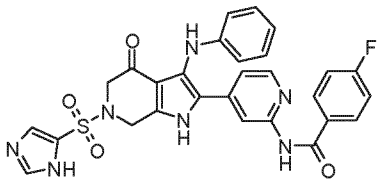


To a mixture of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-1-fluorocyclopropanecarboxamide (132; 40 mg, 0.099 mmol) in pyridine (1.4 mL) was added isopropyl carbonochloridate (197 µL, 1M in toluene, 0.20 mmol) and the reaction was stirred for 1 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (29.6 mg, 58%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.22 (6H), 1.32 (2H), 1.46 (2H), 4.04 (2H), 4.78 (2H), 4.82 (1H), 6.57 (2H), 6.61 (1H), 7.03 (2H), 7.32 (1H), 7.47 (1H), 8.18 (1H), 8.21 (1H), 10.18 (1H), 12.26 (1H)

Example 160

N-{4-[3-Anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-4-fluorobenzamide

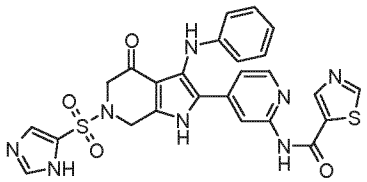


To a mixture of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-4-fluorobenzamide (134; 50 mg, 0.113 mmol) in pyridine (4 mL) was added 1H-imidazole-5-sulfonyl chloride (94 mg, 0.57 mmol) and the reaction was stirred for 2.5 days at 60℃. Methanol was added and the mixture co ncentrated and purified by preparative by preparative HPLC (basic method) to give the title compound (26.8 mg, 39%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.83 (2H), 4.69 (2H), 6.49 (2H), 6.60 (1H), 7.04 (2H), 7.29 (1H), 7.32-7.40 (3H), 7.76 (1H), 7.81 (1H), 8.11 (2H), 8.22 (1H), 8.35 (1H), 10.79 (1H), 12.47 (2H)

Example 161

N-{4-[3-Anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-1,3-thiazole-5-carboxamide

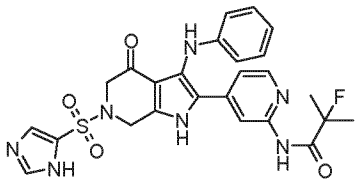


To a mixture of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-1,3-thiazole-5-carboxamide (135; 75 mg, 0.174 mmol) in pyridine (5 mL) was added 1H-imidazole-5-sulfonyl chloride (145 mg, 0.87 mmol) and the reaction was stirred for 2.5 days at 60℃. Methanol was added an d the mixture concentrated and purified by preparative by preparative HPLC (basic method) to give the title compound (34.3 mg, 33%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.82 (2H), 4.69 (2H), 6.49 (2H), 6.60 (1H), 7.04 (2H), 7.30 (1H), 7.38 (1H), 7.75 (1H), 7.81 (1H), 8.23 (1H), 8.31 (1H), 8.89 (1H), 9.34 (1H), 11.16 (1H), 12.47 (2H)

Example 162

N-{4-[3-Anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2-fluoro-2-methylpropanamide

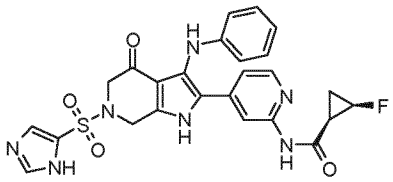


To a mixture of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluoro-2-methylpropanamide (130; 50 mg, 0.123 mmol) in pyridine (4 mL) was added 1H-imidazole-5-sulfonyl chloride (102 mg, 0.61 mmol) and the reaction was stirred for 2.5 days at 60℃. Methanol was added an d the mixture concentrated and purified by preparative by preparative HPLC (basic method) to give the title compound (34.4 mg, 50%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.56 (3H), 1.62 (3H), 3.82 (2H), 4.68 (2H), 6.47 (2H), 6.60 (1H), 7.03 (2H), 7.28 (1H), 7.37 (1H), 7.74 (1H), 7.80 (1H), 8.14-8.22 (2H), 9.78 (1H), 12.47 (2H)

Example 163

rel-(1R,2R)-N-{4-[3-Anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2-fluorocyclopropanecarboxamide



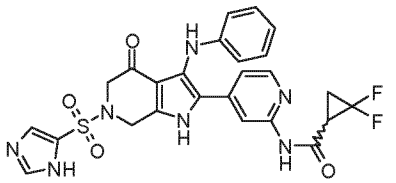
Racemate

To a mixture of rel-(1R,2R)-N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (136; 50 mg, 0.123 mmol) in pyridine (4 mL) was added 1H-imidazole-5-sulfonyl chloride (103 mg, 0.62 mmol) and the reaction was stirred for 2.5 days at 60℃. Methanol was added and the mixture concentrated and purified by preparative by preparative HPLC (basic method) to give the title compound (31.3 mg, 45%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.19 (1H), 1.65 (1H), 2.21 (1H), 3.81 (2H), 4.67 (2H), 4.94 (1H), 6.47 (2H), 6.60 (1H), 7.03 (2H), 7.21 (1H), 7.34 (1H), 7.74 (1H), 7.80 (1H), 8.12 (1H), 8.27 (1H), 10.78 (1H), 12.45 (2H)

Example 164

(1RS)-N-{4-[3-Anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2,2-difluorocyclopropanecarboxamide

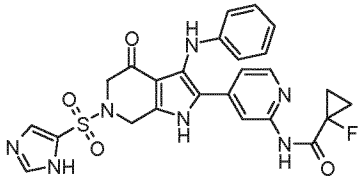


To a mixture of (1RS)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2,2-difluorocyclopropanecarboxamide (137; 50 mg, 0.118 mmol) in pyridine (4 mL) was added 1H-imidazole-5-sulfonyl chloride (98 mg, 0.59 mmol) and the reaction was stirred for 2.5 days at 60℃. Methanol was adde d and the mixture concentrated and purified by preparative by preparative HPLC (basic method) to give the title compound (28.9 mg, 42%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.02 (2H), 3.00 (1H), 3.82 (2H), 4.68 (2H), 6.46 (2H), 6.60 (1H), 7.03 (2H), 7.24 (1H), 7.35 (1H), 7.75 (1H), 7.81 (1H), 8.15 (1H), 8.23 (1H), 10.94 (1H), 12.21 (1H), 12.81 (1H)

Example 165

N-{4-[3-Anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-1-fluorocyclopropanecarboxamide

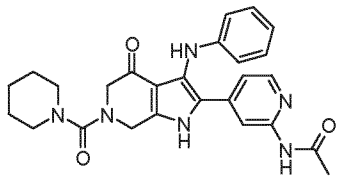


To a mixture of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-1-fluorocyclopropanecarboxamide (132; 50 mg, 0.123 mmol) in pyridine (4 mL) was added 1H-imidazole-5-sulfonyl chloride (103 mg, 0.62 mmol) and the reaction was stirred for 2.5 days at 60℃. Methanol was adde d and the mixture concentrated and purified by preparative by preparative HPLC (basic method) to give the title compound (36.1 mg, 52%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.32 (2H), 1.43 (1H), 1.48 (1H), 3.82 (2H), 4.68 (2H), 6.47 (2H), 6.60 (1H), 7.04 (2H), 7.29 (1H), 7.37 (1H), 7.75 (1H), 7.80 (1H), 8.14 (1H), 8.20 (1H), 10.18 (1H), 12.44 (2H)

Example 166

N-{4-[3-Anilino-4-oxo-6-(piperidin-1-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

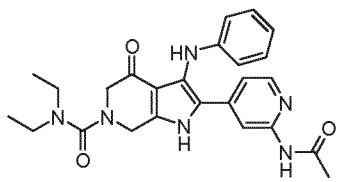


To a mixture of N-{4-[4-Oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) in pyridine (2 mL) was added piperidine-1-carbonyl chloride (35 µL, 0.28 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (50 mg, 73%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.45-1.60 (6H), 2.08 (3H), 3.16 (4H), 3.79 (2H), 4.60 (2H), 6.56 (2H), 6.59 (1H), 7.02 (2H), 7.20 (1H), 7.41 (1H), 8.12 (1H), 8.26 (1H), 10.41 (1H), 12.10 (1H)

Example 167

2-(2-Acetamidopyridin-4-yl)-3-anilino-N,N-diethyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

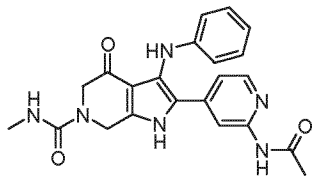


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) in pyridine (2 mL) was added diethylcarbamic chloride (35 µL, 0.28 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (47 mg, 70%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.08 (6H), 2.08 (3H), 3.15 (4H), 3.76 (2H), 4.57 (2H), 6.55 (2H), 6.59 (1H), 7.01 (2H), 7.20 (1H), 7.42 (1H), 8.12 (1H), 8.25 (1H), 10.41 (1H), 12.09 (1H)

Example 168

2-(2-Acetamidopyridin-4-yl)-3-anilino-N-methyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

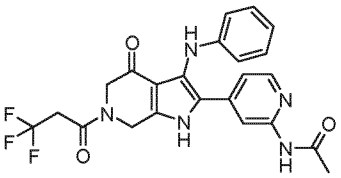


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) in pyridine (2 mL) was added methylcarbamic chloride (26 mg, 0.28 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (28 mg, 45%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 2.58 (3H), 3.98 (2H), 4.70 (2H), 6.55 (2H), 6.59 (1H), 6.79 (1H), 7.02 (2H), 7.22 (1H), 7.39 (1H), 8.12 (1H), 8.27 (1H), 10.39 (1H), 12.19 (1H)

Example 169

N-{4-[3-Anilino-4-oxo-6-(3,3,3-trifluoropropanoyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

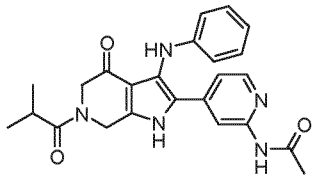


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 40 mg, 0.11 mmol) in pyridine (1.6 mL) was added 3,3,3-trifluoropropanoyl chloride (25 µL, 0.22 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (17 mg, 32%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 3.81+3.93 (2H), 4.16 (2H), 4.82+4.88 (2H), 6.51-6.64 (3H), 7.02 (2H), 7.23 (1H), 7.42+7.45 (1H), 8.14 (1H), 8.28 (1H), 10.41 (1H), 12.28 (1H)

Example 170

N-[4-(3-Anilino-6-isobutyryl-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]acetamide

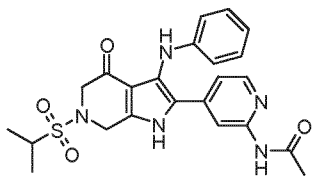


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 40 mg, 0.11 mmol) in pyridine (1.6 mL) was added 2-methylpropanoyl chloride (23 µL, 0.22 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (36 mg, 72%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.93-1.09 (6H), 2.08 (3H), 2.96 (1H), 4.14+4.19 (2H), 4.87+4.91 (2H), 6.56 (2H), 6.59 (1H), 7.02 (2H), 7.22+7.23 (1H), 7.43 (1H), 8.13 (1H), 8.28 (1H), 10.40 (1H), 12.24 (1H)

Example 171

N-{4-[3-Anilino-6-(isopropylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

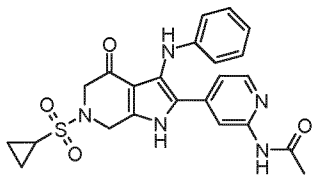


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) in pyridine (2 mL) was added propane-2-sulfonyl chloride (47 µL, 0.42 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (34 mg, 49%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.21 (6H), 2.08 (3H), 3.42 (1H), 3.94 (2H), 4.74 (2H), 6.57 (3H), 7.02 (2H), 7.24 (1H), 7.46 (1H), 8.14 (1H), 8.28 (1H), 10.42 (1H), 12.24 (1H)

Example 172

N-{4-[3-Anilino-6-(cyclopropylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

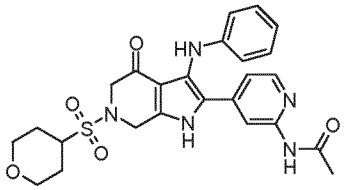


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 40 mg, 0.11 mmol) in pyridine (1.6 mL) was added cyclopropanesulfonyl chloride (23 µL, 0.22 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (36 mg, 66%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.85-0.96 (4H), 2.09 (3H), 2.48 (1H), 3.92 (2H), 4.74 (2H), 6.57 (2H), 6.60 (1H), 7.02 (2H), 7.25 (1H), 7.43 (1H), 8.14 (1H), 8.29 (1H), 10.42 (1H), 12.25 (1H)

Example 173

N-{4-[3-Anilino-4-oxo-6-(tetrahydro-2H-pyran-4-ylsulfonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

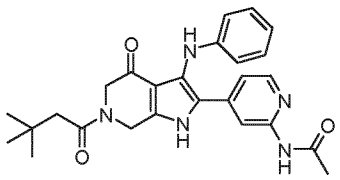


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) in pyridine (2 mL) was added tetrahydro-2H-pyran-4-sulfonyl chloride (51 mg, 0.28 mmol) and the reaction was stirred for 2 h at RT. Methanol was added and the mixture concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (32 mg, 45%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.61 (2H), 1.84 (2H), 2.09 (3H), 3.31 (2H), 3.56 (1H), 3.91 (2H), 3.95 (2H), 4.74 (2H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.24 (1H), 7.46 (1H), 8.14 (1H), 8.28 (1H), 10.42 (1H), 12.24 (1H)

Example 174

N-{4-[3-Anilino-6-(3,3-dimethylbutanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

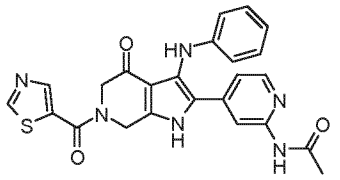


A solution of 3,3-dimethylbutanoic acid (32 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 3 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) and digested with diethyl ether to give the title compound (35 mg, 55%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.96+0.99 (9H), 2.08 (3H), 2.32+2.38 (2H), 4.16+4.19 (2H), 4.89 (2H), 6.55 (2H), 6.59 (1H), 6.98-7.05 (2H), 7.21-7.25 (1H), 7.43 (1H), 8.11-8.16 (1H), 8.28 (1H), 10.41+10.42 (1H), 12.15+12.24 (1H)

Example 175

N-{4-[3-Anilino-4-oxo-6-(1,3-thiazol-5-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

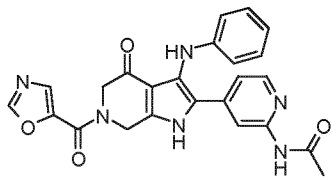


A solution of 1,3-thiazole-5-carboxylic acid (36 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 3 h at RT. The mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) and digested with diethyl ether to give the title compound (29 mg, 45%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 4.33 (2H), 5.09 (2H), 6.58 (2H), 6.60 (1H), 7.03 (2H), 7.22 (1H), 7.45 (1H), 8.13 (1H), 8.27 (1H), 8.32 (1H), 9.31 (1H), 10.41 (1H), 12.17+12.23 (1H)

Example 176

N-{4-[3-Anilino-6-(1,3-oxazol-5-ylcarbonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

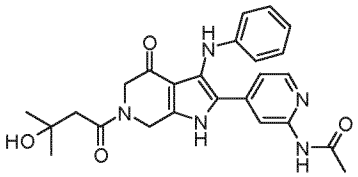


A solution of 1,3-oxazole-5-carboxylic acid (31 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 3 h at RT. The mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) and digested with diethyl ether to give the title compound (17 mg, 27%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.09 (3H), 4.36 (2H), 5.11 (2H), 6.57 (2H), 6.60 (1H), 7.02 (2H), 7.23 (1H), 7.45 (1H), 7.84 (1H), 8.14 (1H), 8.28 (1H), 8.65 (1H), 10.42 (1H), 12.26 (1H)

Example 177

N-{4-[3-Anilino-6-(3-hydroxy-3-methylbutanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

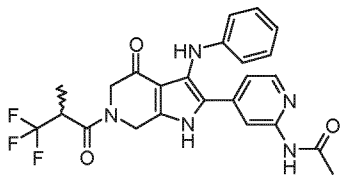


A solution of 3-hydroxy-3-methylbutanoic acid (33 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 3 h at RT. The mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) and digested with diethyl ether to give the title compound (30 mg, 46%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.17+1.21 (6H), 2.08 (3H), 2.53+2.59 (2H), 4.16+4.23 (2H), 4.68+4.75 (1H), 4.89+4.95 (2H), 6.56 (2H), 6.59 (1H), 7.02 (2H), 7.22 (1H), 7.41+7.42 (1H), 8.13 (1H), 8.28 (1H), 10.40 (1H), 12.21+12.24 (1H)

Example 178

N-(4-{3-Anilino-4-oxo-6-[(2RS)-3,3,3-trifluoro-2-methylpropanoyl]-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide

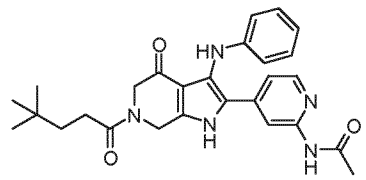


A solution of (2RS)-3,3,3-trifluoro-2-methylpropanoic acid (39 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) and digested with n-hexane to give the title compound (41 mg, 61%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.23+1.29 (3H), 2.08 (3H), 4.17-4.37 (3H), 4.83-5.03 (2H), 6.56 (2H), 6.59 (1H), 6.99-7.05 (2H), 7.21-7.26 (1H), 7.45 (1H), 8.14 (1H), 8.26-8.32 (1H), 10.42 (1H), 12.26+12.29 (1H)

Example 179

N-{4-[3-Anilino-6-(4,4-dimethylpentanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

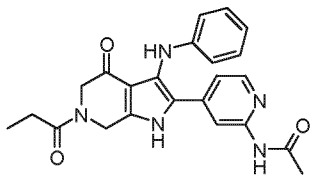


A solution of 4,4-dimethylpentanoic acid (36 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 16 h at RT. The mixture was concentrated and purified by digestion with ethanol to give the title compound (55 mg, 83%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.87+0.91 (9H), 1.36-1.46 (2H), 2.08 (3H), 2.34+2.44 (2H), 4.13+4.16 (2H), 4.85+4.88 (2H), 6.57 (2H), 6.60 (1H), 7.02 (2H), 7.23 (1H), 7.43 (1H), 8.13 (1H), 8.28+8.29 (1H), 10.41 (1H), 12.21+12.23 (1H)

Example 180

N-[4-(3-Anilino-4-oxo-6-propionyl-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]acetamide

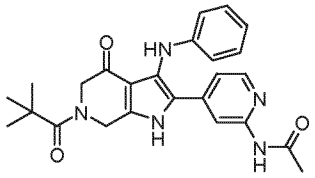


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 40 mg, 0.11 mmol) in pyridine (1.6 mL) was added propanoyl chloride (19 µL, 0.22 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (32 mg, 65%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.99+1.02 (3H), 2.08 (3H), 2.40+2.49 (2H), 4.13 (2H), 4.84+4.85 (2H), 6.56 (2H), 6.59 (1H), 7.02 (2H), 7.23 (1H), 7.41+7.42 (1H), 8.13 (1H), 8.28 (1H), 10.40 (1H), 12.23 (1H)

Example 181

N-{4-[3-Anilino-6-(2,2-dimethylpropanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

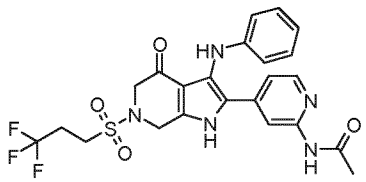


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 40 mg, 0.11 mmol) in pyridine (1.6 mL) was added 2,2-dimethylpropanoyl chloride (27 µL, 0.22 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (36 mg, 70%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.22 (9H), 2.09 (3H), 4.22 (2H), 4.97 (2H), 6.55 (2H), 6.59 (1H), 7.02 (2H), 7.22 (1H), 7.45 (1H), 8.13 (1H), 8.27 (1H), 10.42 (1H), 12.19 (1H)

Example 182

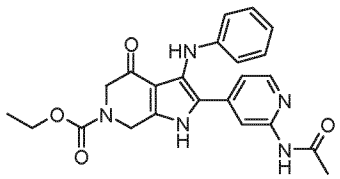
N-(4-{3-Anilino-4-oxo-6-[(3,3,3-trifluoropropyl)sulfonyl]-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamideide



To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 40 mg, 0.11 mmol) in pyridine (1.6 mL) was added 3,3,3-trifluoropropane-1-sulfonyl chloride (28 µL, 0.22 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (46 mg, 76%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.09 (3H), 2.73 (2H), 3.49 (2H), 3.98 (2H), 4.74 (2H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.24 (1H), 7.46 (1H), 8.15 (1H), 8.29 (1H), 10.43 (1H), 12.28 (1H)

Example 183

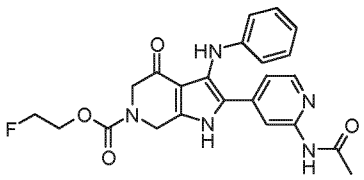
Ethyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 40 mg, 0.11 mmol) in pyridine (1.6 mL) was added ethyl carbonochloridate (21 µL, 0.22 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (39 mg, 77%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.22 (3H), 2.08 (3H), 4.05 (2H), 4.10 (2H), 4.79 (2H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.22 (1H), 7.42 (1H), 8.13 (1H), 8.28 (1H), 10.41 (1H), 12.22 (1H)

Example 184

2-Fluoroethyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

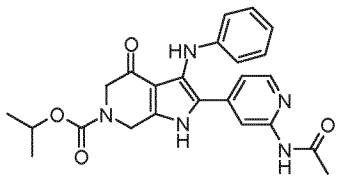


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 40 mg, 0.11 mmol) in pyridine (1.6 mL) was added 2-fluoroethyl carbonochloridate (21 µL, 0.22 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (39 mg, 74%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.09 (3H), 4.07 (2H), 4.32 (2H), 4.64 (2H), 4.83 (2H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.23 (1H), 7.43 (1H), 8.13 (1H), 8.28 (1H), 10.41 (1H), 12.24 (1H)

Example 185

Isopropyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

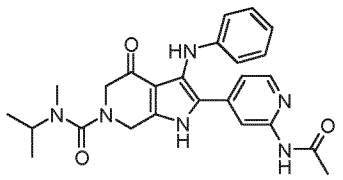


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 40 mg, 0.11 mmol) in pyridine (1.6 mL) was added isopropyl carbonochloridate (221 µL, 0.22 mmol; 1M in toluene) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (36 mg, 70%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.22 (6H), 2.08 (3H), 4.03 (2H), 4.78 (2H), 4.83 (1H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.22 (1H), 7.42 (1H), 8.13 (1H), 8.28 (1H), 10.41 (1H), 12.22 (1H)

Example 186

2-(2-Acetamidopyridin-4-yl)-3-anilino-N-isopropyl-N-methyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

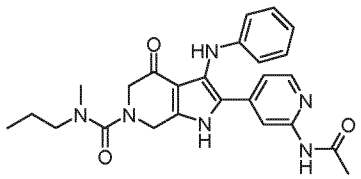


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 40 mg, 0.11 mmol) in pyridine (1.6 mL) was added isopropyl(methyl)carbamic chloride (27 µL, 0.22 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (40 mg, 74%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.09 (6H), 2.08 (3H), 2.65 (3H), 3.75 (2H), 3.92 (1H), 4.56 (2H), 6.56 (2H), 6.59 (1H), 7.02 (2H), 7.19 (1H), 7.41 (1H), 8.11 (1H), 8.25 (1H), 10.40 (1H), 12.07 (1H)

Example 187

2-(2-Acetamidopyridin-4-yl)-3-anilino-N-methyl-4-oxo-N-propyl-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

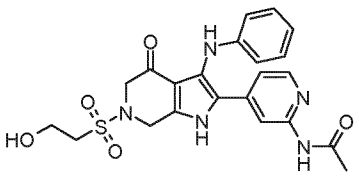


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 40 mg, 0.11 mmol) in pyridine (1.6 mL) was added methyl(propyl)carbamic chloride (28 µL, 0.22 mmol) and the reaction was stirred for 16 h at RT. Methanol was added and the mixture was concentrated and purified by preparative TLC (silica, MeOH:DCM) to give the title compound (34 mg, 64%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.80 (3H), 1.51 (2H), 2.08 (3H), 2.79 (3H), 3.09 (2H), 3.76 (2H), 4.57 (2H), 6.55 (2H), 6.59 (1H), 7.01 (2H), 7.19 (1H), 7.41 (1H), 8.11 (1H), 8.25 (1H), 10.40 (1H), 12.08 (1H)

Example 188

N-(4-{3-Anilino-6-[(2-hydroxyethyl)sulfonyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide

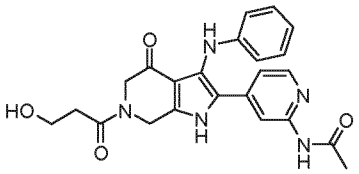


To a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) in pyridine (2.5 mL) was added 2-{[tert-butyl(dimethyl)silyl]oxy}ethanesulfonyl chloride (1.43 g, 5.53 mmol) in three portions and the reaction was stirred for 2.5 days at RT. Methanol was added and the mixture concentrated. THF (6mL), methanol (2 mL) and hydrogen chloride (346 µL, 4M in dioxane) were added and stirring was continued for 16h at RT. Ammonia (25% in water) was added the mixture concentrated and purified by preparative HPLC (basic method) and preparative TLC (silica, MeOH:DCM) to give the title compound (9 mg, 14%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.09 (3H), 3.30 (2H), 3.76 (2H), 3.89 (2H), 4.67 (2H), 5.11 (1H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.24 (1H), 7.43 (1H), 8.13 (1H), 8.29 (1H), 10.41 (1H), 12.26 (1H)

Example 189

N-{4-[3-Anilino-6-(3-hydroxypropanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide



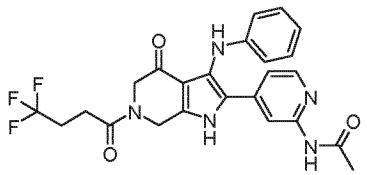
A solution of 3-[(2RS)-tetrahydro-2H-pyran-2-yloxy]propanoic acid (48 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 16 h at 50℃. The mixture was concentrated, THF (5 mL) and hydrogen chloride (346 µL, 4M in dioxane) were added and stirring was continued for 20 h at RT.

