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Pharmaceutical 6,5 Heterobicyclic Ring Derivatives

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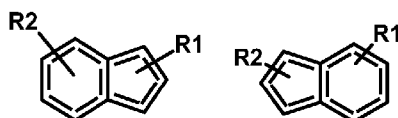
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(54) Title: PHARMACEUTICAL 6,5 HETEROBICYCLIC RING DERIVATIVES



(I)

(57) Abstract: The invention relates to 6,5 heterobicyclic ring derivatives of formula (I), processes for preparing them, pharmaceutical compositions containing them and their use for the treatment of inflammatory conditions driven by STING activation, such as, but not confined to, SLE and geographic atrophy.



PHARMACEUTICAL 6,5 HETEROBICYCLIC RING DERIVATIVES

FIELD OF THE INVENTION

5 The invention relates to 6,5 heterobicyclic ring derivatives, processes for preparing them, pharmaceutical compositions containing them and their use for the treatment of inflammatory conditions driven by STING activation, such as, but not confined to, SLE and geographic atrophy. 6,5 heterobicyclic ring derivatives may be useful as STING (Stimulator of Interferon Genes) antagonists that inhibit the STING pathway.

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BACKGROUND OF THE INVENTION

The response of the body to tissue damage is to mount an inflammatory response. Usually this is self-limiting and functions to remove damaged tissue, counter any infectious microorganisms and restore the tissue to normal function. This innate immune response utilises pattern recognition receptors (PRRs) that can be divided into those that recognise specific microbial products (pathogen associated molecular patterns; PAMPs) and those that recognise host molecules (damage associated molecular patterns; DAMPs). The value in responding to PAMPs is clear but responding to DAMPs is equally important as it amplifies the inflammatory response and allows infections to be controlled early before they have a chance to overwhelm the host.

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DNA from viruses and bacteria and self DNA (nuclear or mitochondrial) can serve as PAMPs and DAMPs respectively (Paludan SR & Bowie AG (2013). Immune sensing of DNA. *Immunity*, 38:870–880). A number of DNA PRRs are recognised including cyclic GMP AMP synthase (cGAS) in the cytoplasmic compartment. cGAS appears to show little discrimination between microbial or self DNA although the extent of activation depends upon the length of the DNA, its' structure and whether or not it is oxidised (Andreeva L et al (2017). cGAS Senses Long and HMGB/TFAM-bound U-Turn DNA by Forming Protein-DNA Ladders. *Nature* 549:394-398). In the absence of infection or tissue damage, cGAS is silent, partly because self DNA is compartmentalised into the nucleus and mitochondria, and partly because of the activity of DNase enzymes that take care of physiological low levels of DNA leakage from cells and organelles.

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When cGAS binds DNA it undergoes a conformational change and acquires enzyme activity utilising ATP and GTP as substrates and producing the cyclic dinucleotide 2',3'-cGAMP as a product. 2',3'-cGAMP engages the adapter protein STING that exists as a dimer on the endoplasmic reticulum. A conformational change to STING triggers a series of events including translocation to the trans Golgi network, recruitment of the tank binding kinase, TBK1, and phosphorylation of substrates IRF3, IKK and STAT 6 leading to the type I interferon response, proinflammatory cytokines and chemokines (Li, Y (2017). Regulating STING in health and

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35

disease. *Journal of Inflammation* 14:11). Activation is also linked to cell death pathways for example through inflammasome activation (Gaidt MM et al (2017). The DNA Inflammasome in Human Myeloid Cells Is Initiated by a STING-Cell Death Program Upstream of NLRP3. *Cell* 171:1110-1124).

5 There are instances where artificially stimulating the cGAS STING pathway may have value. For instance, strengthening the host immune response to infection or boosting immunological responses to tumour cells. STING agonists are being developed for these purposes (Mullard A (2018). Can innate immune system targets turn up the heat on 'cold' tumours? *Nat Rev Drug Discov.* 17:3-5).