The mixture was concentrated and the residue was purified by Biotage (SNAP silica 10g, MeOH:DCM) followed by by preparative TLC (ammino phase, MeOH:DCM) to give the title compound (12 mg, 19%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 2.54+2.62 (2H), 3.59-3.70 (2H), 4.10+4.14 (2H), 4.55+4.60 (1H), 4.83 (2H), 6.54-6.61 (3H), 7.02 (2H), 7.20 (1H), 7.34+7.37 (1H), 8.02-8.14 (1H), 8.30+8.33 (1H), 10.32+10.36 (1H), 12.22 (1H)

Example 190

N-{4-[3-Anilino-4-oxo-6-(4,4,4-trifluorobutanoyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

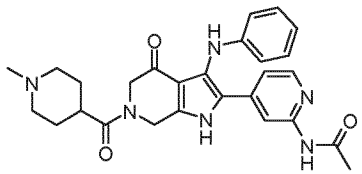


A solution of 4,4,4-trifluorobutanoic acid (39 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 16 h at 50°C. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (39 mg, 55%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08+2.09 (3H), 2.45-2.59 (2H), 2.71+2.81 (2H), 4.15+4.17 (2H), 4.87 (2H), 6.57 (2H), 6.60 (1H), 7.02 (2H), 7.23 (1H), 7.41+7.44 (1H), 8.13 (1H), 8.28+8.29 (1H), 10.41 (1H), 12.19+12.25 (1H)

Example 191

N-(4-{3-Anilino-6-[(1-methylpiperidin-4-yl)carbonyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide

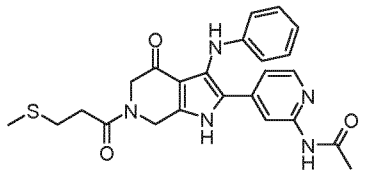


A solution of 1-methylpiperidine-4-carboxylic acid (40 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 16 h at 50°C. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (32 mg, 45%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.50-1.65 (4H), 1.84-1.95 (2H), 2.08+2.09 (3H), 2.13+2.15 (3H), 2.59-2.84 (3H), 4.14+4.19 (2H), 4.87+4.91 (2H), 6.56 (2H), 6.59 (1H), 7.02 (2H), 7.22 (1H), 7.43 (1H), 8.13 (1H), 8.28 (1H), 10.41+10.42 (1H), 12.18+12.25 (1H)

Example 192

N-(4-{3-Anilino-6-[3-(methylsulfanyl)propanoyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide

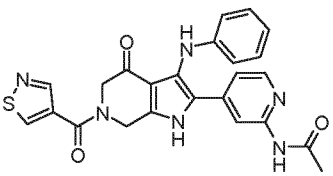


A solution of 3-(methylsulfanyl)propanoic acid (33 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 16 h at 50°C. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (36 mg, 54%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.04-2.10 (6H), 2.62-2.82 (4H), 4.14+4.17 (2H), 4.87 (2H), 6.57 (2H), 6.60 (1H), 7.02 (2H), 7.23 (1H), 7.42+7.44 (1H), 8.13 (1H), 8.28+8.29 (1H), 10.41+10.42 (1H), 12.20+12.25 (1H)

Example 193

N-{4-[3-Anilino-4-oxo-6-(1,2-thiazol-4-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

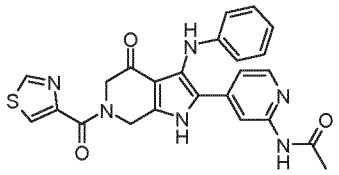


A solution of 1,2-thiazole-4-carboxylic acid (36 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 16 h at 50°C. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (37 mg, 54%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 4.14+4.34 (2H), 4.90+5.08 (2H), 6.58 (2H), 6.60 (1H), 7.03 (2H), 7.21 (1H), 7.45 (1H), 8.13 (1H), 8.23+8.29 (1H), 8.71+8.80 (1H), 9.35+9.45 (1H), 10.41 (1H), 12.07+12.36 (1H)

Example 194

N-{4-[3-Anilino-4-oxo-6-(1,3-thiazol-4-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

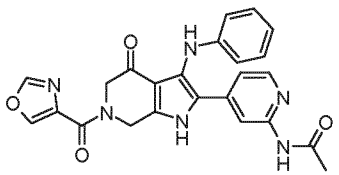


A solution of 1,3-thiazole-4-carboxylic acid (36 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 16 h at 50℃. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (29 mg, 43%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.07+2.09 (3H), 4.34+4.47 (2H), 5.07+5.22 (2H), 6.57 (2H), 6.60 (1H), 7.02 (2H), 7.22 (1H), 7.42+7.45 (1H), 8.12 (1H), 8.24+8.34 (1H), 8.29 (1H), 9.21+9.30 (1H), 10.40+10.42 (1H), 12.18+12.35 (1H)

Example 195

N-{4-[3-Anilino-6-(1,3-oxazol-4-ylcarbonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

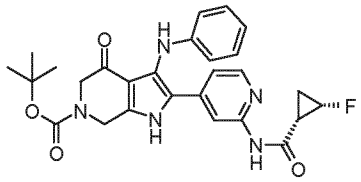


A solution of 1,3-oxazole-4-carboxylic acid (31 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 16 h at 50℃. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (40 mg, 60%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 4.30+4.69 (2H), 5.03+5.43 (2H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.23 (1H), 7.43 (1H), 8.13 (1H), 8.28 (1H), 8.54-8.74 (2H), 10.41 (1H), 12.29+12.32 (1H)

Example 196

tert-Butyl 3-anilino-2-[2-({[(1S,2S)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

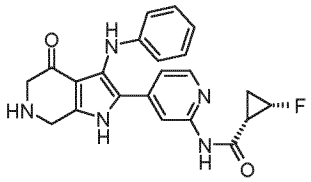


A solution of (1S,2S)-2-fluorocyclopropanecarboxylic acid (25 mg, 0.24 mmol) and HATU (91 mg, 0,24 mmol) in DMA (1 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 50 mg, 0.12 mmol) and DIPEA (42 µL, 0.24 mmol) in DMA (1 mL) and stirred for 16 h at 50℃. The mixture was concentrated and purified by HPLC (basic method) to give the title compound (27 mg, 45%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.19 (1H), 1.43 (9H), 1.65 (1H), 2.21 (1H), 4.00 (2H), 4.73+4.75 (2H), 4.93 (1H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.24 (1H), 7.43 (1H), 8.13 (1H), 8.31 (1H), 10.79 (1H), 12.25 (1H)

Example 197

(1S,2S)-N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide

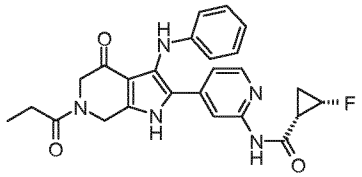


To a solution of tert-butyl 3-anilino-2-[2-({[(1S,2S)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (196; 1.82 g, 3.60 mmol) in DCM (100 mL) was added TFA (4.16 mL) and the mixture was stirred at RT for 16h. The mixture was poured into ammonia (25% in water) extracted with DCM/MeOH, dried over sodium sulfate, filtered and concentrated. The crude product was purified by Biotage (SNAP silica 100g, MeOH:DCM) to give the title compound (947 mg, 65%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.18 (1H), 1.64 (1H), 2.20 (1H), 3.25 (2H), 3.99 (2H), 4.94 (1H), 6.55-6.63 (3H), 7.02 (2H), 7.21 (1H), 7.38 (1H), 8.11 (1H), 8.27 (1H), 10.75 (1H), 11.99 (1H)

Example 198

(1S,2S)-2-Fluoro-N-4-[4-oxo-3-(phenylamino)-6-propanoyl-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide

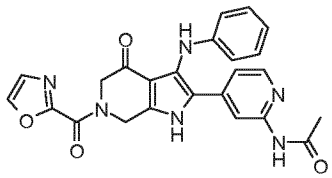


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added propanoyl chloride (21 µL, 0.25 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (42 mg, 70%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.92-1.06 (3H), 1.18 (1H), 1.65 (1H), 2.21 (1H), 2.39+2.48 (2H), 4.12 (2H), 4.81+4.83 (2H), 4.93 (1H), 6.57 (2H), 6.59 (1H), 7.02 (2H), 7.23 (1H), 7.41 (1H), 8.11 (1H), 8.32 (1H), 10.76 (1H), 12.27 (1H)

Example 199

N-4-[6-(1,3-Oxazol-2-ylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide

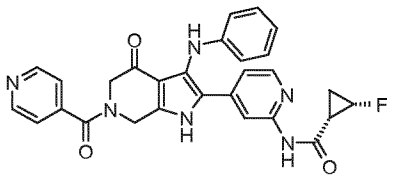


A solution of 1,3-oxazole-2-carboxylic acid (32 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 16 h at 50℃. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (39 mg, 59%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08+2.09 (3H), 4.35+4.80 (2H), 5.07+5.55 (2H), 6.57 (2H), 6.60 (1H), 7.02 (2H), 7.23+7:24 (1H), 7.44 (1H), 7.51+7.57 (1H), 8.13 (1H), 8.29 (1H), 8.36+8.40 (1H), 10.40+10.42 (1H), 12.34 (1H)

Example 200

(1S,2S)-2-Fluoro-N-4-[4-oxo-3-(phenylamino)-6-(pyridin-4-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide

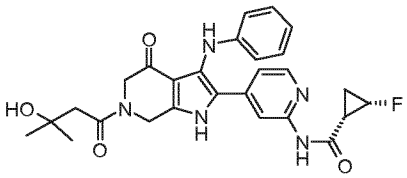


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added isonicotinoyl chloride (44 mg, 0.25 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (22 mg, 63%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.18 (1H), 1.63 (1H), 2.21 (1H), 3.96+4.34 (2H), 4.72+5.07 (2H), 4.93 (1H), 6.55-6.64 (3H), 7.03 (2H), 7.23 (1H), 7.37-7.53 (3H), 8.12+8.15 (1H), 8.23+8.33 (1H), 8.68-8.78 (2H), 10.78+10.81 (1H), 12.04+12.41 (1H)

Example 201

(1S,2S)-2-Fluoro-N-4-[6-(3-hydroxy-3-methylbutanoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide

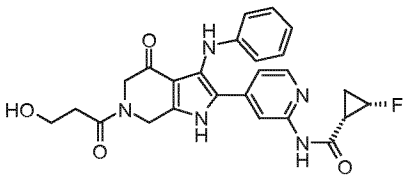


A solution of 3-hydroxy-3-methylbutanoic acid (29 mg, 0.25 mmol) and HATU (94 mg, 0,25 mmol) in DMA (1 mL) was added to a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) 50 mg, 0.12 mmol) and DIPEA (43 µL, 0.25 mmol) in DMA (1 mL) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) followed by preparative TLC (EtOH:DCM) to give the title compound (33 mg, 51%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.13-1.26 (7H), 1.65 (1H), 2.21 (1H), 2.53+2.58 (2H), 4.17+4.24 (2H), 4.67+4.74 (1H), 4.89+4.95 (2H), 4.94 (1H), 6.57 (2H), 6.60 (1H), 7.02 (2H), 7.24 (1H), 7.43+7.44 (1H), 8.14 (1H), 8.30 (1H), 10.78 (1H), 12.22+12.28 (1H)

Example 202

(1S,2S)-2-Fluoro-N-4-[6-(3-hydroxypropanoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide

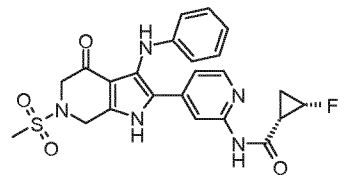


A solution of 3-[(2RS)-tetrahydro-2H-pyran-2-yloxy]propanoic acid (43 mg, 0.25 mmol) and HATU (94 mg, 0.25 mmol) in DMA (0.9 mL) was added to a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) and DIPEA (43 µL, 0.25 mmol) in DMA (0.9 mL) and stirred for 16h at 50℃. The mi xture was concentrated, THF (5mL) and hydrochloric acid (308 µL, 4M) were added and stirred for 16h at RT. N,N-Diethylethanamine (172 µL, 1.23 mmol) was added, the mixture was concentrated and purified by digestion with diethylether to give the title compound (22 mg, 36%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.19 (1H), 1.65 (1H), 2.21 (1H), 2.55+2.63 (2H), 3.59-3.70 (2H), 4.14+4.17 (2H), 4.53+4.61 (1H), 4.86+4.88 (2H), 4.94 (1H), 6.57 (2H), 6.60 (1H), 7.03 (2H), 7.24 (1H), 7.43+7.45 (1H), 8.14 (1H), 8.30 (1H), 10.78+10.79 (1H), 12.22+12.28 (1H)

Example 203

(1S,2S)-2-Fluoro-N-4-[6-(methylsulfonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide

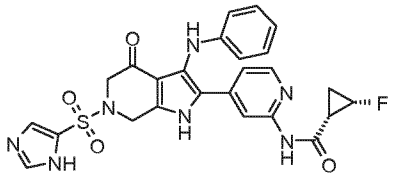


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added methanesulfonyl chloride (19 µL, 0.25 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (43 mg, 68%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.19 (1H), 1.65 (1H), 2.22 (1H), 3.00 (3H), 3.88 (2H), 4.64 (2H), 4.94 (1H), 6.57 (2H), 6.60 (1H), 7.03 (2H), 7.27 (1H), 7.47 (1H), 8.15 (1H), 8.32 (1H), 10.80 (1H), 12.32 (1H)

Example 204

(1S,2S)-2-Fluoro-N-4-[6-(1H-imidazol-5-ylsulfonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide

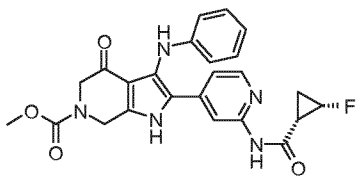


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added 1H-imidazole-5-sulfonyl chloride (151 mg, 0.91 mmol) and stirred for 2h at 80℃. The mixture was concentrated and purifi ed by preparative TLC (EtOH:DCM) to give the title compound (23 mg, 33%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.19 (1H), 1.65 (1H), 2.21 (1H), 3.82 (2H), 4.68 (2H), 4.94 (1H), 6.46 (2H), 6.60 (1H), 7.03 (2H), 7.21 (1H), 7.34 (1H), 7.75 (1H), 7.81 (1H), 8.12 (1H), 8.27 (1H), 10.79 (1H), 12.18 (1H), 12.85 (1H)

Example 205

Methyl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

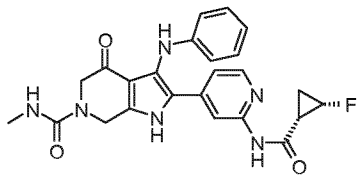


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added methyl carbonochloridate (29 µL, 0.37 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (39 mg, 64%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.19 (1H), 1.65 (1H), 2.21 (1H), 3.66 (3H), 4.04 (2H), 4.79 (2H), 4.94 (1H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.24 (1H), 7.43 (1H), 8.14 (1H), 8.30 (1H), 10.79 (1H), 12.25 (1H)

Example 206

2-[2-([(1S,2S)-2-Fluorocyclopropyl]carbonylamino)pyridin-4-yl]-N-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

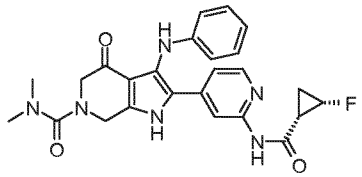


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added methylcarbamic chloride (23 mg, 0.25 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (41 mg, 68%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.18 (1H), 1.64 (1H), 2.21 (1H), 2.58 (3H), 3.98 (2H), 4.69 (2H), 4.93 (1H), 6.56 (2H), 6.59 (1H), 6.78 (1H), 7.02 (2H), 7.23 (1H), 7.41 (1H), 8.13 (1H), 8.30 (1H), 10.77 (1H), 12.22 (1H)

Example 207

2-[2-([(1S,2S)-2-Fluorocyclopropyl]carbonylamino)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

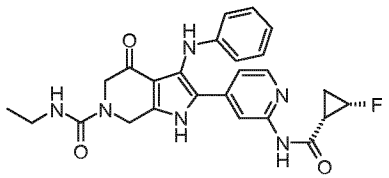


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added dimethylcarbamic chloride (27 mg, 0.25 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (40 mg, 64%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.19 (1H), 1.65 (1H), 2.21 (1H), 2.79 (6H), 3.77 (2H), 4.59 (2H), 4.94 (1H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.21 (1H), 7.42 (1H), 8.12 (1H), 8.29 (1H), 10.78 (1H), 12.12 (1H)

Example 208

N-Ethyl-2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

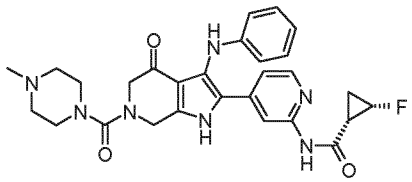


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added isocyanatoethane (20 µL, 0.25 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (43 mg, 69%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.01 (3H), 1.18 (1H), 1.65 (1H), 2.21 (1H), 3.06 (2H), 3.99 (2H), 4.69 (2H), 4.94 (1H), 6.56 (2H), 6.59 (1H), 6.83 (1H), 7.02 (2H), 7.23 (1H), 7.42 (1H), 8.13 (1H), 8.30 (1H), 10.77 (1H), 12.22 (1H)

Example 209

(1S,2S)-2-Fluoro-N-(4-6-[(4-methylpiperazin-1-yl)carbonyl]-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-ylpyridin-2-yl)cyclopropanecarboxamide

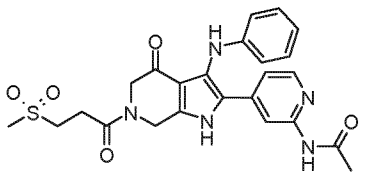


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added 4-methylpiperazine-1-carbonyl chloride (33 µL, 0.25 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (34 mg, 49%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.19 (1H), 1.65 (1H), 2.19 (3H), 2.21 (1H), 2.31 (4H), 3.19 (4H), 3.81 (2H), 4.62 (2H), 4.94 (1H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.21 (1H), 7.42 (1H), 8.12 (1H), 8.29 (1H), 10.79 (1H), 12.13 (1H)

Example 210

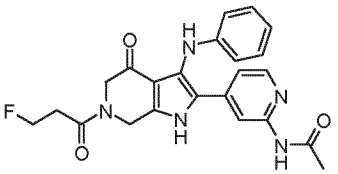
N-(4-6-[3-(Methylsulfonyl)propanoyl]-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-ylpyridin-2-yl)acetamide



To a mixture of N-(4-{3-anilino-6-[3-(methylsulfanyl)propanoyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (192; 30 mg, 0.07 mmol) in DMA (2 mL) was added 3-chlorobenzenecarboperoxoic acid (27 mg, 0.26 mmol) and stirred for 20 h at RT. Diethylethanamine (0.2 mL) was added, the mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (11 mg, 33%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.09 (3H), 2.90+3.01 (2H), 3.02+3.03 (3H), 3.30-3.40 (2H), 4.15+4.20 (2H), 4.87+4.89 (2H), 6.55-6.62 (3H), 7.02 (2H), 7.23 (1H), 7.42 (1H), 8.13 (1H), 8.28+8.30 (1H), 10.40 (1H), 12.24 (1H)

Example 211

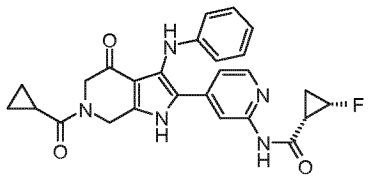
N-4-[6-(3-Fluoropropanoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide



A solution of 3-fluoropropanoic acid (25 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 16 h at 60℃. The mixture was concentrated and purified by preparative HPLC (basic method) followed by preparative TLC (EtOH:DCM) to give the title compound (23 mg, 36%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 2.81-3.02 (2H), 4.16+4.17 (2H), 4.63+4.74 (2H), 4.87+4.88 (2H), 6.54-6.62 (3H), 7.02 (2H), 7.23 (1H), 7.42 (1H), 8.13 (1H), 8.28 (1H), 10.41 (1H), 12.25 (1H)

Example 212

(1S,2S)-N-4-[6-(Cyclopropylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-2-fluorocyclopropanecarboxamide

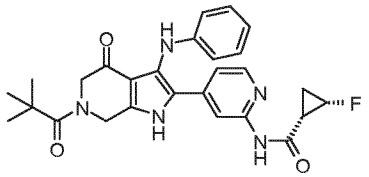


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added cyclopropanecarbonyl chloride (22 µL, 0.25 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (28 mg, 45%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.61-0.80 (4H), 1.17(1H), 1.64 (1H), 2.06 (1H), 2.21 (1H), 4.12+4.37 (2H), 4.86+5.07 (2H), 4.94 (1H), 6.55-6.62 (3H), 7.02 (2H), 7.24 (1H), 7.39+7.42 (1H), 8.11 (1H), 8.31+8.35 (1H), 10.76 (1H), 12.39 (1H)

Example 213

(1S,2S)-N-4-[6-(2,2-Dimethylpropanoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-2-fluorocyclopropanecarboxamide

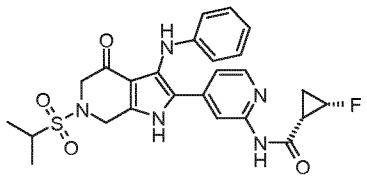


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added 2,2-dimethylpropanoyl chloride (30 µL, mg 0.25 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (38 mg, 60%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.18 (1H), 1.22 (9H), 1.65 (1H), 2.22 (1H), 4.21 (2H), 4.93 (1H), 4.96 (2H), 6.56 (2H), 6.59 (1H), 7.02 (2H), 7.24 (1H), 7.46 (1H), 8.12 (1H), 8.31 (1H), 10.79 (1H), 12.22 (1H)

Example 214

(1S,2S)-2-Fluoro-N-4-[4-oxo-3-(phenylamino)-6-(propan-2-ylsulfonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide

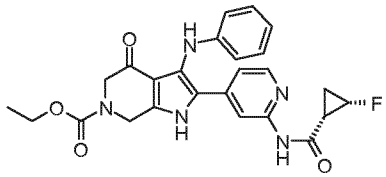


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added propane-2-sulfonyl chloride (28 µL, 0.25 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (15 mg, 22%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.18 (1H), 1.22 (6H), 1.65 (1H), 2.22 (1H), 3.41 (1H), 3.95 (2H), 4.73 (2H), 4.94 (1H), 6.57 (2H), 6.60 (1H), 7.03 (2H), 7.26 (1H), 7.48 (1H), 8.14 (1H), 8.31 (1H), 10.80 (1H), 12.27 (1H)

Example 215

Ethyl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

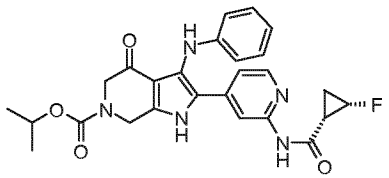


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.7 mL) was added ethyl carbonochloridate (35 µL, 0.37 mmol) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (39 mg, 63%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.14-1.27 (4H), 1.65 (1H), 2.22 (1H), 4.05 (2H), 4.10 (2H), 4.78 (2H), 4.94 (1H), 6.56 (2H), 6.60 (1H), 7.03 (2H), 7.24 (1H), 7.44 (1H), 8.14 (1H), 8.31 (1H), 10.79 (1H), 12.26 (1H)

Example 216

Propan-2-yl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

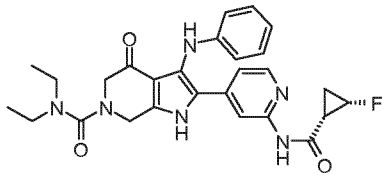


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.7 mL) was added isopropyl carbonochloridate (370 µL, 0.37 mmol, 1M in toluene) and stirred for 2 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (24 mg, 38%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.14-1.88 (7H), 1.65 (1H), 2.22 (1H), 4.03 (2H), 4.78 (2H), 4.83 (1H), 4.93 (1H), 6.56 (2H), 6.60 (1H), 7.03 (2H), 7.24(1H), 7.44 (1H), 8.13 (1H), 8.31 (1H), 10.79 (1H), 12.26 (1H)

Example 217

N,N-Diethyl-2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

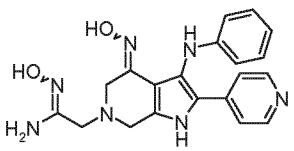


To a mixture of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 0.12 mmol) in pyridine (1.8 mL) was added diethylcarbamic chloride (33 µL, 0.25 mmol) and stirred for 16 h at RT. The mixture was concentrated and purified by preparative TLC (EtOH:DCM) to give the title compound (48 mg, 73%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.08 (6H), 1.19 (1H), 1.65 (1H), 2.21 (1H), 3.15 (4H), 3.75 (2H), 4.57 (2H), 4.94 (1H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.21 (1H), 7.43 (1H), 8.12 (1H), 8.28 (1H), 10.79 (1H), 12.11 (1H)

Example 218

(1E/Z)-N'-Hydroxy-2-[(4E/Z)-4-(hydroxyimino)-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridin-6-yl]ethanimidamide

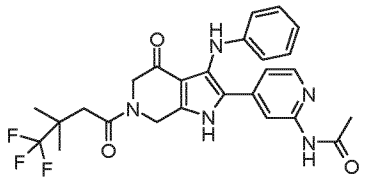


A mixture comprising [4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridin-6-yl]acetonitrile (98; 30 mg, 0.09 mmol), hydroxylamine (24 µL, 0.39 mmol, 50% in water) and ethanol (0.5 mL) was stirred for 16h at 100℃. The mixture was concentrated and purified by preparative HPLC (basic method) followed by digestion with methanol and diethyl ether to give the title compound (5 mg, 13%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.08 (2H), 3.52 (2H), 3.62 (2H), 5.36 (2H), 6.55 (2H), 6.61 (1H), 7.05 (2H), 7.08 (1H), 7.46 (2H), 8.37 (2H), 9.08 (1H), 10.51 (1H), 11.59 (1H)

Example 219

N-{4-[3-Anilino-4-oxo-6-(4,4,4-trifluoro-3,3-dimethylbutanoyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide



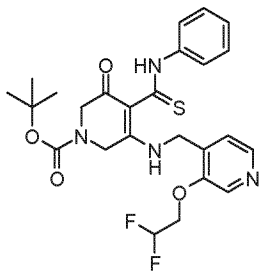
A solution of 4,4,4-trifluoro-3,3-dimethylbutanoic acid (47 mg, 0.28 mmol) and HATU (105 mg, 0,28 mmol) in DMA (1 mL) was added to a mixture of N-{4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide (24; 50 mg, 0.14 mmol) and DIPEA (48 µL, 0.28 mmol) in DMA (1 mL) and stirred for 1 h at RT. The mixture was concentrated and purified by preparative HPLC (basic method) to give the title compound (45 mg, 60%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.22 (3H), 1.24 (3H), 2.09 (3H), 2.63 (1H), 2.72 (1H), 4.17 (2H), 4.89 (2H), 6.56 (2H), 6.59 (1H), 7.02 (2H), 7.23 (1H), 7.43 (1H), 8.13 (1H), 8.28 (1H), 10.41 (1H), 12.19+12.25 (1H)

Example 220

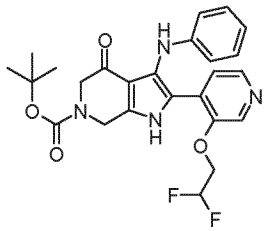
tert-Butyl 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

220-1: tert-Butyl 5-({[3-(2,2-difluoroethoxy)pyridin-4-yl]methyl}amino)-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-Butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 4.00 g, 11.5 mmol) and 1-[3-(2,2-difluoroethoxy)pyridin-4-yl]methanamine (4.32 g, 23.0 mmol) in DMA (30 mL) was heated at 120℃ for 2 h. The mixture was concentrated and purified by repeated Biotage (SNAP silica 340 g, MeOH:DCM) to give the title compound (3.80 g, 64%).

tert-Butyl 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



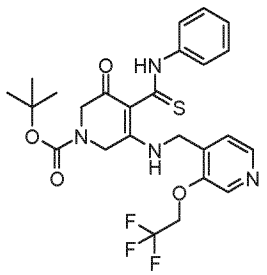
A mixture of tert-butyl 5-({[3-(2,2-difluoroethoxy)pyridin-4-yl]methyl}amino)-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (220-1; 3.59 g, 6.92 mmol), hydrogen peroxide (30% in water, 1.4 mL, 13.8 mmol) in MeOH (110 mL) was stirred at 80℃ for 16 h. The mixture was concentrated and purified by Biotage (SNAP silica 110 g, EtOH:DCM) to give the title compound (1.31 g, 39%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.44 (9H), 4.02 (2H), 4.40 (2H), 4.74 (2H), 6.29 (1H), 6.53 (2H), 6.57 (1H), 6.98 (2H), 7.33 (1H), 7.39 (1H), 8.16 (1H), 8.43 (1H), 11.64 (1H)

Example 221

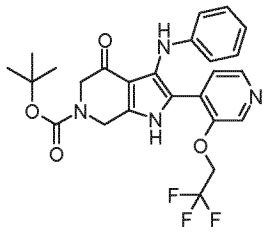
tert-Butyl 3-anilino-4-oxo-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

221-1: tert-Butyl 3-oxo-4-(phenylcarbamothioyl)-5-({[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]methyl}amino)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-Butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 4.00 g, 11.5 mmol) and 1-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]methanamine (4.73 g, 23.0 mmol) in DMA (30 mL) was heated at 120℃ for 2 h. The mixture was concentrated and purified by Biotage (SNAP silica 340 g, EtOAc:Hexane) to give the title compound (4.24 g, 69%).

tert-Butyl 3-anilino-4-oxo-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



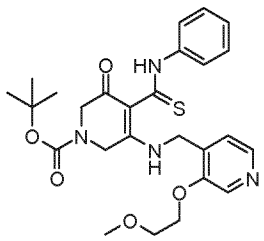
A mixture of tert-butyl 3-oxo-4-(phenylcarbamothioyl)-5-({[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]methyl}amino)-3,6-dihydropyridine-1(2H)-carboxylate (221-1; 4.13 g, 7.70 mmol), hydrogen peroxide (30% in water, 1.57 mL, 15.4 mmol) in MeOH (120 mL) was stirred at 80℃ for 16 h. The mixture was concentrated and pur ified by Biotage (SNAP silica 110 g, EtOH:DCM) to give the title compound (1.61 g, 42%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.44 (9H), 4.02 (2H), 4.72 (2H), 4.88 (2H), 6.51 (2H), 6.57 (1H), 6.97 (2H), 7.31 (1H), 7.32 (1H), 8.18 (1H), 8.51 (1H), 11.67 (1H)

Example 222

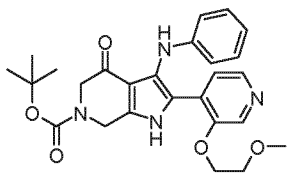
tert-Butyl 3-anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

222-1: tert-Butyl 5-({[3-(2-methoxyethoxy)pyridin-4-yl]methyl}amino)-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-Butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 4.00 g, 11.5 mmol) and 1-[3-(2-methoxyethoxy)pyridin-4-yl]methanamine (4.18 g, 23.0 mmol) in DMA (30 mL) was heated at 120℃ for 2 h. The mixture was concentrated and purified by Biotage (SNAP silica 100 g, EtOAc:Hexane) to give the title compound (3.11 g, 53%).

tert-Butyl 3-anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



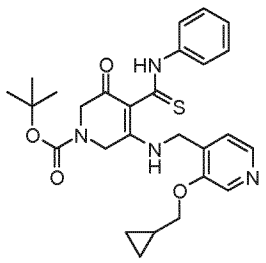
A mixture of tert-butyl 5-({[3-(2-methoxyethoxy)pyridin-4-yl]methyl}amino)-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (222-1; 2.90 g, 5.66 mmol), hydrogen peroxide (30% in water, 1.16 mL, 11.3 mmol) in MeOH (90 mL) was stirred at 80℃ for 16 h. The mixture was concentrated and pur ified by Biotage (SNAP silica 110 g, EtOH:DCM) to give the title compound (1.26 g, 47%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.44 (9H), 3.36 (3H), 3.73 (2H), 4.02 (2H), 4.30 (2H), 4.74 (2H), 6.54 (2H), 6.58 (1H), 7.00 (2H), 7.34 (1H), 7.36 (1H), 8.09 (1H), 8.43 (1H), 11.56 (1H)

Example 223

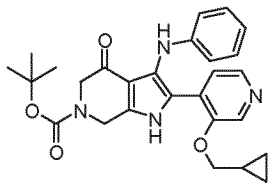
tert-Butyl 3-anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

223-1: tert-Butyl 5-({[3-(cyclopropylmethoxy)pyridin-4-yl]methyl}amino)-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-Butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 4.00 g, 11.5 mmol) and 1-[3-(cyclopropylmethoxy)pyridin-4-yl]methanamine (4.09 g, 23.0 mmol) in DMA (30 mL) was heated at 120℃ for 2 h. The mixture was concentrated and purified by Biotage (SNAP silica 100 g, EtOAc:Hexane) to give the title compound (3.66 g, 63%).

tert-Butyl 3-anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

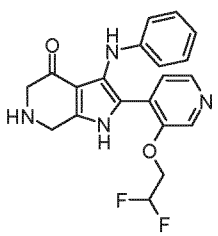


A mixture of tert-butyl 5-({[3-(cyclopropylmethoxy)pyridin-4-yl]methyl}amino)-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (223-1; 3.45 g, 6.78 mmol), hydrogen peroxide (30% in water, 1.39 mL, 13.6 mmol) in MeOH (100 mL) was stirred at 80℃ for 16 h. The mixture was concentrated and purified by Biotage (SNAP silica 110 g, EtOH:DCM) to give the title compound (1.09 g, 34%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.34 (2H), 0.54 (2H), 1.28 (1H), 1.44 (9H), 3.99 (2H), 4.01 (2H), 4.74 (2H), 6.54 (2H), 6.57 (1H), 6.99 (2H), 7.32 (2H), 8.07 (1H), 8.37 (1H), 11.61 (1H)

Example 224

3-Anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

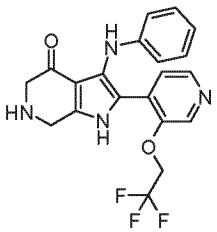


To a solution of tert-butyl 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (220; 1.30 g, 2.68 mmol) in DCM (75 mL) was added TFA (3.1 mL) and the mixture was stirred at RT for 16h. The mixture was poured into ammonia (25% in water) and extracted with DCM/methanol. The organic layer was washed with water and dried over sodium sulphate. After filtration and concentration, the residue was purified by Biotage (SNAP silica 110 g, EtOH:DCM) to give the title compound (529 mg, 51%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.22 (3H), 3.95 (2H), 4.36 (2H), 6.29 (1H), 6.52-6.59 (3H), 6.97 (2H), 7.31 (1H), 7.36 (1H), 8.13 (1H), 8.40 (1H), 11.34 (1H)

Example 225

3-Anilino-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

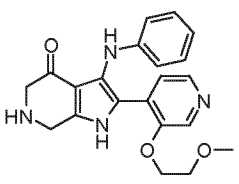


To a solution of tert-butyl 3-anilino-4-oxo-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (221; 1.60 g, 3.18 mmol) in DCM (90 mL) was added TFA (3.7 mL) and the mixture was stirred at RT for 16h. The mixture was poured into ammonia (25% in water) and extracted with DCM/methanol. The organic layer was washed with water and dried over sodium sulphate. After filtration and concentration, the residue was purified by Biotage (SNAP silica 110 g, EtOH:DCM) to give the title compound (511 mg, 40%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.22 (2H), 3.93 (2H), 4.85 (2H), 6.53 (2H), 6.56 (1H), 6.97 (2H), 7.28 (1H), 7.30 (1H), 8.16 (1H), 8.48 (1H), 11.35 (1H)

Example 226

3-Anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

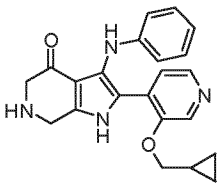


To a solution of tert-butyl 3-anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (222; 1.25 g, 2.61 mmol) in DCM (75 mL) was added TFA (3.0 mL) and the mixture was stirred at RT for 16h. The mixture was poured into ammonia (25% in water) and extracted with DCM/methanol. The organic layer was washed with water and dried over sodium sulphate. After filtration and concentration, the residue was purified by Biotage (SNAP silica 110 g, EtOH:DCM) to give the title compound (367 mg, 37%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.21 (2H), 3.38 (3H), 3.74 (2H), 3.95 (2H), 4.30 (2H), 6.54-6.60 (3H), 6.99 (2H), 7.31-7.35 (2H), 8.06 (1H), 8.40 (1H), 11.22 (1H)

Example 227

3-Anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

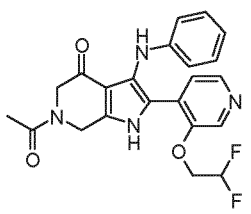


To a solution of tert-butyl 3-anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (223; 1.08 g, 2.28 mmol) in DCM (65 mL) was added TFA (2.6 mL) and the mixture was stirred at RT for 16h. The mixture was poured into ammonia (25% in water) and extracted with DCM/methanol. The organic layer was washed with water and dried over sodium sulphate. After filtration and concentration, the residue was purified by Biotage (SNAP silica 110 g, EtOH:DCM) to give the title compound (325 mg, 38%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.34 (2H), 0.56 (2H), 1.28 (1H), 3.21 (2H), 3.92-3.99 (4H), 6.53-6.59 (3H), 6.98 (2H), 7.27-7.31 (2H), 8.05 (1H), 8.34 (1H), 11.31 (1H)

Example 228

6-Acetyl-3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

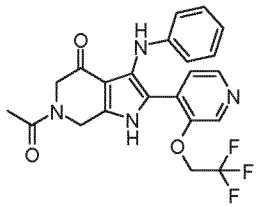


To a solution of 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (224; 50 mg, 130 µmol) in pyridine (53 µL) and THF (2.0 mL) was added acetyl chloride (18 µL, 260 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (25 mg, 42%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.10+2.16 (3H), 4.14+4.15 (2H), 4.40 (2H), 4.83+4.84 (2H), 6.27+6.29 (1H), 6.54 (2H), 6.57 (1H), 6.98 (2H), 7.34 (1H), 7.38+4.39 (1H), 8.15+8.17 (1H), 8.43+8.44 (1H), 11.65 (1H)

Example 229

6-Acetyl-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

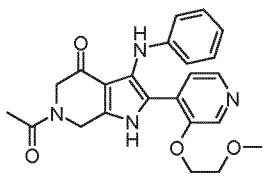


To a solution of 3-anilino-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (225; 50 mg, 124 µmol) in pyridine (50 µL) and THF (2.0 mL) was added acetyl chloride (18 µL, 260 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (26 mg, 45%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.09+2.15 (3H), 4.14+4.15 (2H), 4.81+4.83 (2H), 4.88 (2H), 6.53 (2H), 6.57 (1H), 6.98 (2H), 7.30+7.32 (1H), 7.33 (1H), 8.17-8.20 (1H), 8.51 (1H), 11.68 (1H)

Example 230

6-Acetyl-2-[3-(2-methoxyethoxy)pyridin-4-yl]-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



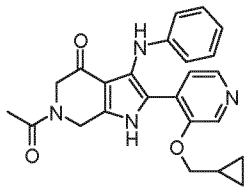
To a solution of 3-anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (226; 70 mg, 185 µmol) in pyridine (75 µL) and THF (3.0 mL)

was added acetyl chloride (26 µL, 370 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (37 mg, 46%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.09+2.17 (3H), 3.36 (3H), 3.73 (2H), 4.13+4.15 (2H), 4.30 (2H), 4.83+4.85 (2H), 6.55 (2H), 6.58 (1H), 7.00 (2H), 7.30-7.37 (2H), 8.08-8.11 (1H), 8.42+8.43 (1H), 11.54+11.58 (1H)

Example 231

6-Acetyl-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

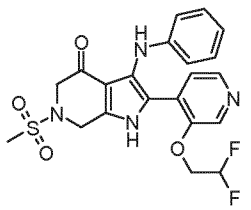


To a solution of 3-anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (227; 50 mg, 134 µmol) in pyridine (54 µL) and THF (2.0 mL) was added acetyl chloride (19 µL, 267 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (26 mg, 45%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.34 (2H), 0.55 (2H), 1.28 (1H), 2.09+2.16 (3H), 3.96-4.02 (2H), 4.14+4.15 (2H), 4.83+4.85 (2H), 6.55 (2H), 6.57 (1H), 6.99 (2H), 7.29-7.36 (2H), 8.05-8.09 (1H), 8.37+8.38 (1H), 11.62 (1H)

Example 232

3-Anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-6-(methylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



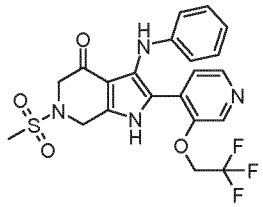
To a solution of 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (224; 50 mg, 130 µmol) in pyridine (1.5 mL) was added methylsulfonyl chloride (20 µL, 260 µmol) and stirred for 2 h at RT. MeOH was added and

the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (29 mg, 46%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.02 (3H), 3.89 (2H), 4.42 (2H), 4.64 (2H), 6.28 (1H), 6.54 (2H), 6.58 (1H), 7.00 (2H), 7.37 (1H), 7.41 (1H), 8.17 (1H), 8.45 (1H), 11.71 (1H)

Example 233

6-(Methylsulfonyl)-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

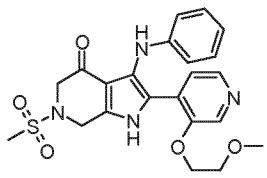


To a solution of 3-anilino-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (225; 50 mg, 124 µmol) in pyridine (1.5 mL) was added methylsulfonyl chloride (19 µL, 249 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (32 mg, 50%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.00 (3H), 3.89 (2H), 4.62 (2H), 4.90 (2H), 6.52 (2H), 6.57 (1H), 6.99 (2H), 7.32-7.37 (2H), 8.20 (1H), 8.53 (1H), 11.76 (1H)

Example 234

2-[3-(2-Methoxyethoxy)pyridin-4-yl]-6-(methylsulfonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

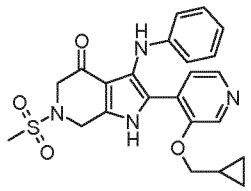


To a solution of 3-anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (226; 70 mg, 185 µmol) in pyridine (2.0 mL) was added methylsulfonyl chloride (29 µL, 370 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (38 mg, 43%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.02 (3H), 3.34 (3H), 3.72 (2H), 3.88 (2H), 4.30 (2H), 4.64 (2H), 6.54 (2H), 6.58 (1H), 7.01 (2H), 7.34 (1H), 7.38 (1H), 8.11 (1H), 8.44 (1H), 11.65 (1H)

Example 235

2-[3-(Cyclopropylmethoxy)pyridin-4-yl]-6-(methylsulfonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

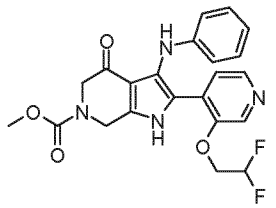


To a solution of 3-anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (227; 50 mg, 134 µmol) in pyridine (1.5 mL) was added methylsulfonyl chloride (21 µL, 267 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (33 mg, 53%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.34 (2H), 0.55 (2H), 1.28 (1H), 3.02 (3H), 3.88 (2H), 4.00 (2H), 4.64 (2H), 6.55 (2H), 6.58 (1H), 7.00 (2H), 7.33-7.37 (2H), 8.09 (1H), 8.39 (1H), 11.69 (1H)

Example 236

Methyl 2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

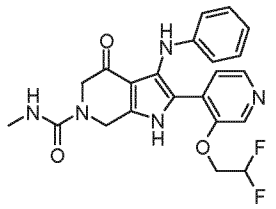


To a solution of 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (224; 50 mg, 130 µmol) in pyridine (1.5 mL) was added methyl carbonochloridate (20 µL, 260 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (34 mg, 55%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.68 (3H), 4.07 (2H), 4.40 (2H), 4.79 (2H), 6.29 (1H), 6.53 (2H), 6.57 (1H), 6.98 (2H), 7.35 (1H), 7.39 (1H), 8.16 (1H), 8.43 (1H), 11.63 (1H)

Example 237

2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-N-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

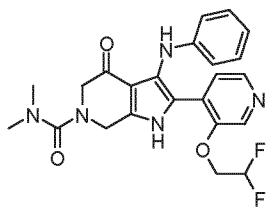


To a solution of 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (224; 50 mg, 130 µmol) in pyridine (1.5 mL) was added methylcarbamic chloride (24 mg, 260 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (26 mg, 44%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.59 (3H), 3.99 (2H), 4.38 (2H), 4.69 (2H), 6.28 (1H), 6.53 (2H), 6.57 (1H), 6.79 (1H), 6.98 (2H), 7.34 (1H), 7.36 (1H), 8.15 (1H), 8.42 (1H), 11.60 (1H)

Example 238

2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

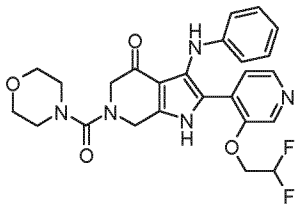


To a solution of 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (224; 50 mg, 130 µmol) in pyridine (1.5 mL) was added dimethylcarbamic chloride (24 µL, 260 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (16 mg, 26%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.79 (6H), 3.80 (2H), 4.38 (2H), 4.58 (2H), 6.30 (1H), 6.53 (2H), 6.57 (1H), 6.97 (2H), 7.33 (1H), 7.38 (1H), 8.14 (1H), 8.41 (1H), 11.52 (1H)

Example 239

2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-6-(morpholin-4-ylcarbonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

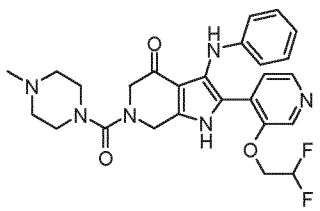


To a solution of 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (224; 50 mg, 130 µmol) in pyridine (1.5 mL) was added morpholine-4-carbonyl chloride (30 µL, 260 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (34 mg, 49%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.20 (4H), 3.60 (4H), 3.85 (2H), 4.37 (2H), 4.63 (2H), 6.29 (1H), 6.52 (2H), 6.57 (1H), 6.97 (2H), 7.33 (1H), 7.41 (1H), 8.15 (1H), 8.41 (1H), 11.56 (1H)

Example 240

2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-6-[(4-methylpiperazin-1-yl)carbonyl]-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

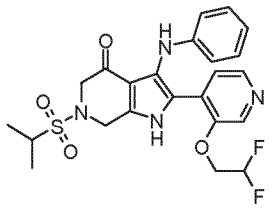


To a solution of 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (224; 50 mg, 130 µmol) in pyridine (1.5 mL) was added 4-methylpiperazine-1-carbonyl chloride (35 µL, 260 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (35 mg, 49%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.19 (3H), 2.29-2.35 (4H), 3.20 (4H), 3.83 (2H), 4.37 (2H), 4.61 (2H), 6.30 (1H), 6.52 (2H), 6.57 (1H), 6.97 (2H), 7.33 (1H), 7.38 (1H), 8.15 (1H), 8.41 (1H), 11.55 (1H)

Example 241

2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-3-(phenylamino)-6-(propan-2-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

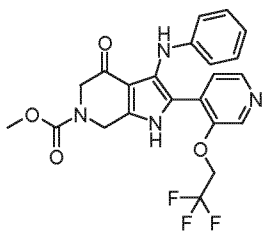


To a solution of 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (224; 50 mg, 130 µmol) in pyridine (1.5 mL) was added propane-2-sulfonyl chloride (29 µL, 260 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (38 mg, 56%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.23 (6H), 3.41 (1H), 3.97 (2H), 4.42 (2H), 4.74 (2H), 6.30 (1H), 6.54 (2H), 6.58 (1H), 6.99 (2H), 7.36 (1H), 7.42 (1H), 8.16 (1H), 8.44 (1H), 11.64 (1H)

Example 242

Methyl 4-oxo-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

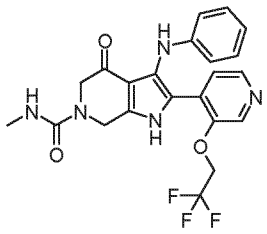


To a solution of 3-anilino-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (225; 50 mg, 124 µmol) in pyridine (1.5 mL) was added methyl carbonochloridate (20 µL, 260 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (27 mg, 45%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.67 (3H), 4.07 (2H), 4.78 (2H), 4.88 (2H), 6.52 (2H), 6.57 (1H), 6.98 (2H), 7.31 (1H), 7.34 (1H), 8.18 (1H), 8.52 (1H), 11.66 (1H)

Example 243

N-Methyl-4-oxo-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

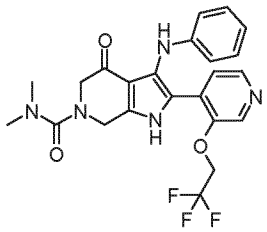


To a solution of 3-anilino-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (225; 50 mg, 124 µmol) in pyridine (1.5 mL) was added methylcarbamic chloride (23 mg, 249 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (25 mg, 42%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.59 (3H), 3.99 (2H), 4.68 (2H), 4.86 (2H), 6.51 (2H), 6.56 (1H), 6.78 (1H), 6.97 (2H), 7.28 (1H), 7.32 (1H), 8.18 (1H), 8.50 (1H), 11.62 (1H)

Example 244

N,N-Dimethyl-4-oxo-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

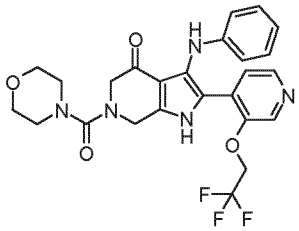


To a solution of 3-anilino-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (225; 50 mg, 124 µmol) in pyridine (1.4 mL) was added dimethylcarbamic chloride (23 µL, 249 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (23 mg, 37%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.79 (6H), 3.80 (2H), 4.57 (2H), 4.86 (2H), 6.52 (2H), 6.56 (1H), 6.97 (2H), 7.30 (1H), 7.32 (1H), 8.17 (1H), 8.50 (1H), 11.53 (1H)

Example 245

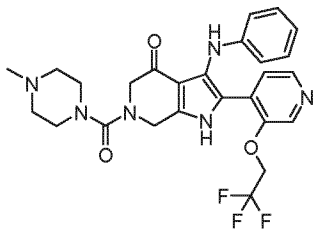
6-(Morpholin-4-ylcarbonyl)-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



To a solution of 3-anilino-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (225; 50 mg, 124 µmol) in pyridine (1.5 mL) was added morpholine-4-carbonyl chloride (29 µL, 249 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (33 mg, 49%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.19 (4H), 3.60 (4H), 3.85 (2H), 4.62 (2H), 4.86 (2H), 6.51 (2H), 6.56 (1H), 6.97 (2H), 7.31 (1H), 7.32 (1H), 8.17 (1H), 8.50 (1H), 11.58 (1H)

Example 246

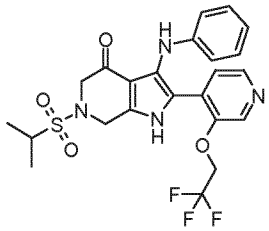
6-[(4-Methylpiperazin-1-yl)carbonyl]-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one



To a solution of 3-anilino-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (225; 50 mg, 124 µmol) in pyridine (1.4 mL) was added 4-methylpiperazine-1-carbonyl chloride (34 µL, 249 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (36 mg, 52%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.19 (3H), 2.32 (4H), 3.19 (4H), 3.82 (2H), 4.60 (2H), 4.86 (2H), 6.51 (2H), 6.56 (1H), 6.97 (2H), 7.29-7.33 (2H), 8.17 (1H), 8.50 (1H), 11.56 (1H)

Example 247

3-(Phenylamino)-6-(propan-2-ylsulfonyl)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

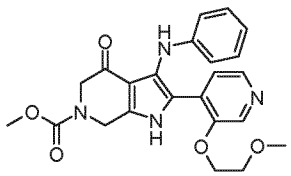


To a solution of 3-anilino-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (225; 50 mg, 124 µmol) in pyridine (1.4 mL) was added propane-2-sulfonyl chloride (28 µL, 249 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (31 mg, 46%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.21 (6H), 3.29-3.44 (1H), 3.97 (2H), 4.72 (2H), 4.89 (2H), 6.52 (2H), 6.57 (1H), 6.98 (2H), 7.33-7.36 (2H), 8.18 (1H), 8.52 (1H), 11.68 (1H)

Example 248

Methyl 2-[3-(2-methoxyethoxy)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

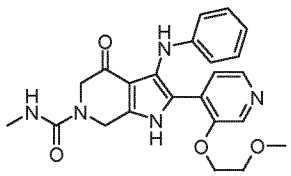


To a solution of 3-anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (226; 70 mg, 185 µmol) in pyridine (2.0 mL) was added methyl carbonochloridate (29 µL, 370 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (29 mg, 34%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.35 (3H), 3.68 (3H), 3.72 (2H), 4.06 (2H), 4.30 (2H), 4.79 (2H), 6.54 (2H), 6.58 (1H), 6.97-7.02 (2H), 7.33 (1H), 7.36 (1H), 8.10 (1H), 8.43 (1H), 11.56 (1H)

Example 249

2-[3-(2-Methoxyethoxy)pyridin-4-yl]-N-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

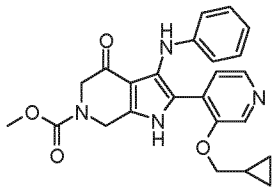


To a solution of 3-anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (226; 70 mg, 185 µmol) in pyridine (2.0 mL) was added methylcarbamic chloride (35 mg, 370 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (38 mg, 44%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.59 (3H), 3.37 (3H), 3.73 (2H), 3.99 (2H), 4.30 (2H), 4.70 (2H), 6.53 (2H), 6.57 (1H), 6.80 (1H), 6.99 (2H), 7.31 (1H), 7.35 (1H), 8.09 (1H), 8.42 (1H), 11.50 (1H)

Example 250

Methyl 2-[3-(cyclopropylmethoxy)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

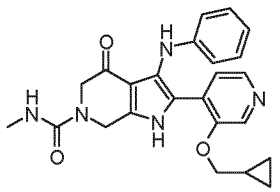


To a solution of 3-anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (227; 50 mg, 134 µmol) in pyridine (1.5 mL) was added methyl carbonochloridate (21 µL, 267 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (30 mg, 49%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.34 (2H), 0.55 (2H), 1.28 (1H), 3.68 (3H), 3.99 (2H), 4.06 (2H), 4.80 (2H), 6.54 (2H), 6.57 (1H), 6.96-7.19 (2H), 7.30-7.35 (2H), 8.07 (1H), 8.38 (1H), 11.60 (1H)

Example 251

2-[3-(Cyclopropylmethoxy)pyridin-4-yl]-N-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

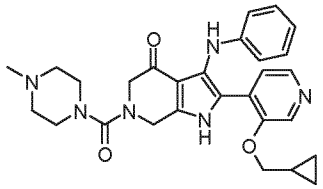


To a solution of 3-anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (227; 50 mg, 134 µmol) in pyridine (1.5 mL) was added methylcarbamic chloride (25 mg, 267 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (30 mg, 50%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.34 (2H), 0.55 (2H), 1.28 (1H), 2.59 (3H), 3.96-4.01 (4H), 4.70 (2H), 6.54 (2H), 6.57 (1H), 6.78 (1H), 6.98 (2H), 7.29 (1H), 7.32 (1H), 8.07 (1H), 8.36 (1H), 11.57 (1H)

Example 252

2-[3-(Cyclopropylmethoxy)pyridin-4-yl]-6-[(4-methylpiperazin-1-yl)carbonyl]-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

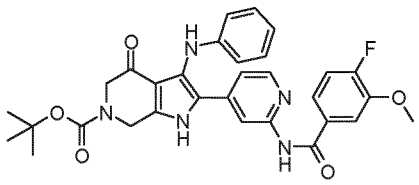


To a solution of 3-anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (227; 50 mg, 134 µmol) in pyridine (1.5 mL) was added 4-methylpiperazine-1-carbonyl chloride (36 µL, 267 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (30 mg, 42%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.34 (2H), 0.55 (2H), 1.28 (1H), 2.19 (3H), 2.32 (4H), 3.20 (4H), 3.82 (2H), 3.97 (2H), 4.62 (2H), 6.53 (2H), 6.57 (1H), 6.98 (2H), 7.29-7.34 (2H), 8.06 (1H), 8.36 (1H), 11.51 (1H)

Example 253

tert-Butyl 2-2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

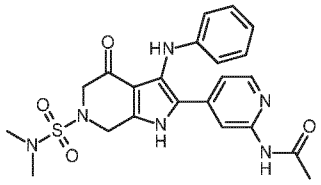


A solution of 4-fluoro-3-methoxybenzoic acid (2.03 g, 11.9 mmol) and HATU (4.53 g, 11.9 mmol) in DMA (40 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 2.00 g, 4.77 mmol) and DIPEA (2.08 mL, 11.9 mmol) in DMA (40 mL) and stirred for 16 h at 50℃. The mixture was concentrated and purified by Biotage (SNAP NH 110g, EtOH:DCM) to give the title compound (2.24 g, 82%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 3.95 (3H), 4.02 (2H), 4.76 (2H), 6.56-6.63 (3H), 7.03 (2H), 7.32 (1H), 7.37 (1H), 7.47 (1H), 7.66 (1H), 7.87 (1H), 8.24 (1H), 8.40 (1H), 10.85 (1H), 12.30 (1H)

Example 254

N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide



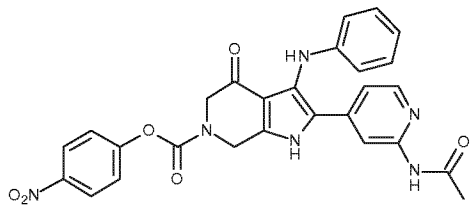
To a solution of N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide (24; 50 mg, 138 µmol) in pyridine (1.5 mL) was added dimethylsulfamyl chloride (30 µL, 249 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (42 mg, 62%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 2.70 (6H), 3.88 (2H), 4.69 (2H), 6.56 (2H), 6.59 (1H), 7.02 (2H), 7.23 (1H), 7.45 (1H), 8.13 (1H), 8.28 (1H), 10.41 (1H), 12.22 (1H)

Example 255

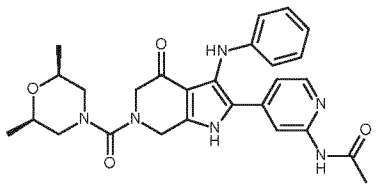
N-4-[6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]carbonyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide

255-1: 4-Nitrophenyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



To a solution of N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide (24; 100 mg, 277 µmol) in pyridine (4.0 mL) was added 4-nitrophenyl carbonochloridate (67 mg, 332 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was used without further purification.

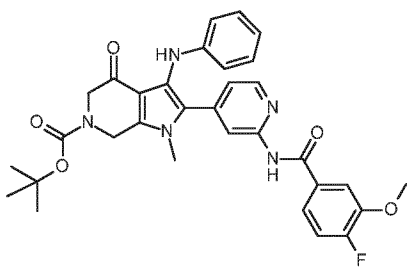
N-4-[6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]carbonyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide



A mixture comprising 4-nitrophenyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (255-1; 140 mg, 266 µmol), potassium carbonate (110 mg), DMA (3.0 mL) and (2R,6S)-2,6-dimethylmorpholine (66 µL) was stirred for 16 h at 60℃. The crude product was pur ified by preparative HPLC (basic method) and crystallized from methanol to give the title compound (31 mg, 22%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.07 (6H), 2.08 (3H), 2.51 (2H), 3.44-3.60 (4H), 3.81 (2H), 4.62 (2H), 6.55 (2H), 6.59 (1H), 7.01 (2H), 7.19 (1H), 7.40 (1H), 8.11 (1H), 8.25 (1H), 10.39 (1H), 12.09 (1H)

Example 256

tert-Butyl 2-2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl-1-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

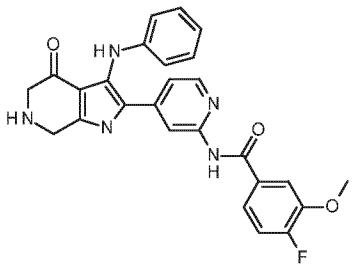


To a solution of tert-butyl 2-2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (253; 67 mg, 116 µmol) in THF (2.0 mL) was added sodium hydride (4.7 mg, 60%) followed by iodomethane (81 µL). The mixture was stirred for 16 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (36 mg, 50%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.46 (9H), 3.65 (3H), 3.95 (3H), 4.02 (2H), 4.81 (2H), 6.51 (2H), 6.53 (1H), 6.96 (2H), 7.13 (1H), 7.28 (1H), 7.35 (1H), 7.65 (1H), 7.85 (1H), 8.18 (1H), 8.34 (1H), 10.96 (1H)

Example 257

4-Fluoro-3-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide

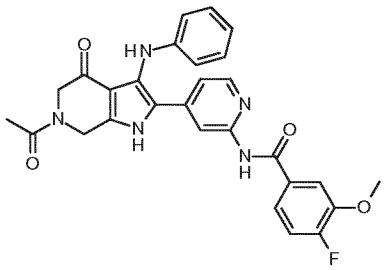


To a solution of tert-butyl 2-2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (253; 2.23 g, 3.90 mmol) in DCM (100 mL) was added TFA (4.5 mL) and stirred at RT for 16h. The mixture was poured into aqueous ammonia (25%), extracted with DCM/MeOH and dried over sodium sulfate. After filtration and concentration the residue was crystallized from ethanol to give the title compound (1.21 g, 66%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.24 (2H), 3.95 (3H), 3.99 (2H), 6.58-6.64 (3H), 7.04 (2H), 7.29 (1H), 7.36 (1H), 7.42 (1H), 7.65 (1H), 7.86 (1H), 8.21 (1H), 8.37 (1H), 10.80 (1H), 12.01 (1H)

Example 258

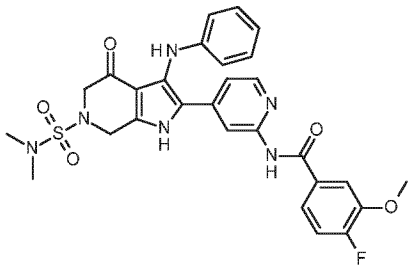
N-4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-3-methoxybenzamide



To a solution of 4-fluoro-3-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (257; 50 mg, 106 µmol) in pyridine (1.5 mL) was added acetyl chloride (15 µL, 212 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (32 mg, 56%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08+2.17 (3H), 3.94 (3H), 4.12+4.14 (2H), 4.85 (2H), 6.56-6.63 (3H), 7.03 (2H), 7.28-7.40 (2H), 7.46 (1H), 7.64 (1H), 7.86 (1H), 8.23 (1H), 8.40 (1H), 10.83 (1H), 12.30 (1H)

Example 259

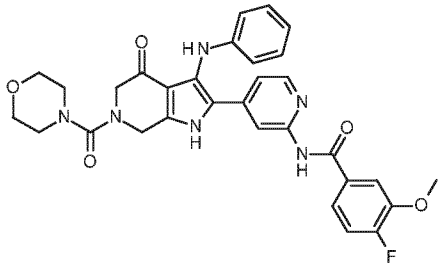
N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-3-methoxybenzamide



To a solution of 4-fluoro-3-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (257; 50 mg, 106 µmol) in pyridine (1.5 mL) was added dimethylsulfamyl chloride (23 µL, 212 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (41 mg, 63%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.71 (6H), 3.89 (2H), 3.95 (3H), 4.70 (2H), 6.57-6.63 (3H), 7.03 (2H), 7.31-7.39 (2H), 7.51 (1H), 7.65 (1H), 7.86 (1H), 8.23 (1H), 8.40 (1H), 10.85 (1H), 12.30 (1H)

Example 260

4-Fluoro-3-methoxy-N-4-[6-(morpholin-4-ylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide



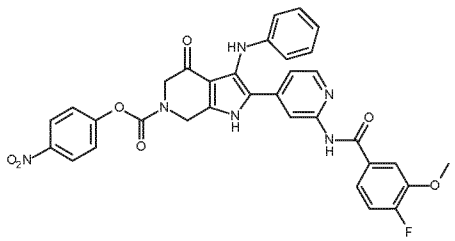
To a solution of 4-fluoro-3-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (257; 50 mg, 106 µmol) in pyridine (1.5 mL) was added morpholine-4-carbonyl chloride (25 µL, 212 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by crystallization from MeOH to give the title compound (61 mg, 93%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.20 (4H), 3.60 (4H), 3.85 (2H), 3.95 (3H), 4.66 (2H), 6.59-6.64 (3H), 7.04 (2H), 7.33-7.42 (2H), 7.57 (1H), 7.64 (1H), 7.84 (1H), 8.25 (1H), 8.28 (1H), 11.06 (1H), 12.29 (1H)

Example 261

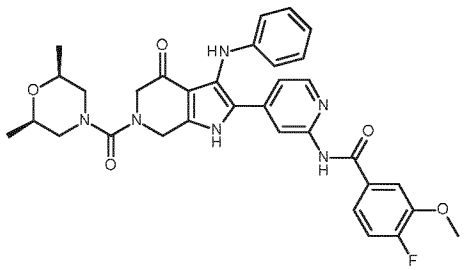
N-4-[6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]carbonyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-3-methoxybenzamide

261-1: 4-Nitrophenyl 3-anilino-2-{2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



To a solution of 4-fluoro-3-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (257; 75 mg, 159 µmol) in pyridine (2.3 mL) was added 4-nitrophenyl carbonochloridate (38 mg, 191 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was used without further purification.

N-4-[6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]carbonyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-3-methoxybenzamide

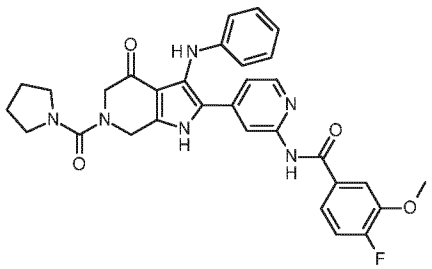


A mixture comprising 4-nitrophenyl 3-anilino-2-{2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (261-1; 101 mg, 159 µmol), potassium carbonate (66 mg), DMA (1.7 mL) and (2R,6S)-2,6-dimethylmorpholine (39 µL) was stirred for 16 h at 60℃. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (37 mg, 36%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.08 (6H), 2.51 (2H), 3.45-3.58 (4H), 3.83 (2H), 3.95 (3H), 4.64 (2H), 6.56-6.62 (3H), 7.02 (2H), 7.29 (1H), 7.36 (1H), 7.46 (1H), 7.64 (1H), 7.86 (1H), 8.22 (1H), 8.38 (1H), 10.84 (1H), 12.16 (1H)

Example 262

4-Fluoro-3-methoxy-N-4-[4-oxo-3-(phenylamino)-6-(pyrrolidin-1-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide

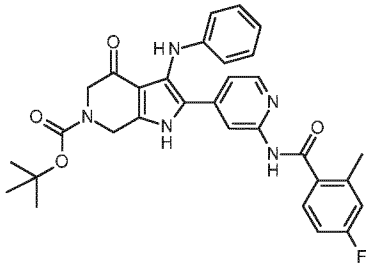


To a solution of 4-fluoro-3-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (257; 50 mg, 106 µmol) in pyridine (1.5 mL) was added pyrrolidine-1-carbonyl chloride (23 µL, 212 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (49 mg, 78%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.76 (4H), 3.30 (4H), 3.83 (2H), 3.94 (3H), 4.64 (2H), 6.56-6.62 (3H), 7.03 (2H), 7.29 (1H), 7.36 (1H), 7.44 (1H), 7.65 (1H), 7.86 (1H), 8.21 (1H), 8.38 (1H), 10.83 (1H), 12.15 (1H)

Example 263

tert-Butyl 2-2-[(4-fluoro-2-methylbenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

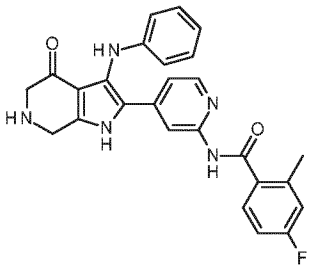


A solution of 4-fluoro-2-methylbenzoic acid (230 mg, 1.49 mmol) and HATU (567 mg, 1.49 mmol) in DMA (5 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 250 mg, 0.60 mmol) and DIPEA (260 µL, 1.49 mmol) in DMA (5 mL) and stirred for 16 h at 50°C. The mixture was concentrated and purified by Biotage (SNAP 55g, EtOAc:Hexane) to give the title compound (195 mg, 56%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 2.38 (3H), 4.01 (2H), 4.76 (2H), 6.58 (2H), 6.60 (1H), 7.03 (2H), 7.10 (1H), 7.16 (1H), 7.30 (1H), 7.47 (1H), 7.50 (1H), 8.18 (1H), 8.35 (1H), 10.71 (1H), 12.27 (1H)

Example 264

4-Fluoro-2-methyl-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide

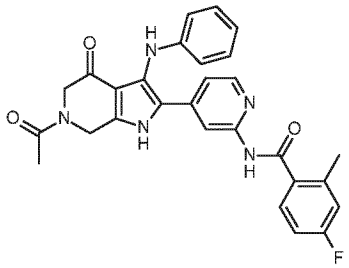


To a solution of tert-butyl 2-2-[(4-fluoro-2-methylbenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (263; 117 mg, 212 µmol) in DCM (6.0 mL) was added TFA (245 µL) and stirred at RT for 16h. The mixture was poured into aqueous ammonia (25%), extracted with DCM/MeOH and dried over sodium sulfate. After filtration and concentration the residue was crystallized from ether/hexane to give the title compound (91 mg, 89%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.38 (3H), 3.21 (2H), 3.97 (2H), 6.56-6.63 (3H), 7.02 (2H), 7.10 (1H), 7.15 (1H), 7.26 (1H), 7.41 (1H), 7.49 (1H), 8.15 (1H), 8.31 (1H), 10.65 (1H), 11.97 (1H)

Example 265

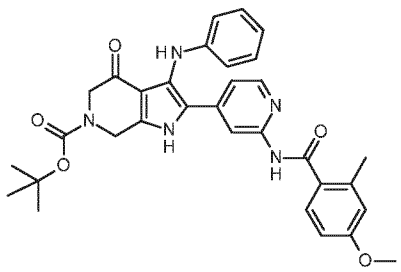
N-4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-2-methylbenzamide



To a solution of 4-fluoro-2-methyl-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (264; 35 mg, 77 µmol) in THF (1.2 mL) and pyridine (31 µL) was added acetyl chloride (11 µL, 154 µmol) and stirred for 0.5 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (26 mg, 66%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08+2.17 (3H), 2.38+2.39 (3H), 4.13+4.15 (2H), 4.85 (2H), 6.57-6.63 (3H), 7.03 (2H), 7.10 (1H), 7.16 (1H), 7.30 (1H), 7.46 (1H), 7.50 (1H), 8.18 (1H), 8.36 (1H), 10.70 (1H), 12.28 (1H)

Example 266

tert-Butyl 2-2-[(4-methoxy-2-methylbenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



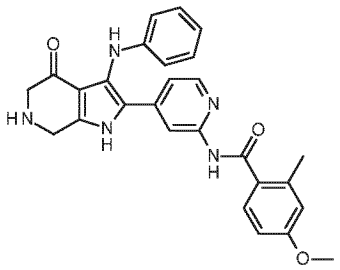
A solution of 4-methoxy-2-methylbenzoic acid (248 mg, 1.49 mmol) and HATU (567 mg, 1.49 mmol) in THF (5 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 250 mg, 0.60 mmol) and DIPEA (260 µL, 1.49 mmol) in THF (5 mL) and heated for 3.5 h at

120℃. The mixture was concentrated and purified by Biotage (SNAP 28g, EtOAc:Hexane) to give the title compound (82 mg, 23%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 2.29 (3H), 3.77 (3H), 4.01 (2H), 4.76 (2H), 6.58 (2H), 6.60 (1H), 6.94 (1H), 7.00 (1H), 7.03 (2H), 7.19 (1H), 7.29 (1H), 7.46 (1H), 8.18 (1H), 8.36 (1H), 10.65 (1H), 12.27 (1H)

Example 267

4-Methoxy-2-methyl-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide

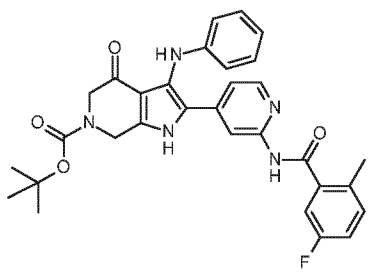


To a solution of tert-butyl 2-2-[(4-methoxy-2-methylbenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (266; 81 mg, 143 µmol) in DCM (4.1 mL) was added TFA (165 µL) and stirred at RT for 16h. The mixture was poured into aqueous ammonia (25%), extracted with DCM/MeOH and dried over sodium sulfate. After filtration and concentration the residue was crystallized from ether to give the title compound (61 mg, 86%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.39 (3H), 3.21 (2H), 3.79 (3H), 3.96 (2H), 6.56-6.63 (3H), 6.77-6.86 (2H), 7.03 (2H), 7.24 (1H), 7.39 (1H), 7.45 (1H), 8.13 (1H), 8.31 (1H), 10.44 (1H), 11.96 (1H)

Example 268

tert-Butyl 2-2-[(5-fluoro-2-methylbenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

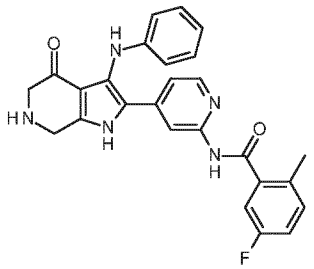


A solution of 5-fluoro-2-methylbenzoic acid (184 mg, 1.19 mmol) and HATU (453 mg, 1.19 mmol) in DMA (4 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 200 mg, 477 µmol) and DIPEA (208 µL, 1.19 mmol) in DMA (4 mL) and heated for 16 h at 50°C. The mixture was concentrated and purified by Biotage (SNAP 55g, EtOAc:Hexane) to give the title compound (20 mg, 7%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 2.32 (3H), 4.01 (2H), 4.76 (2H), 6.58 (2H), 6.60 (1H), 7.03 (2H), 7.19-7.34 (4H), 7.47 (1H), 8.19 (1H), 8.35 (1H), 10.77 (1H), 12.28 (1H)

Example 269

5-Fluoro-2-methyl-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide

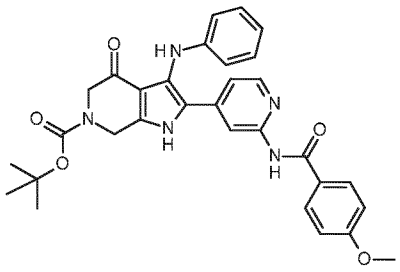


To a solution of tert-butyl 2-2-[(5-fluoro-2-methylbenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (268; 130 mg, 235 µmol) in DCM (6.7 mL) was added TFA (272 µL) and stirred at RT for 16h. The mixture was poured into aqueous ammonia (25%), extracted with DCM/MeOH and dried over sodium sulfate. After filtration and concentration the residue was crystallized from ether/hexane to give the title compound (79 mg, 70%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.32 (3H), 3.21 (2H), 3.97 (2H), 6.56-6.64 (3H), 7.03 (2H), 7.19-7.34 (4H), 7.41 (1H), 8.16 (1H), 8.31 (1H), 10.72 (1H), 11.98 (1H)

Example 270

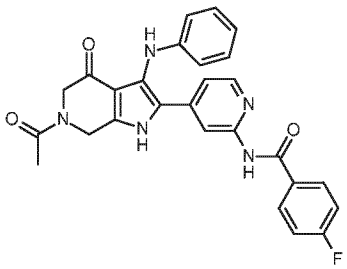
tert-Butyl 2-2-[(4-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



A solution of 4-methoxybenzoic acid (181 mg, 1.19 mmol) and HATU (453 mg, 1.19 mmol) in DMA (4 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 200 mg, 477 µmol) and DIPEA (208 µL, 1.19 mmol) in DMA (4 mL) and heated for 16 h at 50℃. The mixture was concentrated and purified by Biotage (SNAP 55g, EtOAc:Hexane) and preparative TLC (silica, EtOH:DCM) to give the title compound (22 mg, 8%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 3.84 (3H), 4.01 (2H), 4.75 (2H), 6.55-6.62 (3H), 6.99-7.07 (4H), 7.29 (1H), 7.46 (1H), 8.05 (2H), 8.20 (1H), 8.39 (1H), 10.57 (1H), 12.28 (1H)

Example 271

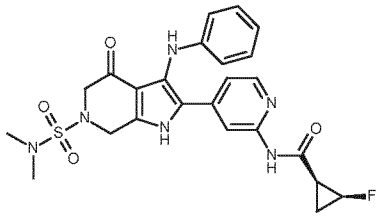
N-4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluorobenzamide



To a solution of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-4-fluorobenzamide (134; 83 mg, 187 µmol) in THF (2.8 mL) and pyridine (76 µL) was added acetyl chloride (27 µL, 374 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (51 mg, 54%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08+2.17 (3H), 4.13+4.14 (2H), 4.85 (2H), 6.56-6.63 (3H), 7.03 (2H), 7.28-7.39 (3H), 7.47 (1H), 8.11 (2H), 8.23 (1H), 8.39 (1H), 10.79 (1H), 12.30 (1H)

Example 272

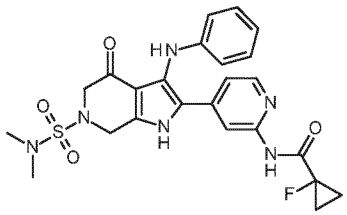
(1S,2S)-N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-2-fluorocyclopropanecarboxamide



To a solution of (1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 123 µmol) in pyridine (1.4 mL) was added dimethylsulfamyl chloride (26 µL, 247 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (48 mg, 72%). ^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.18 (1H), 1.64 (1H), 2.21 (1H), 2.69 (6H), 3.88 (2H), 4.68 (2H), 4.93 (1H), 6.57 (2H), 6.60 (1H), 7.02 (2H), 7.25 (1H), 7.47 (1H), 8.13 (1H), 8.30 (1H), 10.79 (1H), 12.25 (1H)

Example 273

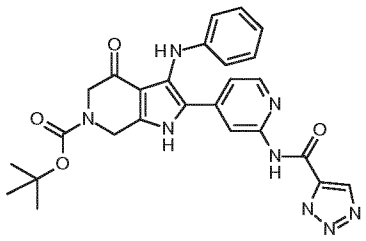
N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-1-fluorocyclopropanecarboxamide



To a solution of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-1-fluorocyclopropanecarboxamide (132; 40 mg, 99 µmol) in pyridine (1.2 mL) was added dimethylsulfamyl chloride (21 µL, 197 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (42 mg, 78%). ^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.32 (2H), 1.44 (2H), 2.70 (6H), 3.88 (2H), 4.68 (2H), 6.57 (2H), 6.60 (1H), 7.03 (2H), 7.33 (1H), 7.50 (1H), 8.17 (1H), 8.21 (1H), 10.18 (1H), 12.25 (1H)

Example 274

tert-Butyl 4-oxo-3-(phenylamino)-2-2-[(1H-1,2,3-triazol-5-ylcarbonyl)amino]pyridin-4-yl-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

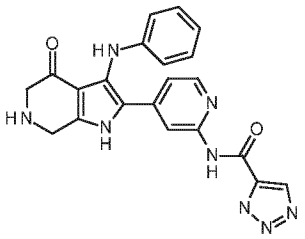


A solution of 1H-1,2,3-triazole-5-carboxylic acid (135 mg, 1.19 mmol) and HATU (453 mg, 1.19 mmol) in DMA (4 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 200 mg, 477 µmol) and DIPEA (208 µL, 1.19 mmol) in DMA (4 mL) and heated for 16 h at 50℃. The mixture was concentrated and purified by Biotage (SNAP 55g, EtOAc:Hexane) to give the title compound (113 mg, 44%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 4.01 (2H), 4.75 (2H), 6.57-6.62 (4H), 7.03 (2H), 7.31 (1H), 7.47 (1H), 8.21 (1H), 8.40 (1H), 8.58 (1H), 10.04 (1H), 12.33 (1H)

Example 275

N-4-[4-Oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-1H-1,2,3-triazole-5-carboxamide



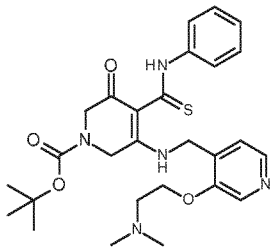
To a solution of tert-butyl 4-oxo-3-(phenylamino)-2-2-[(1H-1,2,3-triazol-5-ylcarbonyl)amino]pyridin-4-yl-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (274; 170 mg, 331 µmol) in DCM (9.4 mL) was added TFA (382 µL) and stirred at RT for 16h. The mixture was poured into aqueous ammonia (25%), the aqueous layer was adjusted to pH 5, extracted with DCM and dried over sodium sulfate. After filtration and concentration the residue was crystallized from ether/hexane to give the title compound (53 mg, 37%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.65 (2H), 4.41 (2H), 6.57-6.63 (3H), 7.03 (2H), 7.16 (1H), 7.29 (1H), 7.37 (1H), 7.41 (1H), 7.54 (1H), 8.25 (1H), 8.41 (1H), 8.67 (1H), 10.12 (1H),

Example 276

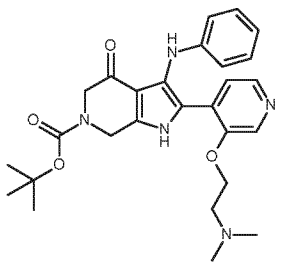
tert-Butyl 2-3-[2-(dimethylamino)ethoxy]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

276-1: tert-Butyl 5-[({3-[2-(dimethylamino)ethoxy]pyridin-4-yl}methyl)amino]-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 357 mg, 1.02 mmol) and 2-{[4-(aminomethyl)pyridin-3-yl]oxy}-N,N-dimethylethanamine (400 mg, 2.05 mmol) in DMA (3 mL) was heated at 120℃ for 1 h. The mixture was concentrated and purified by Biotage (SNAP 110g, EtOH:DCM) to give the title compound (438 mg, 81%).

tert-Butyl 2-3-[2-(dimethylamino)ethoxy]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

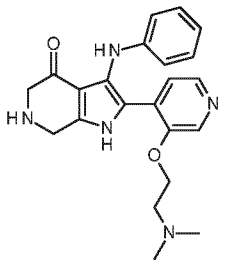


A mixture of tert-butyl 5-[({3-[2-(dimethylamino)ethoxy]pyridin-4-yl}methyl)amino]-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (276-1; 100 mg, 190 mmol), hydrogen peroxide (30% in water, 78 µL, 761 µmol), TFA (29 µL, 380 µmol) in MeOH (3.5 mL) was stirred for 16 h at 50℃. The mixture was c oncentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (25 mg, 25%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.44 (9H), 2.34 (6H), 2.74 (2H), 4.02 (2H), 4.42 (2H), 4.75 (2H), 6.57 (2H), 6.60 (1H), 7.02 (2H), 7.44 (1H), 7.50 (1H), 8.02 (1H), 8.49 (1H), 12.64 (1H)

Example 277

2-3-[2-(Dimethylamino)ethoxy]pyridin-4-yl-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

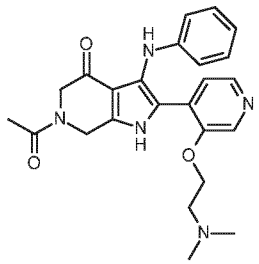


To a solution of tert-butyl 2-3-[2-(dimethylamino)ethoxy]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (276; 600 mg, 1.22 mmol) in DCM (35 mL) was added TFA (1.41 mL) and stirred at RT for 16h. The mixture was poured into aqueous ammonia (25%), extracted with DCM/MeOH and dried over sodium sulfate. After filtration and concentration the residue was purified by Biotage (SNAP 100g, EtOH:DCM) to give the title compound (265 mg, 55%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.31 (6H), 2.71 (2H), 3.22 (2H), 3.96 (2H), 4.41 (2H), 6.56-6.62 (3H), 7.01 (2H), 7.39 (1H), 7.46 (1H), 7.98 (1H), 8.46 (1H), 12.35 (1H)

Example 278

6-Acetyl-2-3-[2-(dimethylamino)ethoxy]pyridin-4-yl-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

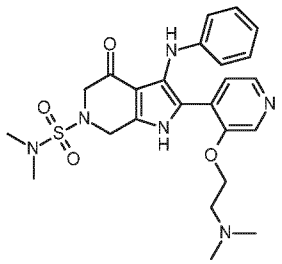


To a solution of 2-3-[2-(dimethylamino)ethoxy]pyridin-4-yl-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (277; 50 mg, 128 µmol) in THF (1.8 mL) was added pyridine (52 µL), acetyl chloride (18 µL, 255 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (22 mg, 37%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.09+2.19 (3H), 2.33+2.34 (6H), 2.73 (2H), 4.13+4.15 (2H), 4.41+4.42 (2H), 4.84 (2H), 6.53-6.62 (3H), 7.01 (2H), 7.43 (1H), 7.48 (1H), 8.02 (1H), 8.48 (1H), 12.63+12.68 (1H)

Example 279

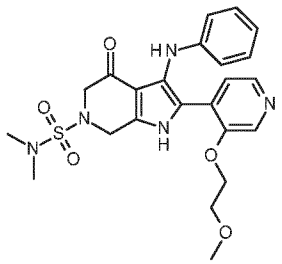
2-3-[2-(Dimethylamino)ethoxy]pyridin-4-yl-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-sulfonamide



To a solution of 2-3-[2-(dimethylamino)ethoxy]pyridin-4-yl-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (277; 50 mg, 128 µmol) in pyridine (1.5 mL) was added dimethylsulfamyl chloride (27 µL, 255 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (38 mg, 56%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.31 (6H), 2.69-2.76 (8H), 3.90 (2H), 4.40 (2H), 4.68 (2H), 6.57 (2H), 6.59 (1H), 7.02 (2H), 7.44 (1H), 7.51 (1H), 8.03 (1H), 8.48 (1H), 12.59 (1H)

Example 280

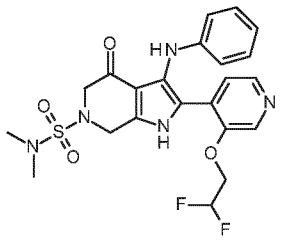
2-[3-(2-Methoxyethoxy)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-sulfonamide



To a solution of 3-anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (226; 75 mg, 198 µmol) in pyridine (2.3 mL) was added dimethylsulfamyl chloride (43 µL, 396 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (24 mg, 24%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.71 (6H), 3.33 (3H), 3.72 (2H), 3.89 (2H), 4.30 (2H), 4.69 (2H), 6.54 (2H), 6.57 (1H), 6.97-7.02 (2H), 7.33-7.38 (2H), 8.09 (1H), 8.42 (1H), 11.56 (1H)

Example 281

3-Anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-N,N-dimethyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-sulfonamide

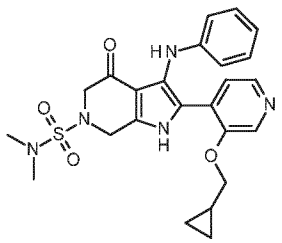


To a solution of 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (224; 50 mg, 130 µmol) in pyridine (1.5 mL) was added dimethylsulfamyl chloride (28 µL, 260 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (32 mg, 48%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.70 (6H), 3.90 (2H), 4.42 (2H), 4.70 (2H), 6.31 (1H), 6.54 (2H), 6.57 (1H), 6.98 (2H), 7.35 (1H), 7.41 (1H), 8.15 (1H), 8.44 (1H), 11.63 (1H)

Example 282

2-[3-(Cyclopropylmethoxy)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-sulfonamide

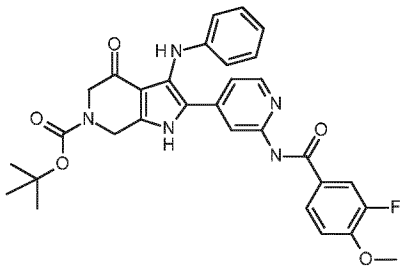


To a solution of 3-anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (227; 50 mg, 134 µmol) in pyridine (1.5 mL) was added dimethylsulfamyl chloride (29 µL, 267 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (31 mg, 46%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 0.33 (2H), 0.53 (2H), 1.27 (1H), 2.70 (6H), 3.90 (2H), 4.00 (2H), 4.70 (2H), 6.55 (2H), 6.57 (1H), 6.99 (2H), 7.31-7.39 (2H), 8.06 (1H), 8.38 (1H), 11.61 (1H)

Example 283

tert-Butyl 2-2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

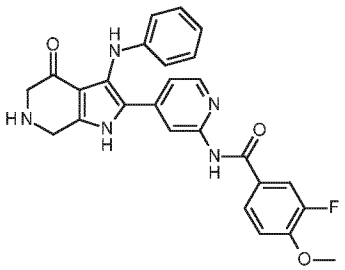


A solution of 3-fluoro-4-methoxybenzoic acid (2.03 g, 11.9 mmol) and HATU (4.53 g, 11.9 mmol) in DMA (40 mL) was added to a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (13; 2.0 g, 4.77 mmol) and DIPEA (2.08 mL, 11.9 mmol) in DMA (40 mL) and stirred for 16 h at 50°C. The mixture was concentrated and purified by Biotage (SNAP 340g, EtOH:DCM) to give the title compound (1.60 g, 58%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 3.93 (3H), 4.01 (2H), 4.75 (2H), 6.56-6.63 (3H), 7.03 (2H), 7.31 (2H), 7.46 (1H), 7.90-7.97 (2H), 8.21 (1H), 8.38 (1H), 10.68 (1H), 12.29 (1H)

Example 284

3-Fluoro-4-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide

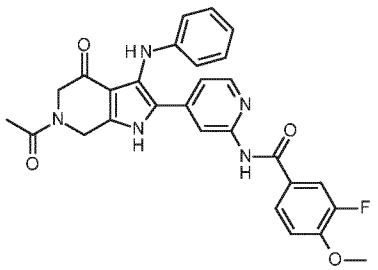


To a solution of tert-butyl 2-2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (283; 791 mg, 1.38 mmol) in DCM (35 mL) was added TFA (1.6 mL) and stirred at RT for 16h. The mixture was poured into aqueous ammonia (25%), extracted with DCM/MeOH and dried over sodium sulfate. After filtration and concentration the residue was purified by crystallization from EtOH/Ether to give the title compound (520 mg, 76%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.21 (2H), 3.93 (3H), 3.97 (2H), 6.58-6.64 (3H), 7.04 (2H), 7.27-7.33 (2H), 7.41 (1H), 7.90-7.96 (2H), 8.19 (1H), 8.34 (1H), 10.65 (1H), 11.99 (1H)

Example 285

N-4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide

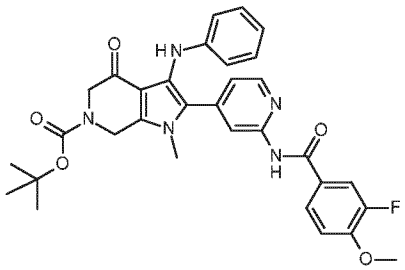


To a solution of tert-butyl 2-2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (283; 50 mg, 106 µmol) in THF (1.5 mL) was added pyridine (43 µL), acetyl chloride (15 µL, 212 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by crystallization from MeOH to give the title compound (47 mg, 82%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.09+2.17 (3H), 3.94 (3H), 4.14+4.16 (2H), 4.87 (2H), 6.61-6.67 (3H), 7.06 (2H), 7.34 (1H), 7.44 (1H), 7.70 (1H), 7.88-7.96 (2H), 8.22 (1H), 8.27+8.29 (1H), 11.19 (1H), 12.53 (1H)

Example 286

tert-Butyl 2-2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl-1-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

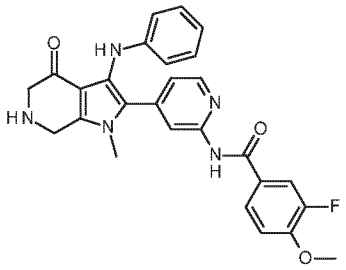


To a solution of tert-butyl 2-2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (283; 250 mg, 437 µmol) in THF (7.5 mL) was added sodium hydride (17 mg, 60%) followed by iodomethane (272 µL). The mixture was stirred for 16 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (86 mg, 32%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.45 (9H), 3.63 (3H), 3.92 (3H), 4.01 (2H), 4.80 (2H), 6.48-6.54 (3H), 6.95 (2H), 7.11 (1H), 7.24-7.32 (2H), 7.89-7.95 (2H), 8.15 (1H), 8.32 (1H), 10.80 (1H)

Example 287

3-Fluoro-4-methoxy-N-4-[1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide

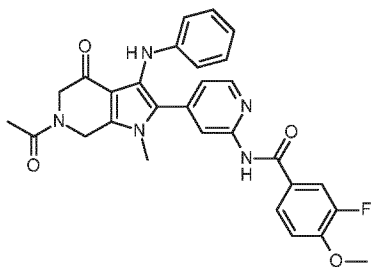


To a solution of tert-butyl 2-2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl-1-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (286; 235 mg, 401 µmol) in DCM (11 mL) was added TFA (618 µL) and stirred at RT for 16h. The mixture was poured into aqueous ammonia (25%), extracted with DCM/MeOH and dried over sodium sulfate. After filtration and concentration the residue was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (60 mg, 29%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.22 (2H), 3.58 (3H), 3.92 (3H), 4.06 (2H), 6.49-6.54 (3H), 6.94 (2H), 7.10 (1H), 7.22 (1H), 7.29 (1H), 7.89-7.95 (2H), 8.14 (1H), 8.29 (1H), 10.78 (1H)

Example 288

N-4-[6-Acetyl-1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide



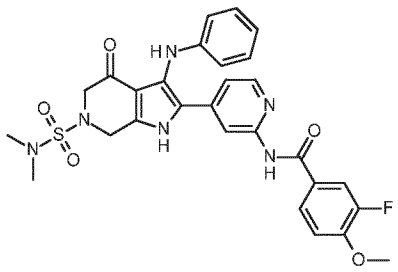
To a solution of 3-fluoro-4-methoxy-N-4-[1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (287; 35 mg, 72 µmol) in THF (1.0 mL) was added pyridine (19 µL), acetyl chloride (10 µL, 144 µmol) and stirred

for1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by crystallization from MeOH to give the title compound (26 mg, 65%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.11+2.22 (3H), 3.65+3.67 (3H), 3.92 (3H), 4.12+4.15 (2H), 4.89+4.93 (2H), 6.47-6.55 (3H), 6.95 (2H), 7.11 (1H), 7.24-7.33 (2H), 7.89-7.95 (2H), 8.15 (1H), 8.33 (1H), 10.81 (1H)

Example 289

N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide

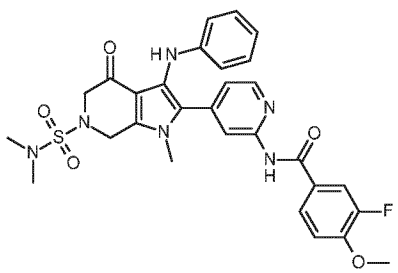


To a solution of 3-fluoro-4-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (284; 50 mg, 106 µmol) in pyridine (1.5 mL) was added dimethylsulfamyl chloride (23 µL, 212 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by crystallization from MeOH to give the title compound (54 mg, 83%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.72 (6H), 3.91 (2H), 3.94 (3H), 4.72 (2H), 6.60-6.66 (3H), 7.06 (2H), 7.34 (1H), 7.43 (1H), 7.70 (1H), 7.88-7.96 (2H), 8.23 (1H), 8.28 (1H), 11.14 (1H), 12.51 (1H)

Example 290

N-4-[6-(Dimethylsulfamoyl)-1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide

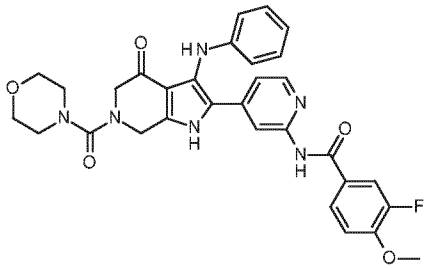


To a solution of 3-fluoro-4-methoxy-N-4-[1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (287; 35 mg, 72 µmol) in pyridine (1.0 mL) was added dimethylsulfamyl chloride (15 µL, 144 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by crystallization from MeOH to give the title compound (29 mg, 64%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.76 (6H), 3.65 (3H), 3.89 (2H), 3.92 (3H), 4.76 (2H), 6.48-6.55 (3H), 6.95 (2H), 7.12 (1H), 7.26-7.32 (2H), 7.88-7.95 (2H), 8.15 (1H), 8.33 (1H), 10.81 (1H)

Example 291

3-Fluoro-4-methoxy-N-4-[6-(morpholin-4-ylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide



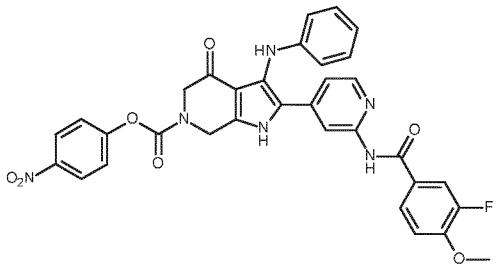
To a solution of 3-fluoro-4-methoxy-N-4-[1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (287; 50 mg, 106 µmol) in pyridine (1.5 mL) was added morpholine-4-carbonyl chloride (25 µL, 212 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by crystallization from MeOH to give the title compound (58 mg, 89%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 3.20 (4H), 3.60 (4H), 3.85 (2H), 3.93 (3H), 4.66 (2H), 6.60-6.65 (3H), 7.04 (2H), 7.31-7.38 (2H), 7.62 (1H), 7.88-7.94 (2H), 8.20-8.26 (2H), 11.03 (1H), 12.33 (1H)

Example 292

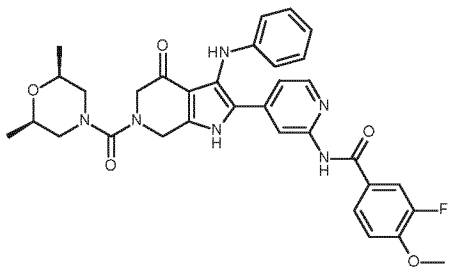
N-4-[6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]carbonyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide

292-1: 4-Nitrophenyl 3-anilino-2-{2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



To a solution of 3-fluoro-4-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (284; 75 mg, 159 µmol) in pyridine (2.3 mL) was added 4-nitrophenyl carbonochloridate (38 mg, 191 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was used without further purification.

N-4-[6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]carbonyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide

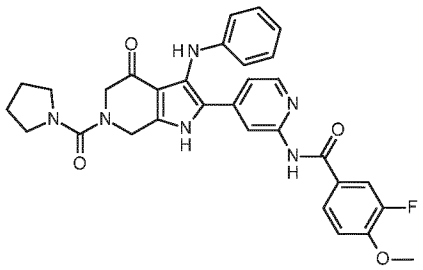


A mixture comprising 4-nitrophenyl 3-anilino-2-{2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (292-1; 101 mg, 159 µmol), potassium carbonate (66 mg), DMA (1.7 mL) and (2R,6S)-2,6-dimethylmorpholine (39 µL) was stirred for 16 h at 60℃. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (25 mg, 24%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.08 (6H), 2.53 (2H), 3.49 (2H), 3.55 (2H), 3.82 (2H), 3.93 (3H), 4.64 (2H), 6.56-6.62 (3H), 7.02 (2H), 7.26-7.33 (2H), 7.45 (1H), 7.90-7.97 (2H), 8.20 (1H), 8.35 (1H), 10.68 (1H), 12.16 (1H)

Example 293

3-Fluoro-4-methoxy-N-4-[4-oxo-3-(phenylamino)-6-(pyrrolidin-1-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide



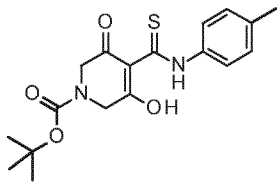
To a solution of 3-fluoro-4-methoxy-N-4-[1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (287; 50 mg, 106 µmol) in pyridine (1.5 mL) was added pyrrolidine-1-carbonyl chloride (23 µL, 212 µmol) and stirred for 1 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (48 mg, 76%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.78 (4H), 3.30 (4H), 3.83 (2H), 3.93 (3H), 4.64 (2H), 6.56-6.62 (3H), 7.03 (2H), 7.26-7.33 (2H), 7.45 (1H), 7.90-7.96 (2H), 8.20 (1H), 8.35 (1H), 10.68 (1H), 12.14 (1H)

Example 294

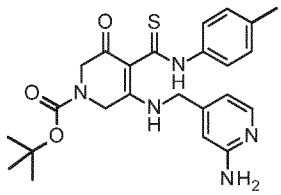
tert-butyl 2-(2-Aminopyridin-4-yl)-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

294-2: tert-Butyl 5-hydroxy-4-[(4-methylphenyl)carbamothioyl]-3-oxo-3,6-dihydropyridine-1(2H)-carboxylate



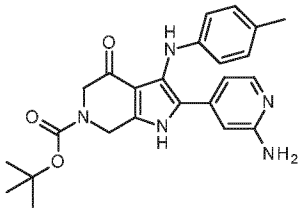
To a solution of 1-benzylpiperidine-3,5-dione (8.00 g, 37.5 mmol) and 1-isothiocyanato-4-methylbenzene (8.40 g, 56.3 mmol) in MeCN (67 mL) was added DBU (10 mL) and the mixture was stirred at RT for 16 h. The mixture was concentrated and purified by Biotage (SNAP silica 340g, EtOAc:Hexane) to give the title compound (3.76 g, 26%).

294-1: tert-Butyl 5-{[(2-aminopyridin-4-yl)methyl]amino}-4-[(4-methylphenyl)carbamothioyl]-3-oxo-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-butyl 5-hydroxy-4-[(4-methylphenyl)carbamothioyl]-3-oxo-3,6-dihydropyridine-1(2H)-carboxylate (294-2; 3.48 g, 9.59 mmol) and 4-(methylamino)pyridine (2.36 g, 19.2 mmol) in DMA (52 mL) was heated at 120℃ for 2 h. The mixture was concentrated and purified by Biotage (SNAP silica 100g, EtOAc:Hexane) to give the title compound (3.01 g, 67%).

tert-Butyl 2-(2-Aminopyridin-4-yl)-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

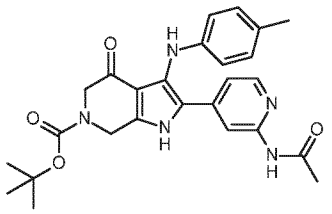


A mixture of tert-butyl 5-{[(2-aminopyridin-4-yl)methyl]amino}-4-[(4-methylphenyl)carbamothioyl]-3-oxo-3,6-dihydropyridine-1(2H)-carboxylate (294-1; 79 mg, 169 mmol), hydrogen peroxide (30% in water, 35 µL, 338 µmol), TFA (26 µL, 338 µmol) in MeOH (2.6 mL) was stirred for 16 h at 50℃. Aqueous sodium thiosulfate and TEA (49 µmol) were added and the mixture was concentrated. The residue was purified by Biotage (SNAP NH 10g, MeOH:DCM to give the title compound (24 mg, 31%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.42 (9), 2.13 (3H), 3.97 (2H), 4.71 (2H), 5.87 (2H), 6.47 (2H), 6.59 (1H), 6.70 (1H), 6.83 (2H), 7.12 (1H), 7.78 (1H), 11.98 (1H)

Example 295

tert-Butyl 2-(2-acetamidopyridin-4-yl)-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



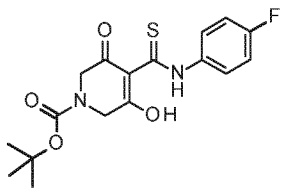
To a solution of tert-butyl 2-(2-aminopyridin-4-yl)-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (294; 16 mg, 36 µmol) in THF (1.0 mL) were added pyridine (21 µL, 268 µmol) acetyl chloride (10 µL, 144 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, MeOH:DCM) to give the title compound (13 mg, 69%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.42 (9H), 2.08 (3H), 2.12 (3H), 3.99 (2H), 4.73 (2H), 6.47 (2H), 6.83 (2H), 7.18 (1H), 7.23 (1H), 8.10 (1H), 8.26 (1H), 10.39 (1H), 12.18 (1H)

Example 296

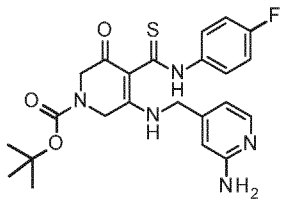
tert-Butyl 2-(2-aminopyridin-4-yl)-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

296-2: tert-Butyl 4-[(4-fluorophenyl)carbamothioyl]-5-hydroxy-3-oxo-3,6-dihydropyridine-1(2H)-carboxylate



To a solution of 1-benzylpiperidine-3,5-dione (8.00 g, 37.5 mmol) and 1-fluoro-4-isothiocyanatobenzene (6.0 g, 39.4 mmol) in MeCN (67 mL) was added DBU (10 mL) and the mixture was stirred at RT for 16 h. The mixture was concentrated and purified by Biotage (SNAP silica 340g, EtOAc:Hexane) to give the title compound (3.69 g, 24%).

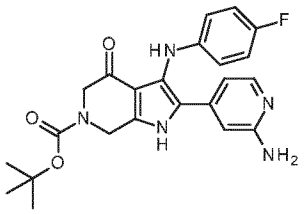
296-1: tert-Butyl 5-{[(2-aminopyridin-4-yl)methyl]amino}-4-[(4-fluorophenyl)carbamothioyl]-3-oxo-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-butyl 4-[(4-fluorophenyl)carbamothioyl]-5-hydroxy-3-oxo-3,6-dihydropyridine-1(2H)-carboxylate (296-2; 3.23 g, 8.18 mmol) and 4-(methylamino)pyridine (2.17 g, 17.6 mmol) in DMA (48 mL) was heated at 120℃ for 2 h.

The mixture was concentrated and purified by Biotage (SNAP silica 100g, EtOAc:Hexane) to give the title compound (2.92 g, 70%).

tert-Butyl 2-(2-aminopyridin-4-yl)-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

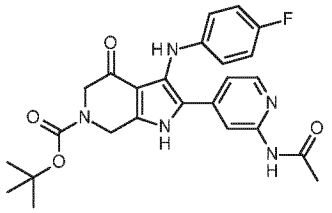


A mixture of tert-butyl 5-{[(2-aminopyridin-4-yl)methyl]amino}-4-[(4-fluorophenyl)carbamothioyl]-3-oxo-3,6-dihydropyridine-1(2H)-carboxylate (296-1; 79 mg, 168 mmol), hydrogen peroxide (30% in water, 34 µL, 335 µmol), TFA (26 µL, 335 µmol) in MeOH (2.6 mL) was stirred for 16 h at 50℃. Aqueous sodium thiosulfate and TEA (49 µmol) were added and the mixture was concentrated. The residue was purified by Biotage (SNAP NH 10g, MeOH:DCM to give the title compound (24 mg, 31%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.42 (9H), 3.97 (2H), 4.71 (2H), 5.91 (2H), 6.54 (2H), 6.60 (1H), 6.71 (1H), 6.87 (2H), 7.30 (1H), 7.81 (1H), 12.01 (1H)

Example 297

tert-Butyl 2-(2-acetamidopyridin-4-yl)-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



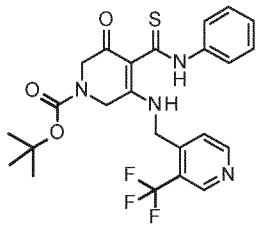
To a solution of tert-butyl 2-(2-aminopyridin-4-yl)-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (296; 15 mg, 35 µmol) in THF (1.0 mL) were added pyridine (21 µL, 268 µmol) acetyl chloride (10 µL, 144 µmol) and stirred for 2 h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, MeOH:DCM) to give the title compound (9 mg, 51%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.42 (9H), 2.07 (3H), 3.99 (2H), 4.74 (2H), 6.54 (2H), 6.86 (2H), 7.21 (1H), 7.40 (1H), 8.14 (1H), 8.27 (1H), 10.39 (1H), 12.21 (1H)

Example 298

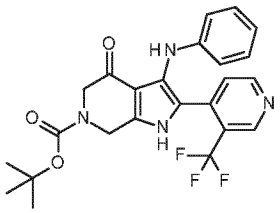
tert-Butyl 4-oxo-3-(phenylamino)-2-[3-(trifluoromethyl)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

298-1: tert-Butyl 3-oxo-4-(phenylcarbamothioyl)-5-({[3-(trifluoromethyl)pyridin-4-yl]methyl}amino)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-butyl 5-hydroxy-3-oxo-4-(phenylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (2-2; 300 mg, 861 µmol) and 1-[3-(trifluoromethyl)pyridin-4-yl]methanamine (429 mg, 1.72 mmol) in DMA (2.6 mL) was heated at 100℃ for 1.5 h. The mixture was concentrated and purified by Biotage (SNAP silica 25g, EtOAc:Hexane) to give the title compound (329 mg, 75%).

tert-Butyl 4-oxo-3-(phenylamino)-2-[3-(trifluoromethyl)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

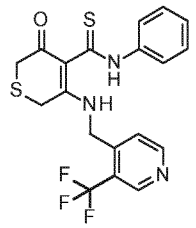


A mixture comprising tert-butyl 3-oxo-4-(phenylcarbamothioyl)-5-({[3-(trifluoromethyl)pyridin-4-yl]methyl}amino)-3,6-dihydropyridine-1(2H)-carboxylate (298-1; 325 mg, 642 µmol), DMA (13 mL), TFA (49 µL, 642 µmol) and palladium on charcoal (10%, 683 mg, 642 µmol) was heated at 120℃ for 16 h. TEA (200 µL) was added, the mixture concentrated and purified by Biotage (SNAP NH 28g, EtOH:DCM) and preparative TLC (silica, EtOH:DCM) to give the title compound (22 mg, 7%).
^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.44 (9H), 4.01 (2H), 4.71 (2H), 6.48-6.54 (3H), 6.94 (2H), 7.29 (1H), 7.41 (1H), 8.73 (1H), 8.96 (1H), 11.70 (1H)

Example 299

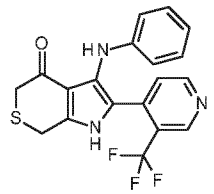
3-(Phenylamino)-2-[3-(trifluoromethyl)pyridin-4-yl]-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one

299-1: 3-Oxo-N-phenyl-5-({[3-(trifluoromethyl)pyridin-4-yl]methyl}amino)-3,6-dihydro-2H-thiopyran-4-carbothioamide



A solution of 5-hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-thiopyran-4-carbothioamide (4-1; 300 mg, 1.13 mmol) and 1-[3-(trifluoromethyl)pyridin-4-yl]methanamine (415 mg, 1.58 mmol) in DMA (3.0 mL) was heated at 80℃ for 1 h. T he mixture was concentrated, the residue digested with ether to give the title compound (130 mg, 26%).

3-(Phenylamino)-2-[3-(trifluoromethyl)pyridin-4-yl]-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one



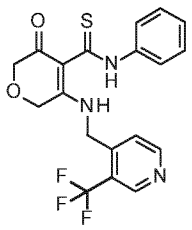
A mixture comprising 3-oxo-N-phenyl-5-({[3-(trifluoromethyl)pyridin-4-yl]methyl}amino)-3,6-dihydro-2H-thiopyran-4-carbothioamide (299-1; 125 mg, 295 µmol), DMA (5.3 mL) and palladium on charcoal (10%, 314 mg, 295 µmol) was heated at 120℃ for 3 h. The mixture was concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound (11 mg, 9%).

^{1}H-NMR (400 MHz, CD_2Cl_2), δ [ppm]= 3.47 (2H), 3.92 (2H), 6.69 (2H), 6.73 (1H), 7.01 (2H), 7.29 (1H), 7.62 (1H), 8.36 (1H), 8.50 (1H), 8.87 (1H)

Example 300

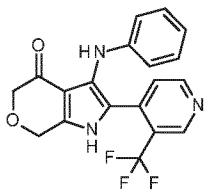
3-(Phenylamino)-2-[3-(trifluoromethyl)pyridin-4-yl]-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

300-1: 3-Oxo-N-phenyl-5-({[3-(trifluoromethyl)pyridin-4-yl]methyl}amino)-3,6-dihydro-2H-pyran-4-carbothioamide



A solution of 5-hydroxy-3-oxo-N-phenyl-3,6-dihydro-2H-pyran-4-carbothioamide (6-2; 250 mg, 1.00 mmol) and 1-[3-(trifluoromethyl)pyridin-4-yl]methanamine (500 mg, 2.00 mmol) in DMA (3.0 mL) was heated at 85℃ for 2 h. The mix ture was concentrated, and purified by Biotage (SNAP silica 25g, EtOAc:Hexane) to give the title compound (307 mg, 75%).

3-(Phenylamino)-2-[3-(trifluoromethyl)pyridin-4-yl]-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one

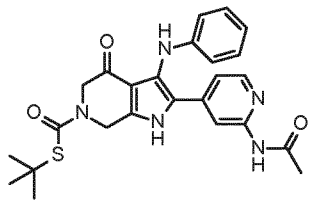


A mixture comprising 3-oxo-N-phenyl-5-({[3-(trifluoromethyl)pyridin-4-yl]methyl}amino)-3,6-dihydro-2H-pyran-4-carbothioamide (300-1; 203 mg, 498 µmol), DMA (10 mL), TFA (38 µL, 498 µmol) and palladium on charcoal (10%, 530 mg, 498 µmol) was heated at 125℃ for 16 h. TEA (100 µL) was added, the mixture concentrated and purified by Biotage (SNAP NH 28g, EtOH:DCM) and preparative TLC (silica, EtOH:DCM) to give the title compound (26 mg, 14%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 4.06 (2H), 4.87 (2H), 6.49-6.56 (3H), 6.96 (2H), 7.31 (1H), 7.42 (1H), 8.76 (1H), 8.97 (1H), 11.64 (1H)

Example 301

S-tert-butyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate



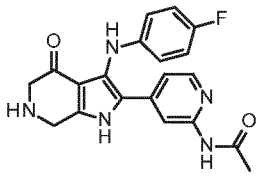
To a solution of N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]acetamide (24; 50 mg, 138 µmol) in pyridine (2.0 mL) was added S-tert-

butyl carbonochloridothioate (44 µL, 277 µmol) and stirred for 1h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (46 mg, 66%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.46 (9H), 2.08 (3H), 4.11 (2H), 4.87 (2H), 6.53-6.61 (3H), 7.02 (2H), 7.22 (1H), 7.43 (1H), 8.13 (1H), 8.28 (1H), 10.41 (1H), 12.25 (1H)

Example 302

N-(4-{3-[(4-Fluorophenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide

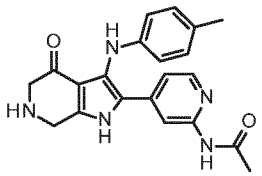


To a solution of tert-butyl 2-(2-acetamidopyridin-4-yl)-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (297; 533 mg, 1.11 mmol) in DCM (31 mL) was added TFA (1.3 mL) and stirred at RT for 16h. The mixture was poured into aqueous ammonia (25%), extracted with DCM/MeOH and dried over sodium sulfate. After filtration and concentration the residue was crystallized from ether to give the title compound (331 mg, 78%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.06 (3H), 3.19 (2H), 3.94 (2H), 6.53-6.59 (2H), 6.85 (2H), 7.18 (1H), 7.34 (1H), 8.11 (1H), 8.23 (1H), 10.35 (1H), 11.91 (1H)

Example 303

N-(4-{3-[(4-Methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide

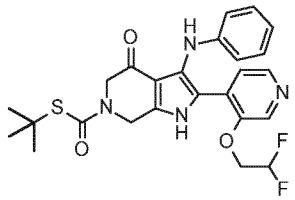


To a solution of tert-butyl 2-(2-acetamidopyridin-4-yl)-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (295; 570 mg, 1.20 mmol) in DCM (33 mL) was added TFA (1.4 mL) and stirred at RT for 16h. The mixture was poured into aqueous ammonia (25%), extracted with DCM/MeOH and dried over sodium sulfate. After filtration and concentration the residue was crystallized from ether to give the title compound (377 mg, 84%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.07 (3H), 2.12 (3H), 3.19 (2H), 3.94 (2H), 6.49 (2H), 6.83 (2H), 7.14 (1H), 7.18 (1H), 8.07 (1H), 8.22 (1H), 10.35 (1H), 11.88 (1H)

Example 304

S-tert-Butyl 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate

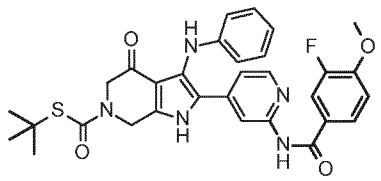


To a solution of 3-Anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one (224; 50 mg, 130 µmol) in pyridine (1.8 mL) was added S-tert-butyl carbonochloridothioate (41 µL, 260 µmol) and stirred for 1h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (35 mg, 51%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.47 (9H), 4.13 (2H), 4.40 (2H), 4.87 (2H), 6.28 (1H), 6.52 (2H), 6.57 (1H), 6.98 (2H), 7.35 (1H), 7.39 (1H), 8.15 (1H), 8.43 (1H), 11.66 (1H)

Example 305

S-tert-butyl 3-anilino-2-{2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate

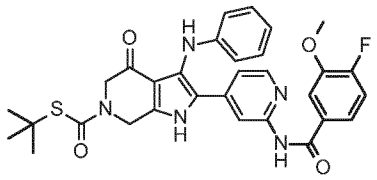


To a solution of 3-Fluoro-4-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (284; 50 mg, 106 µmol) in pyridine (1.5 mL) was added S-tert-butyl carbonochloridothioate (33 µL, 212 µmol) and stirred for 1h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (57 mg, 86%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.47 (9H), 3.94 (3H), 4.15 (2H), 4.91 (2H), 6.61-6.66 (3H), 7.05 (2H), 7.34 (1H), 7.43 (1H), 7.69 (1H), 7.89-7.96 (2H), 8.23 (1H), 8.28 (1H), 11.17 (1H), 12.55 (1H)

Example 306

S-tert-butyl 3-anilino-2-{2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate

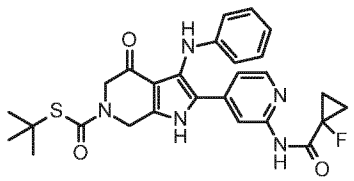


To a solution of 4-Fluoro-3-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide (257; 50 mg, 106 µmol) in pyridine (1.5 mL) was added S-tert-butyl carbonochloridothioate (33 µL, 212 µmol) and stirred for 1h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (43 mg, 65%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.47 (9H), 3.95 (3H), 4.13 (2H), 4.89 (2H), 6.56-6.63 (3H), 7.03 (2H), 7.32 (1H), 7.35 (1H), 7.48 (1H), 7.65 (1H), 7.86 (1H), 8.24 (1H), 8.40 (1H), 10.85 (1H), 12.32 (1H)

Example 307

S-tert-Butyl 3-anilino-2-(2-{[(1-fluorocyclopropyl)carbonyl]amino}pyridin-4-yl)-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate

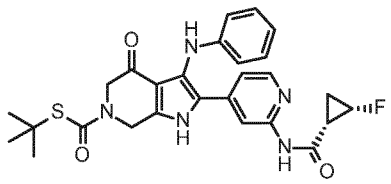


To a solution of N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-1-fluorocyclopropanecarboxamide (132; 50 mg, 123 µmol) in pyridine (1.8 mL) was added S-tert-butyl carbonochloridothioate (39 µL, 247 µmol) and stirred for 1h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (54 mg, 79%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.32 (2H), 1.44 (2H), 1.46 (9H), 4.12 (2H), 4.87 (2H), 6.56 (2H), 6.60 (1H), 7.02 (2H), 7.31 (1H), 7.47 (1H), 8.17 (1H), 8.21 (1H), 10.18 (1H), 12.28 (1H)

Example 308

S-tert-Butyl 3-anilino-2-[2-({[(1S,2S)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate



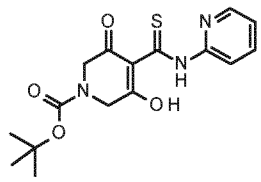
To a solution of (1S,2S)-N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide (197; 50 mg, 123 µmol) in pyridine (1.8 mL) was added S-tert-butyl carbonochloridothioate (39 µL, 247 µmol) and stirred for 1h at RT. MeOH was added and the reaction mixture was concentrated. The crude product was purified by preparative TLC (silica, EtOH:DCM) to give the title compound (47 mg, 69%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.18 (1H), 1.46 (9H), 1.64 (1H), 2.21 (1H), 4.11 (2H), 4.86 (2H), 4.94 (1H), 6.55 (2H), 6.59 (1H), 7.02 (2H), 7.24 (1H), 7.44 (1H), 8.13 (1H), 8.30 (1H), 10.79 (1H), 12.27 (1H)

Example 309

tert-Butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(pyridin-2-ylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

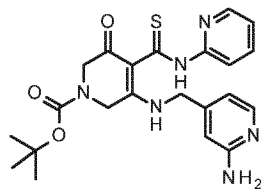
309-2: tert-Butyl 5-hydroxy-3-oxo-4-(pyridin-2-ylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



To a solution of 1-benzylpiperidine-3,5-dione (12.0 g, 56.3 mmol) and 2-isothiocyanatopyridine (10.7 g, 78.8 mmol) in MeCN (140 mL) was added DBU (15 mL) at

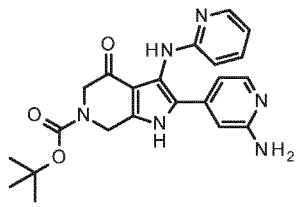
0℃ and the mixture was stirred at RT for 16 h. The mixture was concentrated and purified by Biotage (SNAP silica 340g, EtOAc:Hexane) to give the title compound (2.05 g, 10%).

309-1: tert-Butyl 5-{[(2-aminopyridin-4-yl)methyl]amino}-3-oxo-4-(pyridin-2-ylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of tert-butyl 5-hydroxy-3-oxo-4-(pyridin-2-ylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (309-2; 2.04 g, 5.8 mmol) and 4-(methylamino)pyridine (1.44 g, 11.7 mmol) in DMA (31 mL) was heated at 120℃ for 2 h. T he mixture was concentrated and purified by Biotage (SNAP silica 50g, MeOH:DCM) to give the title compound (1.32 g, 37%).

tert-Butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(pyridin-2-ylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

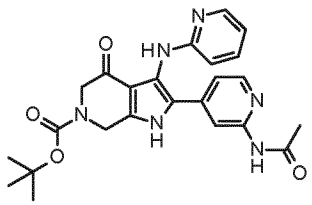


A mixture of tert-butyl 5-{[(2-aminopyridin-4-yl)methyl]amino}-3-oxo-4-(pyridin-2-ylcarbamothioyl)-3,6-dihydropyridine-1(2H)-carboxylate (309-1; 1.32 g, 2.9 mmol), hydrogen peroxide (30% in water, 593 µL, 5.8 mmol), TFA (670 µL, 1.5 mmol) in MeOH (45 mL) was stirred for 16 h at 50℃. Aqueous sodiu m thiosulfate and TEA (1.3 mL) were added and the mixture was concentrated. The residue was purified by Biotage (SNAP NH 50g, MeOH:DCM) and preparative TLC (silica, EtOH:DCM) to give the title compound (48 mg, 4%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.42 (9H), 3.95 (2H), 4.71 (2H), 5.84 (2H), 6.35 (1H), 6.55 (1H), 6.62 (1H), 6.73 (1H), 7.36 (1H), 7.82 (1H), 7.89 (1H), 7.93 (1H), 11.99 (1H)

Example 310

tert-Butyl 2-(2-acetamidopyridin-4-yl)-4-oxo-3-(pyridin-2-ylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

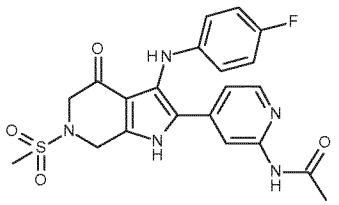


To a mixture of tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(pyridin-2-ylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate (309; 47 mg, 0.11 mmol) in pyridine (91 µL) and THF (3.1 mL) was added acetyl chloride(36 µL, 0.5 mmol) and stirred for 16 h at RT. MeOH was added, the mixture concentrated and purified by preparative TLC (silica, EtOH:DCM) to give the title compound together with bisacetylated product (34 mg, max. 66%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.43 (9H), 2.07 (3H), 3.91-4.08 (2H), 4.60-4.85 (2H), 6.42 (1H), 6.55 (1H), 7.29 (1H), 7.37 (1H), 7.90 (1H), 8.02 (1H), 8.16 (1H), 8.28 (1H), 10.40 (1H), 12.21 (1H)

Example 311

N-(4-(3-[(4-Fluorophenyl)amino]-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide

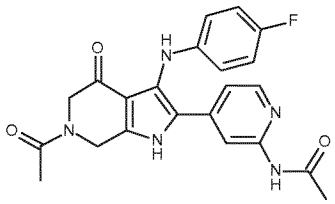


To a mixture of N-(4-{3-[(4-fluorophenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (302; 50 mg, 132 µmol) in pyridine (1.9 mL) was added methylsulfonyl chloride (30 mg, 264 µmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (44 mg, 70%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 3.00 (3H), 3.87 (2H), 4.63 (2H), 6.56 (2H), 6.86 (2H), 7.23 (1H), 7.44 (1H), 8.16 (1H), 8.28 (1H), 10.41 (1H), 12.27 (1H)

Example 312

N-(4-(6-Acetyl-3-[(4-fluorophenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide

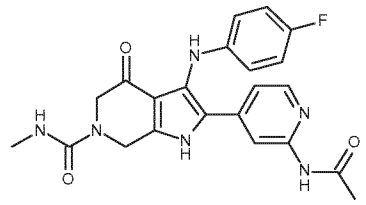


To a mixture of N-(4-{3-[(4-fluorophenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (302; 40 mg, 105 µmol) in pyridine (1.3 mL) was added acetyl chloride (15 µL, 211 µmol) and stirred for 1 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (32 mg, 68%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.07+2.16 (6H), 34.11+4.13 (2H), 4.82 (2H), 6.55 (2H), 6.86 (2H), 7.21 (1H), 7.39+7.42 (1H), 8.15 (1H), 8.27+8.28 (1H), 10.39 (1H), 12.22 (1H)

Example 313

2-[2-(Acetylamino)pyridin-4-yl]-3-[(4-fluorophenyl)amino]-N-methyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

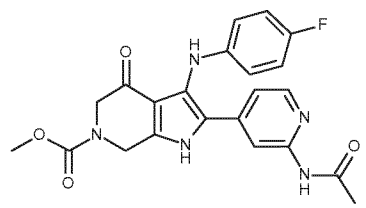


To a mixture of N-(4-{3-[(4-fluorophenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (302; 50 mg, 132 µmol) in pyridine (1.9 mL) was added methylcarbamic chloride (30 mg, 264 µmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (43 mg, 70%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.07 (3H), 2.57 (3H), 3.97 (2H), 4.69 (2H), 6.54 (2H), 6.78 (1H), 6.85 (2H), 7.20 (1H), 7.38 (1H), 8.14 (1H), 8.26 (1H), 10.38 (1H), 12.17 (1H)

Example 314

Methyl 2-[2-(acetylamino)pyridin-4-yl]-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

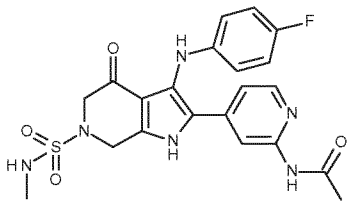


To a mixture of N-(4-{3-[(4-fluorophenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (302; 50 mg, 132 µmol) in pyridine (1.9 mL) was added methyl carbonochloridate (25 mg, 264 µmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (37 mg, 61%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.07 (3H), 3.66 (3H), 4.04 (2H), 4.78 (2H), 6.55 (2H), 6.86 (2H), 7.20 (1H), 7.40 (1H), 8.15 (1H), 8.26 (1H), 10.40 (1H), 12.21 (1H)

Example 315

N-(4-(3-[(4-Fluorophenyl)amino]-6-(methylsulfamoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide

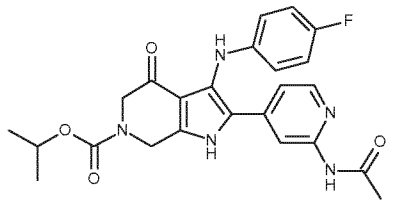


To a mixture of N-(4-{3-[(4-fluorophenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (302; 50 mg, 132 µmol) in pyridine (1.9 mL) was added methylsulfamyl chloride (34 mg, 264 µmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (27 mg, 41%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.07 (3H), 2.47 (3H), 3.80 (2H), 4.60 (2H), 6.55 (2H), 6.86 (2H), 7.21 (1H), 7.42 (1H), 7.45 (1H), 8.15 (1H), 8.27 (1H), 10.40 (1H), 12.20 (1H)

Example 316

Propan-2-yl 2-[2-(acetylamino)pyridin-4-yl]-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

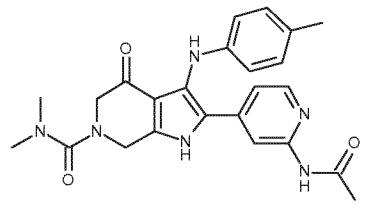


To a mixture of N-(4-{3-[(4-fluorophenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (302; 50 mg, 132 µmol) in pyridine (1.9 mL) was added isopropyl carbonochloridate (32 mg, 264 µmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (36 mg, 55%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.21 (6H), 2.07 (3H), 4.03 (2H), 4.77 (2H), 4.82 (1H), 6.55 (2H), 6.86 (2H), 7.21 (1H), 7.41 (1H), 8.15 (1H), 8.27 (1H), 10.40 (1H), 12.21 (1H)

Example 317

2-[2-(Acetylamino)pyridin-4-yl]-N,N-dimethyl-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

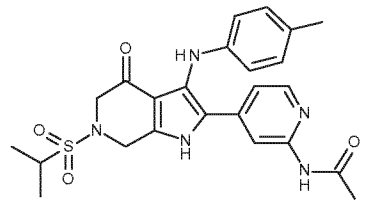


To a mixture of N-(4-{3-[(4-methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (303; 50 mg, 133 µmol) in pyridine (1.9 mL) was added dimethylcarbamic chloride (29 mg, 264 µmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (44 mg, 71%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 2.12 (3H), 2.78 (6H), 3.77 (2H), 4.57 (2H), 6.47 (2H), 6.83 (2H), 7.15 (1H), 7.22 (1H), 8.09 (1H), 8.24 (1H), 10.38 (1H), 12.05 (1H)

Example 318

N-(4-(3-[(4-Methylphenyl)amino]-4-oxo-6-(propan-2-ylsulfonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide

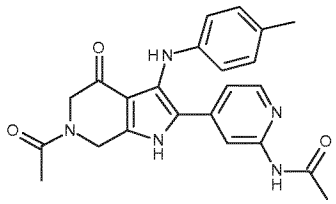


To a mixture of N-(4-{3-[(4-methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (303; 50 mg, 133 µmol) in pyridine (1.9 mL) was added propane-2-sulfonyl chloride (38 mg, 266 µmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (38 mg, 57%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.21 (6H), 2.08 (3H), 2.12 (3H), 3.41 (1H), 3.94 (2H), 4.72 (2H), 6.48 (2H), 6.83 (2H), 7.20 (1H), 7.28 (1H), 8.12 (1H), 8.26 (1H), 10.41 (1H), 12.19 (1H)

Example 319

N-(4-(6-Acetyl-3-[(4-methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide

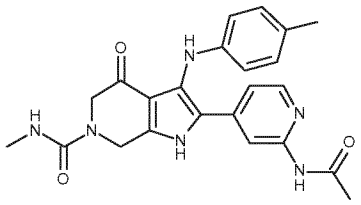


To a mixture of N-(4-{3-[(4-methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (303; 40 mg, 107 µmol) in pyridine (1.3 mL) was added acetyl chloride (17 mg, 213 µmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (25 mg, 53%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.05-2.12 (9H), 4.11+4.12 (2H), 4.82 (2H), 6.48 (2H), 6.83 (2H), 7.19 (1H), 7.24 (1H), 8.11 (1H), 8.26+8.27 (1H), 10.39 (1H), 12.19 (1H)

Example 320

2-[2-(Acetylamino)pyridin-4-yl]-N-methyl-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

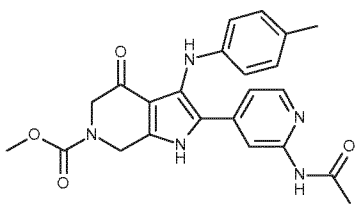


To a mixture of N-(4-{3-[(4-methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (303; 50 mg, 133 µmol) in pyridine (1.9 mL) was added methylcarbamic chloride (25 mg, 266 µmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (51 mg, 85%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 2.12 (3H), 2.57 (3H), 3.97 (2H), 4.69 (2H), 6.47 (2H), 6.78 (1H), 6.82 (2H), 7.17 (1H), 7.21 (1H), 8.10 (1H), 8.25 (1H), 10.38 (1H), 12.14 (1H)

Example 321

Methyl 2-[2-(acetylamino)pyridin-4-yl]-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

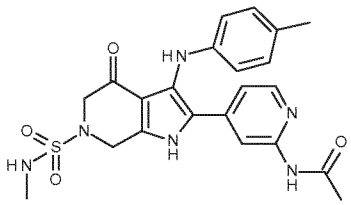


To a mixture of N-(4-{3-[(4-methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (303; 50 mg, 133 µmol) in pyridine (1.9 mL) was added methyl carbonochloridate (25 mg, 266 µmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (26 mg, 43%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 2.12 (3H), 3.66 (3H), 4.04 (2H), 4.78 (2H), 6.47 (2H), 6.83 (2H), 7.18 (1H), 7.24 (1H), 8.11 (1H), 8.25 (1H), 10.40 (1H), 12.18 (1H)

Example 322

N-(4-(3-[(4-Methylphenyl)amino]-6-(methylsulfamoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide

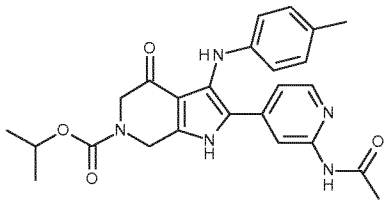


To a mixture of N-(4-{3-[(4-methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (303; 50 mg, 133 µmol) in pyridine (1.9 mL) was added methylsulfamyl chloride (35 mg, 266 µmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (37 mg, 57%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 2.08 (3H), 2.12 (3H), 2.46 (3H), 3.79 (2H), 4.59 (2H), 6.48 (2H), 6.83 (2H), 7.19 (1H), 7.25 (1H), 7.45 (1H), 8.12 (1H), 8.26 (1H), 10.40 (1H), 12.18 (1H)

Example 323

Propan-2-yl 2-[2-(acetylamino)pyridin-4-yl]-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate



To a mixture of N-(4-{3-[(4-methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide (303; 50 mg, 133 µmol) in pyridine (1.9 mL) was added isopropyl carbonochloridate (33 mg, 266 µmol) and stirred for 16 h at RT. MeOH was added, followed by toluene and the reaction mixture was concentrated. The crude product was purified by Biotage (SNAP NH 10g, MeOH:DCM) to give the title compound (40 mg, 62%).

^{1}H-NMR (400 MHz, DMSO-d6), δ [ppm]= 1.21 (6H), 2.08 (3H), 2.12 (3H), 4.03 (2H), 4.77 (2H), 4.82 (1H), 6.47 (2H), 6.83 (2H), 7.18 (1H), 7.24 (1H), 8.11 (1H), 8.26 (1H), 10.40 (1H), 12.19 (1H)

Biological investigations

The following assays can be used to illustrate the commercial utility of the compounds according to the present invention.

Examples were tested in selected biological assays one or more times. When tested more than once, data are reported as either average values or as median values, wherein

- the average value, also referred to as the arithmetic mean value, represents the sum of the values obtained divided by the number of times tested, and
- the median value represents the middle number of the group of values when ranked in ascending or descending order. If the number of values in the data set is odd, the median is the middle value. If the number of values in the data set is even, the median is the arithmetic mean of the two middle values.

Examples were synthesized one or more times. When synthesized more than once, data from biological assays represent average values calculated utilizing data sets obtained from testing of one or more synthetic batch.

Bub1 kinase assay

Bub1-inhibitory activities of compounds described in the present invention were quantified using a time-resolved fluorescence energy transfer (TR-FRET) kinase assay which measures phosphorylation of the synthetic peptide Biotin-Ahx-VLLPKKSFAEPG (C-terminus in amide form), purchased from e.g. Biosyntan (Berlin, Germany) by the (recombinant) catalytic domain of human Bub1 (amino acids 704-1085), expressed in Hi5 insect cells with an N-terminal His6-tag and purified by affinity- (Ni-NTA) and size exclusion chromatography.

In a typical assay 11 different concentrations of each compound (0.1 nM, 0.33 nM, 1.1 nM, 3.8 nM, 13 nM, 44 nM, 0.15 µM, 0.51 µM, 1.7 µM, 5.9 µM and 20 µM) were tested in duplicate within the same microtiter plate. To this end, 100-fold concentrated compound solutions (in DMSO) were previously prepared by serial dilution (1:3.4) of 2 mM stocks in a clear low volume 384-well source microtiter plate (Greiner Bio-One, Frickenhausen, Germany), from which 50 nl of compounds were transferred into a black low volume test microtiter plate from the same supplier. Subsequently, 2 µL of Bub1 (the final concentration of Bub1 was adjusted depending on the activity of the enzyme lot in order to be within the linear dynamic range of the assay: typically ~ 200 ng/mL were used) in

aqueous assay buffer [50 mM Tris/HCl pH 7.5, 10 mM magnesium chloride ($MgCl_2$), 200 mM potassium chloride (KCl), 1.0 mM dithiothreitol (DTT), 0.1 mM sodium ortho-vanadate, 1% (v/v) glycerol, 0.01 % (w/v) bovine serum albumine (BSA), 0.005% (v/v) Trition X-100 (Sigma), 1x Complete EDTA-free protease inhibitor mixture (Roche)] were added to the compounds in the test plate and the mixture was incubated for 15 min at 22℃ to allow pre-equilibration of the putative enz yme-inhibitor complexes before the start of the kinase reaction, which was initiated by the addition of 3 µL 1.67-fold concentrated solution (in assay buffer) of adenosine-tri-phosphate (ATP, 10 µM final concentration) and peptide substrate (1 µM final concentration). The resulting mixture (5 µL final volume) was incubated at 22℃ during 60 min., and the reaction was stopped by the addition of 5 µL of an aqueous EDTA-solution (50 mM EDTA, in 100 mM HEPES pH 7.5 and 0.2 % (w/v) bovine serum albumin) which also contained the TR-FRET detection reagents (0.2 µM streptavidin-XL665 [Cisbio Bioassays, Codolet, France] and 1 nM anti-phosho-Serine antibody [Merck Millipore, cat. # 35-002] and 0.4 nM LANCE EU-W1024 labeled anti-mouse IgG antibody [Perkin-Elmer, product no. AD0077, alternatively a Terbium-cryptate-labeled anti-mouse IgG antibody from Cisbio Bioassays can be used]). The stopped reaction mixture was further incubated 1 h at 22℃ in order to allow the formation of complexes between peptides and detection reagents. Subsequently, the amount of product was evaluated by measurement of the resonance energy transfer from the Eu-chelate-antibody complex recognizing the Phosphoserine residue to the streptavidin-XL665 bound to the biotin moiety of the peptide. To this end, the fluorescence emissions at 620 nm and 665 nm after excitation at 330-350 nm were measured in a TR-FRET plate reader, e.g. a Rubystar or Pherastar (both from BMG Labtechnologies, Offenburg, Germany) or a Viewlux (Perkin-Elmer) and the ratio of the emissions (665 nm/622 nm) was taken as indicator for the amount of phosphorylated substrate. The data were normalised using two sets of control wells for high- (= enzyme reaction without inhibitor = 0 % = Minimum inhibition) and low- (= all assay components without enzyme = 100 % = Maximum inhibition) Bub1 activity. IC50 values were calculated by fitting the normalized inhibition data to a 4-parameter logistic equation (Minimum, Maximum, IC50, Hill; Y = Max + (Min - Max) / (1 + (X/IC50)Hill)).

Table 1: Inhibition of Bub1 kinase

Example No.	IC_{50} [nM]
1	67
2	236
3	10
4	19
5	5
6	42
7	4
8	4
9	4
10	6
11	8
12	102
13	40
14	47
15	1200
16	949
17	6
18	6
19	8
20	152
21	794
22	503
23	1660
24	154
25	254

Example No.	IC_{50} [nM]
26	97
27	59
28	13
29	24
30	7
31	7
32	4
33	17
34	60
35	55
36	79
37	482
38	40
39	81
40	1470
41	233
42	77
43	84
44	50
45	59
46	93
47	341
48	115
49	51
50	26

Example No.	IC_{50} [nM]
51	44
52	10
53	82
54	77
55	98
56	5
57	8
58	8
59	10
60	67
61	40
62	15
63	9
64	1400
65	1680
66	9
67	6
68	5
69	4
70	7
71	8
72	7
73	8
74	6
75	6

Table 1 (cont.): Inhibition of Bub1 kinase

Example No.	IC_{50} [nM]
76	7
77	11
78	73
79	8
80	11
81	4
82	4
83	12
84	9
85	13
86	11
87	11
88	21
89	31
90	21
91	14
92	4
93	4
94	3
95	9
96	55
97	59
98	16
99	205
100	26

Example No.	IC_{50} [nM]
101	43
102	17
103	138
104	9
105	12
106	6
107	6
108	8
109	7
110	6
111	7
112	9
113	34
114	63
115	45
116	26
117	9
118	149
119	42
120	9
121	10
122	6
123	3
124	4
125	10

Example No.	IC_{50} [nM]
126	7
127	29
128	8
129	7
130	662
131	23
132	299
133	28
134	36
135	51
136	81
137	64
138	224
139	7
140	31
141	7
142	76
143	6
144	20
145	16
146	10
147	8
148	4
149	4
150	5

Table 1 (cont.): Inhibition of Bub1 kinase

Example No.	IC_{50} [nM]
151	4
152	437
153	510
154	19
155	60
156	12
157	7
158	8
159	22
160	4
161	5
162	38
163	6
164	6
165	14
166	3
167	6
168	5
169	5
170	5
171	3
172	5
173	6
174	8
175	8

Example No.	IC_{50} [nM]
176	16
177	23
178	5
179	63
180	5
181	5
182	4
183	9
184	8
185	14
186	3
187	3
188	4
189	16
190	135
191	143
192	30
193	19
194	46
195	24
196	7
197	40
198	3
199	20
200	7

Example No.	IC_{50} [nM]
201	6
202	8
203	2
204	3
205	3
206	4
207	3
208	5
209	7
210	3
211	4
212	3
213	2
214	3
215	4
216	6
217	4
218	79
219	22
220	18
221	104
222	9
223	14
224	222
225	1020

Table 1 (cont.): Inhibition of Bub1 kinase

Example No.	IC_{50} [nM]
226	72
227	140
228	33
229	163
230	16
231	40
232	12
233	36
234	5
235	6
236	16
237	18
238	8
239	20
240	66
241	13
242	57
243	55
244	18
245	73
246	319
247	65
248	5
249	5
250	9

Example No.	IC_{50} [nM]
251	12
252	48
253	42
254	4
255	375
256	936
257	35
258	10
259	3
260	8
261	351
262	8
263	38
264	81
265	6
266	72
267	Nd
268	58
269	149
270	37
271	5
272	4
273	11
274	10
275	113

Example No.	IC_{50} [nM]
276	7
277	102
278	23
279	6
280	6
281	10
282	12
283	38
284	52
285	6
286	1050
287	2060
288	404
289	6
290	73
291	6
292	214
293	10
294	499
295	363
296	172
297	55
298	896
299	7360
300	8210

Table 1 (cont.): Inhibition of Bub1 kinase

Example No.	IC_{50} [nM]
301	33
302	297
303	1150
304	233
305	233
306	171
307	182
308	31

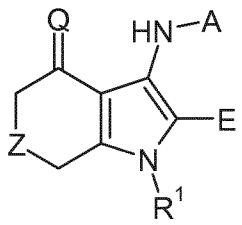
Example No.	IC_{50} [nM]
309	nd
310	79
311	4
312	16
313	17
314	8
315	4
316	25

Example No.	IC_{50} [nM]
317	50
318	31
319	192
320	178
321	113
322	41
323	229

nd: not determined

Claims

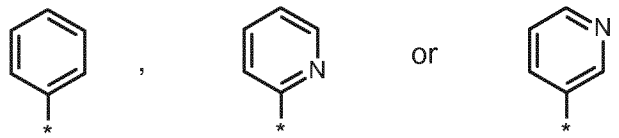
1. A compound of formula (I),



(I)

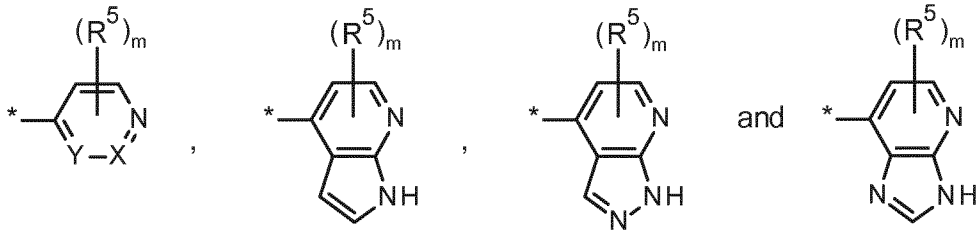
in which:

A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule and said group is optionally substituted, one, two or three times, independently from each other, with R^{3c};

E represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule;

Q represents O or N-OH;

X represents CR^{4a} or N;

Y represents CR^{4b} or N,

wherein when X represents N, Y represents CR^{4b}, and when Y represents N, X represents CR^{4a},

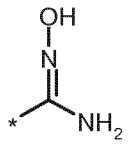
Z represents O, S, SO or NR^2;

R^1 represents hydrogen, C_1-C_4-alkyl or C_1-C_4-alkoxy-C_2-C_4-alkyl-;

R^2 represents hydrogen, C_1-C_4-alkyl, C_3-C_6-cycloalkyl, R^{8a}-C(O)-, R^{8b}O-C(O)-, R^{8c}S-C(O)-, R^6R^7N-C(O)-, $R^{10}R^{11}$N-SO_2-, R^9SO_2-, phenyl-C_1-C_3-alkyl or heteroaryl-C_1-C_3-alkyl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_4-alkyl and C_3-C_6-cycloalkyl are optionally substituted, one, two or three times, independently from each other, with R^{3b} or once with a group



wherein * indicates the point of attachment of said group with the rest of the molecule;

R^{3a}, R^{3b}, R^{3c}, R^{3d} represent, independently from each other, hydroxy, halogen, cyano, $R^{10}R^{11}$N-, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl, C_1-C_4-haloalkyl or C_1-C_4-haloalkoxy;

R^{4a}, R^{4b} represent hydrogen, halogen, hydroxy, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{10}R^{11}$N-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}$N-C(O)-NH-;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b};

wherein C_1-C_4-alkoxy is optionally substituted, one, two or three times, independently from each other, with R^{3d};

R^5 represents, independently from each other, halogen, hydroxy, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{12a}R^{12b}$N-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{12a}R^{12b}$N-C(O)-NH-;

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkoxy-C_2-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,
wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkoxy-C_2-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl- and 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b}; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 4- to 7-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing groups selected from O, S, C(=O) or NR^{12a}, and which may be optionally substituted, one, two or three times, independently from each other, with R^{3a};

R^{8a} represents, independently from each other, C_1-C_6-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a}; and

wherein C_1-C_6-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{8b} represents, independently from each other, C_1-C_6-alkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a}; and

wherein C_1-C_6-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{8c} represents C_1-C_4-alkyl;

R^9 represents, independently from each other, C_1-C_4-alkyl, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, 4- to 7-membered heterocycloalkyl-C_1-C_4-alkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a}; and

wherein C_1-C_4-alkyl, C_3-C_6-cycloalkyl and 4- to 7-membered heterocycloalkyl-C_1-C_4-alkyl groups are optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{10}, R^{11} represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, R^{12a}-O-C(O)- or phenyl,

wherein said C_1-C_6-alkyl is optionally substituted, one or more times, independently from each other, with halogen, hydroxy, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_3-C_6-cycloalkyl or $R^{12a}R^{12b}N$-,

wherein said phenyl group is optionally substituted, one or more times, independently from each other, with with halogen, hydroxy, C_1-C_3-alkyl, C_1-C_3-alkoxy or C_1-C_3-haloalkoxy;

or,

R^{10} and R^{11} together with the nitrogen atom to which they are attached form a 4- to 7-membered nitrogen containing heterocyclic ring, optionally containing one additional heteroatom selected from O, NR^{12a} and S, and which may be optionally substituted, one or more times, independently from each other, with halogen or C_1-C_3-alkyl;

R^{12a}, R^{12b} represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl or -C(=O)-(C_1-C_6-alkyl) ;

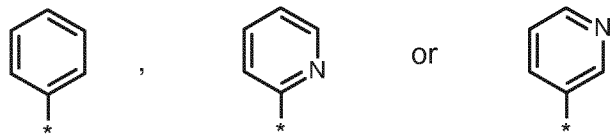
m represents 0, 1 or 2;

or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

2. The compound of formula (I) according to claim 1:

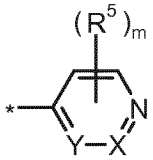
wherein:

A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule and said group is optionally substituted, one, two or three times, independently from each other, with R^{3c};

E represents a group:



wherein * indicates the point of attachment of said group with the rest of the molecule;

Q represents O or N-OH;

X represents CR^{4a};

Y represents CR^{4b} or N,

Z represents O, S, SO or NR^2;

R^1 represents hydrogen or C_1-C_4-alkyl;

R^2 represents hydrogen, C_1-C_4-alkyl, C_3-C_6-cycloalkyl, R^{8a}-C(O)-, R^{8b}O-C(O)-, R^{8c}S-C(O)-, R^6R^7N-C(O)-, $R^{10}R^{11}$N-SO_2-, R^9SO_2-, phenyl-C_1-C_3-alkyl or heteroaryl-C_1-C_3-alkyl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_4-alkyl and C_3-C_6-cycloalkyl are optionally substituted, one, two or three times, independently from each other, with R^{3b} or once with a group

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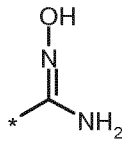


wherein * indicates the point of attachment of said group with the rest of the molecule;

R^{3a} represents, independently from each other, halogen, $R^{10}R^{11}N$-, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl;

R^{3b} represents, independently from each other, hydroxy, halogen, cyano, $R^{10}R^{11}N$-, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl;

R^{3c} represents, independently from each other, hydroxy, halogen, cyano, $R^{10}R^{11}N$-, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl, C_1-C_4-haloalkyl or C_1-C_4-haloalkoxy;

R^{3d} represents, independently from each other, halogen, $R^{10}R^{11}N$-, C_1-C_4-alkyl, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl;

R^{4a} represents hydrogen, halogen, hydroxy, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{10}R^{11}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}N$-C(O)-NH-;

R^{4b} represents hydrogen, halogen, hydroxy, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{10}R^{11}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}N$-C(O)-NH-;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b};

wherein C_1-C_4-alkoxy is optionally substituted, one, two or three times, independently from each other, with R^{3d};

R^5 represents, independently from each other, halogen, hydroxy, nitro, cyano, C_1-C_4-alkyl, C_1-C_4-alkoxy, $R^{12a}R^{12b}N$-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{12a}R^{12b}N$-C(O)-NH-;

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkoxy-C_2-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,
wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkoxy-C_2-C_4-alkoxy-C_2-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl- and 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b}; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 4- to 6-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing groups selected from O, S, C(=O) or NR^{12a}, and which may be optionally substituted, one, two or three times, independently from each other, with R^{3a};

R^{8a} represents, independently from each other, C_1-C_6-alkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl-, C_1-C_4-alkyl-S-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO-C_1-C_4-alkyl-, C_1-C_4-alkyl-SO_2-C_1-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a}; and

wherein C_1-C_6-alkyl, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{8b} represents, independently from each other, C_1-C_6-alkyl, C_1-C_4-alkoxy-C_2-C_4-alkyl-, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a}; and

wherein C_1-C_6-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{8c} represents C_1-C_4-alkyl;

R^9 represents, independently from each other, C_1-C_4-alkyl, C_3-C_6-cycloalkyl, 4- to 7-membered heterocycloalkyl, 4- to 7-membered heterocycloalkyl-C_1-C_4-alkyl, phenyl or heteroaryl,
wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with R^{3a}; and

wherein C_1-C_4-alkyl and C_3-C_6-cycloalkyl are optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{10}, R^{11} represent, independently from each other, hydrogen, C_1-C_3-alkyl, C_3-C_4-cycloalkyl, R^{12a}-O-C(O)- or phenyl,

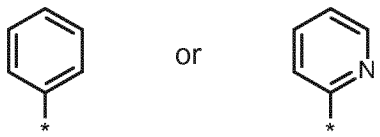
R^{12a}, R^{12b} represent, independently from each other, hydrogen, C_1-C_3-alkyl;

m represents 0 or 1;

or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

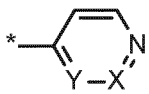
3. The compound of formula (I) according to claim 1 or 2, wherein:

A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule and said group is optionally substituted once with R^{3c};

E represents a group:



wherein * indicates the point of attachment of said group with the rest of the molecule;

Q represents O or N-OH;

X represents CR^{4a};

Y represents CR^{4b} or N,

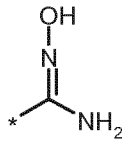
Z represents O, S, SO or NR^2;

R^1 represents hydrogen or C_1-C_4-alkyl;

R^2 represents hydrogen, C_1-C_4-alkyl, R^{8a}-C(O)-, R^{8b}O-C(O)-, R^{8c}S-C(O)-, R^6R^7N-C(O)-, $R^{10}R^{11}$N-SO_2-, R^9SO_2- or phenyl-C_1-C_3-alkyl,

wherein phenyl is optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b} or once with a group



wherein * indicates the point of attachment of said group with the rest of the molecule;

R^{3a} represents, independently from each other, halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy;

R^{3b} represents, independently from each other, hydroxy, halogen, cyano, $R^{10}R^{11}$N-, C_1-C_4-alkyl;

R^{3c} represents, independently from each other, halogen, or C_1-C_2-alkyl;

R^{3d} represents, independently from each other, halogen, $R^{10}R^{11}$N-, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl;

R^{4a} represents hydrogen, C_1-C_4-alkyl, $R^{10}R^{11}$N-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}$N-C(O)-NH-;

R^{4b} represents hydrogen, halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b},

wherein C_1-C_4-alkoxy is optionally substituted, one, two or three times, independently from each other, with R^{3d};

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_4-alkyl, C_3-C_4-cycloalkyl, methoxy-ethyl-, methoxy-ethoxy-ethyl-, methylsulfanyl-ethyl-, methylsulfinyl-ethyl-, methylsulfonyl-ethyl-, 5- to 6-membered heterocycloalkyl, or heteroaryl,;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with halogen; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 5- to 6-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing group selected from O, C(=O) or NR^{12a}, and which may be optionally substituted, one or two times, independently from each other, with R^{3a};

R^{8a} represents, independently from each other, C_1-C_6-alkyl, C_1-alkoxy-C_1-C_2-alkyl-, methylsulfanyl-C_1-C_2-alkyl-, methylsulfinyl-C_1-C_2-alkyl-, methylsulfonyl-C_1-C_2-alkyl-, C_3-C_4-cycloalkyl, 4- to 6-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with halogen, methyl or methoxy; and

wherein C_1-C_6-alkyl, cyclopropyl and 4- to 6-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with R^{3b};

R^{8b} represents, independently from each other, C_1-C_5-alkyl,

wherein C_1-C_5-alkyl is optionally substituted, one, two or three times, independently from each other, with halogen or methoxy;

R^{8c} represents C_1-C_4-alkyl;

R^9 represents, independently from each other, C_1-C_3-alkyl, C_3-C_4-cycloalkyl, 4- to 6-membered heterocycloalkyl, 4- to 6-membered heterocycloalkyl-C_1-C_2-alkyl-, or heteroaryl,
wherein heteroaryl is optionally substituted, one, two or three time, with R^{3a}; and

wherein C_1-C_3-alkyl is optionally substituted, one, two or three times, independently from each other, with hydroxy or fluoro;

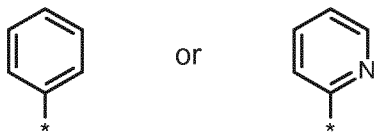
R^{10}, R^{11} represent, independently from each other, hydrogen, C_1-C_3-alkyl, C_3-C_4-cycloalkyl,

R^{12a} represents hydrogen, or C_1-C_2-alkyl;

or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

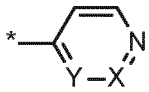
4. The compound of formula (I) according to any of claims 1 to 3, wherein

A represents a group selected from:



wherein * indicates the point of attachment of said group with the rest of the molecule and said group is optionally substituted once with R^{3c};

E represents a group:



wherein * indicates the point of attachment of said group with the rest of the molecule;

Q represents O or N-OH;

X represents CR^{4a};

Y represents CR^{4b} or N,

Z represents O, S, SO or NR^2;

R^1 represents hydrogen or C_1-C_4-alkyl;

R^2 represents hydrogen, C_1-C_4-alkyl, R^{8a}-C(O)-, R^{8b}O-C(O)-, R^{8c}S-C(O)-, R^6R^7N-C(O)-, $R^{10}R^{11}$N-SO_2-, R^9SO_2- or phenyl-C_1-C_3-alkyl,

wherein phenyl is optionally substituted, one, two or three times, independently from each other, with R^{3a};

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with R^{3b} or one time with a group

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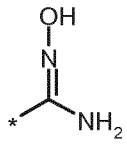


wherein * indicates the point of attachment of said group with the rest of the molecule;

R^{3a} represents, independently from each other, halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy;

R^{3b} represents, independently from each other, hydroxy, halogen, cyano, C_1-C_4-alkyl;

R^{3c} represents, independently from each other, halogen, or C_1-C_2-alkyl;

R^{3d} represents, independently from each other, halogen, $(CH_3)_2N$-, C_1-C_4-alkoxy, C_3-C_6-cycloalkyl;

R^{4a} represents hydrogen, C_1-C_4-alkyl, H_2N-, R^{8a}-C(O)-NH-, R^{8b}O-C(O)-NH- or $R^{10}R^{11}$N-C(O)-NH-;

R^{4b} represents hydrogen, halogen, C_1-C_4-alkyl, C_1-C_4-alkoxy;

wherein C_1-C_4-alkoxy is optionally substituted, one, two or three times, independently from each other, with R^{3d};

R^6, R^7 represent, independently from each other, hydrogen, C_1-C_4-alkyl, cyclopropyl, methoxy-ethyl-, methoxy-ethoxy-ethyl-, methylsulfanyl-ethyl-, methylsulfinyl-ethyl-, methylsulfonyl-ethyl-, tetrahydro-2H-pyran-4-yl or pyridyl;

wherein C_1-C_4-alkyl is optionally substituted, one, two or three times, independently from each other, with halogen; or

R^6 and R^7 together with the nitrogen atom to which they are attached form a 5- to 6-membered nitrogen containing heterocyclic ring, optionally containing one or two additional heteroatom containing group selected from O, C(=O) or NR^{12a}, and which may be optionally substituted, one or two times, independently from each other, with methyl;

R^{8a} represents, independently from each other, C_1-C_6-alkyl, methoxymethyl-, methylsulfanyl-C_1-C_2-alkyl-, methylsulfinyl-C_1-C_2-alkyl-, methylsulfonyl-C_1-C_2-alkyl-, cyclopropyl, 4- to 6-membered heterocycloalkyl, phenyl or heteroaryl,

wherein phenyl and heteroaryl are optionally substituted, one, two or three times, independently from each other, with fluoro, methyl or methoxy; and

wherein C_1-C_6-alkyl, cyclopropyl and 4- to 6-membered heterocycloalkyl, are optionally substituted, one, two or three times, independently from each other, with hydroxy, fluoro, methyl or $(CH_3)_2N$-;

R^{8b} represents, independently from each other, C_1-C_5-alkyl,

wherein C_1-C_5-alkyl is optionally substituted, one, two or three times, independently from each other, with fluoro or methoxy;

R^{8c} represents C_1-C_4-alkyl;

R^9 represents, independently from each other, C_1-C_3-alkyl, cyclopropyl, 4 to 6 membered heterocycloalkyl, 4 to 6 membered heterocycloalkyl-C_1-C_2-alkyl-, or heteroaryl,
wherein heteroaryl is optionally substituted, once with methyl; and

wherein C_1-C_3-alkyl is optionally substituted, one, two or three times, independently from each other, with hydroxy or fluoro;

R^{10}, R^{11} represent, independently from each other, hydrogen, C_1-C_3-alkyl, C_3-C_4-cycloalkyl,

R^{12a} represents hydrogen, or C_1-C_2-alkyl;

or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

5. The compound according to any of claims 1 to 4, which is selected from the group consisting of:
6-benzyl-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-(3-chloropyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
tert-butyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
3-(phenylamino)-2-(pyridin-4-yl)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one,

6-(cyclopropylcarbonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
6-acetyl-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-6-propanoyl-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(2,2-dimethylpropanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
N-ethyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide
tert-butyl 2-(3-fluoropyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-butyl 2-(2-methylpyrimidin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-(2-methylpyrimidin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
2-(2-methylpyrimidin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(2-methylpropanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
methyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
6-(methylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one 6-oxide,
2-(2-aminopyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-(2-aminopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
tert-butyl 2-[2-(acetylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,

N-ethyl-2-(2-methylpyrimidin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
6-acetyl-2-(2-methylpyrimidin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
methyl 2-(2-methylpyrimidin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2-[2-(acetylamino)pyridin-4-yl]-N-ethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
2-(2-methylpyrimidin-4-yl)-6-(methylsulfonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
N-4-[6-(cyclopropylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
methyl 2-[2-(acetylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-4-[6-(methylsulfonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
2-(3-fluoropyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylacetamide,
N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylcyclopropanecarboxamide,
3,3,3-trifluoro-N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylpropanamide,
2-(3-methylpyridin-4-yl)-3-(phenylamino)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one,
2-(3-chloropyridin-4-yl)-3-(phenylamino)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one,
2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one,
2-(3-methylpyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
2-(3-bromopyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
2-(3-chloropyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylpropanamide,

2-methoxy-N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylacetamide,
2-(methylsulfanyl)-N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylacetamide,
2-(methylsulfinyl)-N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylacetamide,
2-(methylsulfonyl)-N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylacetamide,
N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl-1,3-thiazole-4-carboxamide,
N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl-1,3-oxazole-5-carboxamide,
N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-yl-1,3-thiazole-5-carboxamide,
4-fluoro-N-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylbenzamide,
methyl 4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylcarbamate,
1-ethyl-3-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylurea,
1-cyclopropyl-3-4-[4-oxo-3-(phenylamino)-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl]pyridin-2-ylurea,
6-(3-hydroxypropanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(3-hydroxy-3-methylbutanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(3,3-dimethylbutanoyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(1H-imidazol-5-ylcarbonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-[(1-methyl-1H-imidazol-4-yl)carbonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-2-ylcarbonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-3-ylcarbonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,

3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-4-ylcarbonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
1-methyl-6-(methylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
1-ethyl-6-(methylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(cyclopropylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-6-(propan-2-ylsulfonyl)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-[(difluoromethyl)sulfonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-[(3,3,3-trifluoropropyl)sulfonyl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(tetrahydro-2H-pyran-4-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-[(tetrahydro-2H-pyran-4-ylmethyl)sulfonyl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(1H-imidazol-5-ylsulfonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-2-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(pyridin-3-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
ethyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
propan-2-yl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2,2-dimethylpropyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2-fluoroethyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2-methoxyethyl 4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

N-methyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N,N-dimethyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-(2,2-difluoroethyl)-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-cyclopropyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-tert-butyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-(2-methoxyethyl)-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-[2-(methylsulfanyl)ethyl]-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-2-[(S)-methylsulfinyl]ethyl-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-[2-(methylsulfonyl)ethyl]-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-[2-(2-methoxyethoxy)ethyl]-4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
6-[(2-oxoimidazolidin-1-yl)carbonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-2-(pyridin-4-yl)-6-(pyrrolidin-1-ylcarbonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-(phenylamino)-6-(piperidin-1-ylcarbonyl)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(morpholin-4-ylcarbonyl)-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-[(4-methylpiperazin-1-yl)carbonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-N-(tetrahydro-2H-pyran-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
4-oxo-3-(phenylamino)-N-(pyridin-3-yl)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
[4-oxo-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridin-6-yl]acetonitrile,

tert-butyl 2-(3-methylpyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-butyl 2-(3-bromopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2-(3-fluoropyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
tert-butyl 2-(3-methoxypyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
methyl 2-(3-methoxypyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
6-acetyl-2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(2,2-dimethylpropanoyl)-2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-(3-methoxypyridin-4-yl)-6-(methylsulfonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(cyclopropylcarbonyl)-2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-(3-methoxypyridin-4-yl)-3-(phenylamino)-6-(propan-2-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-[(difluoromethyl)sulfonyl]-2-(3-methoxypyridin-4-yl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-(3-methoxypyridin-4-yl)-3-(phenylamino)-6-[(3,3,3-trifluoropropyl)sulfonyl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
N-4-[6-acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-4-[6-(1H-imidazol-5-ylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-4-[4-oxo-3-(phenylamino)-6-(pyridin-2-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-4-[4-oxo-3-(phenylamino)-6-(pyridin-3-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-4-[4-oxo-3-(phenylamino)-6-(pyridin-4-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,

N-4-[6-(1H-imidazol-5-ylsulfonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-(4-6-[(1-methyl-1H-imidazol-4-yl)carbonyl]-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-ylpyridin-2-yl)acetamide,
tert-butyl 2-2-[(2-fluoro-2-methylpropanoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-butyl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-butyl 2-[2-([(1S)-2,2-difluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-butyl 4-oxo-3-(phenylamino)-2-2-[(1,3-thiazol-5-ylcarbonyl)amino]pyridin-4-yl-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
6-[(2-hydroxyethyl)sulfonyl]-3-(phenylamino)-2-(pyridin-4-yl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-[2-(acetylamino)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-{4-[3-anilino-6-(morpholin-4-ylcarbonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
N-4-[4-oxo-3-(phenylamino)-6-(pyrrolidin-1-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
N-(4-{3-anilino-6-[(4-methylpiperazin-1-yl)carbonyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide,
tert-butyl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 3-anilino-2-[2-({[(rel-1S,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate
2-fluoro-2-methyl-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylpropanamide,
tert-butyl 2-(2-[(1-fluorocyclopropyl)carbonyl]aminopyridin-4-yl)-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
1-fluoro-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
4-fluoro-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,
N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-1,3-thiazole-5-carboxamide,

(1S,2S)-2-fluoro-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
(1S)-2,2-difluoro-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
(1S,2S)-2-fluoro-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
methyl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-[4-(3-anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-4-fluoro-3-methoxybenzamide,
methyl 3-anilino-2-[2-({[(1R,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
(1S,2R)-N-[4-(3-Anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide,
methyl 3-anilino-2-[2-({[(1S,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
methyl 3-anilino-2-{2-[(2-fluoro-2-methylpropanoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-[4-(3-anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-1H-pyrazole-5-carboxamide
methyl 3-anilino-2-[2-({[(1RS)-2,2-difluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
methyl 3-anilino-2-(2-{[(1-fluorocyclopropyl)carbonyl]amino}pyridin-4-yl)-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
rel-(1R,2R)-N-{4-[3-anilino-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2-fluorocyclopropanecarboxamide,
(1RS)-N-{4-[3-anilino-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2,2-difluorocyclopropanecarboxamide,
N-{4-[3-anilino-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-1-fluorocyclopropanecarboxamide,
N-{4-[3-anilino-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-1,3-thiazole-5-carboxamide,
N-[4-(3-anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-2-hydroxy-2-methylpropanamide,
N-[4-(3-anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-N2,N2-dimethylglycinamide,

N-[4-(3-Anilino-4-oxo-1,4,5,7-tetrahydropyrano[3,4-b]pyrrol-2-yl)pyridin-2-yl]-3,4-difluorobenzamide,

isopropyl 3-anilino-2-{2-[(2-fluoro-2-methylpropanoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

isopropyl 3-anilino-4-oxo-2-{2-[(1,3-thiazol-5-ylcarbonyl)amino]pyridin-4-yl}-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

isopropyl 3-anilino-2-[2-({[rel-(1R,2R)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

isopropyl 3-anilino-2-[2-({[(1RS)-2,2-difluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

isopropyl 3-anilino-2-(2-{[(1-fluorocyclopropyl)carbonyl]amino}pyridin-4-yl)-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

N-{4-[3-anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-4-fluorobenzamide,

N-{4-[3-anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-1,3-thiazole-5-carboxamide,

N-{4-[3-anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2-fluoro-2-methylpropanamide,

rel-(1R,2R)-N-{4-[3-anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2-fluorocyclopropanecarboxamide,

(1RS)-N-{4-[3-anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-2,2-difluorocyclopropanecarboxamide,

N-{4-[3-anilino-6-(1H-imidazol-5-ylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}-1-fluorocyclopropanecarboxamide,

N-{4-[3-anilino-4-oxo-6-(piperidin-1-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

2-(2-acetamidopyridin-4-yl)-3-anilino-N,N-diethyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,

2-(2-acetamidopyridin-4-yl)-3-anilino-N-methyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,

N-{4-[3-anilino-4-oxo-6-(3,3,3-trifluoropropanoyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-[4-(3-anilino-6-isobutyryl-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]acetamide,

N-{4-[3-anilino-6-(isopropylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-{4-[3-anilino-6-(cyclopropylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

N-{4-[3-anilino-4-oxo-6-(tetrahydro-2H-pyran-4-ylsulfonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide

N-{4-[3-anilino-6-(3,3-dimethylbutanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-{4-[3-anilino-4-oxo-6-(1,3-thiazol-5-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-{4-[3-anilino-6-(1,3-oxazol-5-ylcarbonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-{4-[3-anilino-6-(3-hydroxy-3-methylbutanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-(4-{3-anilino-4-oxo-6-[(2RS)-3,3,3-trifluoro-2-methylpropanoyl]-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide,

N-{4-[3-anilino-6-(4,4-dimethylpentanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-[4-(3-anilino-4-oxo-6-propionyl-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]acetamide,

N-{4-[3-anilino-6-(2,2-dimethylpropanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-(4-{3-anilino-4-oxo-6-[(3,3,3-trifluoropropyl)sulfonyl]-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamideide,

ethyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

2-fluoroethyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

isopropyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

2-(2-acetamidopyridin-4-yl)-3-anilino-N-isopropyl-N-methyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,

2-(2-acetamidopyridin-4-yl)-3-anilino-N-methyl-4-oxo-N-propyl-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

N-(4-{3-anilino-6-[(2-hydroxyethyl)sulfonyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide

N-{4-[3-anilino-6-(3-hydroxypropanoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,

N-{4-[3-anilino-4-oxo-6-(4,4,4-trifluorobutanoyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
N-(4-{3-anilino-6-[(1-methylpiperidin-4-yl)carbonyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide,
N-(4-{3-anilino-6-[3-(methylsulfanyl)propanoyl]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide,
N-{4-[3-anilino-4-oxo-6-(1,2-thiazol-4-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
N-{4-[3-anilino-4-oxo-6-(1,3-thiazol-4-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
N-{4-[3-anilino-6-(1,3-oxazol-4-ylcarbonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
tert-butyl 3-anilino-2-[2-({[(1S,2S)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
(1S,2S)-N-[4-(3-anilino-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl]-2-fluorocyclopropanecarboxamide,
(1S,2S)-2-fluoro-N-4-[4-oxo-3-(phenylamino)-6-propanoyl-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
N-4-[6-(1,3-oxazol-2-ylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
(1S,2S)-2-fluoro-N-4-[4-oxo-3-(phenylamino)-6-(pyridin-4-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
(1S,2S)-2-fluoro-N-4-[6-(3-hydroxy-3-methylbutanoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
(1S,2S)-2-fluoro-N-4-[6-(3-hydroxypropanoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide
(1S,2S)-2-fluoro-N-4-[6-(methylsulfonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
(1S,2S)-2-fluoro-N-4-[6-(1H-imidazol-5-ylsulfonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
methyl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-N-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,

N-ethyl-2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
(1S,2S)-2-fluoro-N-(4-6-[(4-methylpiperazin-1-yl)carbonyl]-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-ylpyridin-2-yl)cyclopropanecarboxamide,
N-(4-6-[3-(methylsulfonyl)propanoyl]-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-ylpyridin-2-yl)acetamide,
N-4-[6-(3-fluoropropanoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,
(1S,2S)-N-4-[6-(cyclopropylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-2-fluorocyclopropanecarboxamide,
(1S,2S)-N-4-[6-(2,2-dimethylpropanoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-2-fluorocyclopropanecarboxamide,
(1S,2S)-2-fluoro-N-4-[4-oxo-3-(phenylamino)-6-(propan-2-ylsulfonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylcyclopropanecarboxamide,
ethyl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
propan-2-yl 2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N,N-diethyl-2-[2-([(1S,2S)-2-fluorocyclopropyl]carbonylamino)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
(1E/Z)-N'-hydroxy-2-[(4E/Z)-4-(hydroxyimino)-3-(phenylamino)-2-(pyridin-4-yl)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridin-6-yl]ethanimidamide,
N-{4-[3-Anilino-4-oxo-6-(4,4,4-trifluoro-3,3-dimethylbutanoyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl}acetamide,
tert-Butyl 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 3-anilino-4-oxo-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 3-anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 3-anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
3-Anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-Anilino-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,

3-Anilino-2-[3-(2-methoxyethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-Anilino-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-Acetyl-3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-Acetyl-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-Acetyl-2-[3-(2-methoxyethoxy)pyridin-4-yl]-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-Acetyl-2-[3-(cyclopropylmethoxy)pyridin-4-yl]-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
3-Anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-6-(methylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-(Methylsulfonyl)-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-[3-(2-Methoxyethoxy)pyridin-4-yl]-6-(methylsulfonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-[3-(Cyclopropylmethoxy)pyridin-4-yl]-6-(methylsulfonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one
Methyl 2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate
2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-N-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide
2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide
2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-6-(morpholin-4-ylcarbonyl)-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one
2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-6-[(4-methylpiperazin-1-yl)carbonyl]-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one
2-[3-(2,2-Difluoroethoxy)pyridin-4-yl]-3-(phenylamino)-6-(propan-2-ylsulfonyl)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one
Methyl 4-oxo-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate
N-Methyl-4-oxo-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

N,N-Dimethyl-4-oxo-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

6-(Morpholin-4-ylcarbonyl)-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

6-[(4-Methylpiperazin-1-yl)carbonyl]-3-(phenylamino)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

3-(Phenylamino)-6-(propan-2-ylsulfonyl)-2-[3-(2,2,2-trifluoroethoxy)pyridin-4-yl]-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

Methyl 2-[3-(2-methoxyethoxy)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

2-[3-(2-Methoxyethoxy)pyridin-4-yl]-N-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

Methyl 2-[3-(cyclopropylmethoxy)pyridin-4-yl]-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate

2-[3-(Cyclopropylmethoxy)pyridin-4-yl]-N-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide

2-[3-(Cyclopropylmethoxy)pyridin-4-yl]-6-[(4-methylpiperazin-1-yl)carbonyl]-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one

tert-Butyl 2-2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,

N-4-[6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]carbonyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylacetamide,

tert-Butyl 2-2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl-1-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

4-Fluoro-3-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,

N-4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-3-methoxybenzamide,

N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-3-methoxybenzamide,

4-Fluoro-3-methoxy-N-4-[6-(morpholin-4-ylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,

N-4-[6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]carbonyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-3-methoxybenzamide,

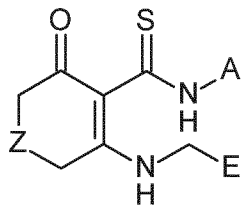
4-Fluoro-3-methoxy-N-4-[4-oxo-3-(phenylamino)-6-(pyrrolidin-1-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,
tert-Butyl 2-2-[(4-fluoro-2-methylbenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
4-Fluoro-2-methyl-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,
N-4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluoro-2-methylbenzamide,
tert-Butyl 2-2-[(4-methoxy-2-methylbenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
4-Methoxy-2-methyl-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,
tert-Butyl 2-2-[(5-fluoro-2-methylbenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
5-Fluoro-2-methyl-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,
tert-Butyl 2-2-[(4-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-4-fluorobenzamide,
(1S,2S)-N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-2-fluorocyclopropanecarboxamide,
N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-1-fluorocyclopropanecarboxamide,
tert-Butyl 4-oxo-3-(phenylamino)-2-2-[(1H-1,2,3-triazol-5-ylcarbonyl)amino]pyridin-4-yl-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-4-[4-Oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-1H-1,2,3-triazole-5-carboxamide,
tert-Butyl 2-3-[2-(dimethylamino)ethoxy]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2-3-[2-(Dimethylamino)ethoxy]pyridin-4-yl-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
6-Acetyl-2-3-[2-(dimethylamino)ethoxy]pyridin-4-yl-3-(phenylamino)-1,5,6,7-tetrahydro-4H-pyrrolo[2,3-c]pyridin-4-one,
2-3-[2-(Dimethylamino)ethoxy]pyridin-4-yl-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-sulfonamide,

2-[3-(2-Methoxyethoxy)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-sulfonamide,
3-Anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-N,N-dimethyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-sulfonamide,
2-[3-(Cyclopropylmethoxy)pyridin-4-yl]-N,N-dimethyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-sulfonamide,
tert-Butyl 2-2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
3-Fluoro-4-methoxy-N-4-[4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,
N-4-[6-Acetyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide,
tert-Butyl 2-2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl-1-methyl-4-oxo-3-(phenylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
3-Fluoro-4-methoxy-N-4-[1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide
N-4-[6-Acetyl-1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide,
N-4-[6-(Dimethylsulfamoyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide,
N-4-[6-(Dimethylsulfamoyl)-1-methyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide,
3-Fluoro-4-methoxy-N-4-[6-(morpholin-4-ylcarbonyl)-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,
N-4-[6-[(2R,6S)-2,6-Dimethylmorpholin-4-yl]carbonyl-4-oxo-3-(phenylamino)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-yl-3-fluoro-4-methoxybenzamide,
3-Fluoro-4-methoxy-N-4-[4-oxo-3-(phenylamino)-6-(pyrrolidin-1-ylcarbonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl]pyridin-2-ylbenzamide,
tert-butyl 2-(2-Aminopyridin-4-yl)-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 2-(2-acetamidopyridin-4-yl)-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 2-(2-aminopyridin-4-yl)-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-Butyl 2-(2-acetamidopyridin-4-yl)-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,

tert-Butyl 4-oxo-3-(phenylamino)-2-[3-(trifluoromethyl)pyridin-4-yl]-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
3-(Phenylamino)-2-[3-(trifluoromethyl)pyridin-4-yl]-1,7-dihydrothiopyrano[3,4-b]pyrrol-4(5H)-one,
3-(Phenylamino)-2-[3-(trifluoromethyl)pyridin-4-yl]-1,7-dihydropyrano[3,4-b]pyrrol-4(5H)-one,
S-tert-butyl 2-(2-acetamidopyridin-4-yl)-3-anilino-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate,
N-(4-{3-[(4-Fluorophenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide,
N-(4-{3-[(4-methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl}pyridin-2-yl)acetamide,
S-tert-butyl 3-anilino-2-[3-(2,2-difluoroethoxy)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate,
S-tert-butyl 3-anilino-2-{2-[(3-fluoro-4-methoxybenzoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate,
S-tert-butyl 3-anilino-2-{2-[(4-fluoro-3-methoxybenzoyl)amino]pyridin-4-yl}-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate,
S-tert-butyl 3-anilino-2-(2-{[(1-fluorocyclopropyl)carbonyl]amino}pyridin-4-yl)-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate,
S-tert-butyl 3-anilino-2-[2-({[(1S,2S)-2-fluorocyclopropyl]carbonyl}amino)pyridin-4-yl]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carbothioate,
tert-butyl 2-(2-aminopyridin-4-yl)-4-oxo-3-(pyridin-2-ylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
tert-butyl 2-(2-acetamidopyridin-4-yl)-4-oxo-3-(pyridin-2-ylamino)-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-(4-(3-[(4-fluorophenyl)amino]-6-(methylsulfonyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide,
N-(4-(6-acetyl-3-[(4-fluorophenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide,
2-[2-(acetylamino)pyridin-4-yl]-3-[(4-fluorophenyl)amino]-N-methyl-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
methyl 2-[2-(acetylamino)pyridin-4-yl]-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-(4-(3-[(4-fluorophenyl)amino]-6-(methylsulfamoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide,

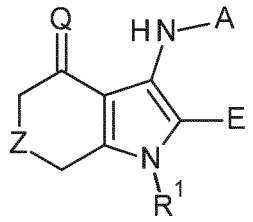
propan-2-yl 2-[2-(acetylamino)pyridin-4-yl]-3-[(4-fluorophenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
2-[2-(acetylamino)pyridin-4-yl]-N,N-dimethyl-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
N-(4-(3-[(4-methylphenyl)amino]-4-oxo-6-(propan-2-ylsulfonyl)-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide,
N-(4-(6-acetyl-3-[(4-methylphenyl)amino]-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide,
2-[2-(acetylamino)pyridin-4-yl]-N-methyl-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxamide,
methyl 2-[2-(acetylamino)pyridin-4-yl]-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate,
N-(4-(3-[(4-methylphenyl)amino]-6-(methylsulfamoyl)-4-oxo-4,5,6,7-tetrahydro-1H-pyrrolo[2,3-c]pyridin-2-yl)pyridin-2-yl)acetamide,
propan-2-yl 2-[2-(acetylamino)pyridin-4-yl]-3-[(4-methylphenyl)amino]-4-oxo-1,4,5,7-tetrahydro-6H-pyrrolo[2,3-c]pyridine-6-carboxylate
or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

6. A method of preparing a compound of general formula (I) according to any of claims 1 to 5, said method comprising the step of allowing an intermediate compound of general formula (1-2) :



1-2

in which A, E and Z are as defined for the compound of formula (I) in any of claims 1 to 5, to react
with a base and/or oxidizing reagent, preferably an oxidizing agent, such as, for example hydrogen peroxide or SIBX,
optionally being further reacted with an alkylating agent which contains a suitable leaving group,
thereby giving a compound of general formula (I) :



(I)

in which R^1, A, E and Z are as defined for the compound of formula (I) in any of claims 1 to 5, R^1 is a hydrogen atom and Q is an oxygen atom.

7. Use of a compound according to any of claims 1 to 5 for the treatment or prophylaxis of a disease.

8. Use according to claim 7, whereby the disease is a hyperproliferative disease and/or disorder responsive to induction of cell death.

9. Use according to claim 8, whereby the hyperproliferative disease and/or disorder responsive to induction of cell death is a haematological tumour, solid tumour and/or metastases thereof.

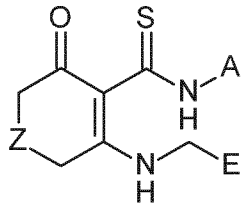
10. Use according to claim 9, whereby the tumor is cervical -, breast -, non-small cell lung -, prostate -, colon - and melanoma tumor and/or metastases thereof.

11. A pharmaceutical composition comprising at least one compound according to any of claims 1 to 5, together with at least one pharmaceutically acceptable auxiliary.

12. A composition according to claim 11, for the treatment of a haematological tumour, a solid tumour and/or metastases thereof.

13. A combination comprising one or more first active ingredients selected from a compound according to any of claims 1 to 5, and one or more second active ingredients selected from chemotherapeutic anti-cancer agents and target-specific anti-cancer agents.

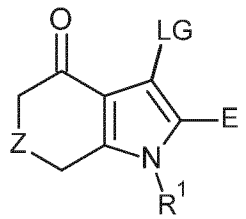
14. A compound which is selected from:



1-2

whereby A, E and Z have the meaning according to any of claims 1 to 5;

and,



I-h

whereby R^1, E and Z have the meaning according to any of claims 1 to 5 and LG represents a leaving group, such as, Cl, Br, I, aryl sulfonates, such as p-toluene sulfonate, or alkyl sulfonates, such as methane sulfonate or trifluoromethane sulfonate.

15. The use of a compound according to claim 14 for preparing a compound of formula (I) according to any of claims 1 to 5, or an N-oxide, a salt, a tautomer or a stereoisomer of said compound, or a salt of said N-oxide, tautomer or stereoisomer.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2016/080640

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☒ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/080640

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D471/04 C07D491/04 C07D495/04 A61K31/35 A61K31/382
A61K31/407 A61K31/437 A61P35/00
ADD.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2014/147203 A1 (BAYER PHARMA AG [DE]) 25 September 2014 (2014-09-25) page 4, line 24 - line 29 page 5; compound (I) page 57, line 24 - page 58, line 6 examples 2-5-4 page 150; table claims 1, 9-13 -----	1-15

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 February 2017	21/03/2017

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Hoepfner, Wolfgang

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2016/080640

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2014147203 A1	25-09-2014	AR 095706 A1	04-11-2015
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		CN 105209455 A	30-12-2015
		EP 2976336 A1	27-01-2016
		JP 2016514718 A	23-05-2016
		TW 201514166 A	16-04-2015
		US 2016046610 A1	18-02-2016
		UY 35500 A	31-10-2014
		WO 2014147203 A1	25-09-2014