10 The reverse is also true. For whilst activation of the cGAS STING pathway is an important response to tissue injury and infection, inflammatory changes induced by excessive activation of the pathway may be detrimental. Mutations in human STING that give rise to a constitutive activation of the protein cause SAVI (STING associated vasculopathy of infants) (Liu, Y (2014). Activated STING in a Vascular and Pulmonary Syndrome. *The New England Journal of Medicine*, 371:507–518) with affected children having skin rash, skin ulceration and interstitial lung disease (all symptoms that can be found in severe SLE). And in SLE, measurement of 2',3'-cGAMP in peripheral blood mononuclear cells was associated with patients with higher disease scores (An J et al (2017). Expression of Cyclic GMP-AMP Synthase in Patients With Systemic Lupus Erythematosus. *Arthritis Rheumatol.* 69:800-807) indicating the cGAS STING pathway to be active in patients with more severe SLE and suggesting the therapeutic potential of STING inhibitors.

There are other conditions where DNA sensing pathways and the cGAS STING pathway in particular, may drive pathological changes and where STING inhibitors may have utility. Extensive tissue damage, as seen in systemic inflammatory response syndrome (SIRS) and in critical care patients, is associated with symptoms similar to sepsis that may be explained by extensive engagement of innate immune receptors by DNA derived from tissue damage (Boyapati, RK et al. (2017). Advances in the understanding of mitochondrial DNA as a pathogenic factor in inflammatory diseases. *F1000Research* 6: 169). And in tissues where repair processes are limited, such as the heart and the brain, the inflammatory response to tissue injury can contribute to tissue damage. Experimental evidence suggests a damaging role for the cGAS STING pathway in myocardial infarction (King, KR et al (2017). IRF3 and type I interferons fuel a fatal response to myocardial infarction. *Nat. Med.* 23:1481-1487) and expression of cGAS and STING in CNS cells (Jeffries AM & Marriott I (2017). Human microglia and astrocytes express cGAS-STING viral sensing components. *Neurosci Lett.* 658:53-56) suggests similar mechanisms could be active in stroke.

35 Although the inflammatory response is essential to host defence, there are instances when the vigour of the host response to an infectious microorganism is itself a problem. For example the high mortality of N5N1 infection (avian flu) is caused by the local accumulation of exudate in the

lungs from damaged cells attacked by the patient's own immune response (Short KR et al (2016). Influenza virus damages the alveolar barrier by disrupting epithelial cell tight junctions. Eur Respir J. 47:954-66). In such circumstances there may be a need to limit the extent of the innate immune response and inhibitors, that may include STING inhibitors, could have value in those circumstances.

Another area receiving attention relates to tissue degeneration. Many diseases are associated with mitochondrial stress and this has been linked to the release into the cytoplasm of mitochondrial DNA that can activate the cGAS STING pathway. This mechanism leads to the death of retinal pigmented epithelial cells and causes blindness in geographic atrophy (Kerur N et al (2018). cGAS drives noncanonical-inflammasome activation in age-related macular degeneration. Nat. Med. 24:50-61). The mechanism may also be active in other neurodegenerative diseases such as Parkinson's disease, amyotrophic lateral sclerosis, Alzheimer's disease and peripheral degenerative diseases such as chondrocyte death in osteoarthritis, loss of pancreatic islet cells etc.

Thus, there is a clear need to develop STING antagonists to explore their therapeutic potential in a range of human conditions with high unmet medical need.

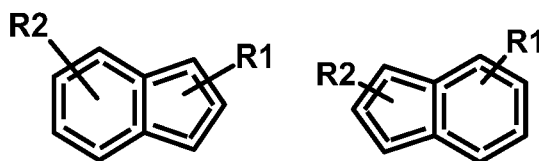
SUMMARY OF THE INVENTION

The present invention relates to 6,5 heterobicyclic ring derivatives, processes for preparing them, pharmaceutical compositions containing them and their use for the treatment of inflammatory conditions driven by STING activation, such as, but not confined to, SLE and geographic atrophy. A further aspect of the present invention consists of novel compounds that demonstrate the ability to functionally antagonise STING activation.

Further aspects of the invention will become apparent from the detailed specification.

DESCRIPTION

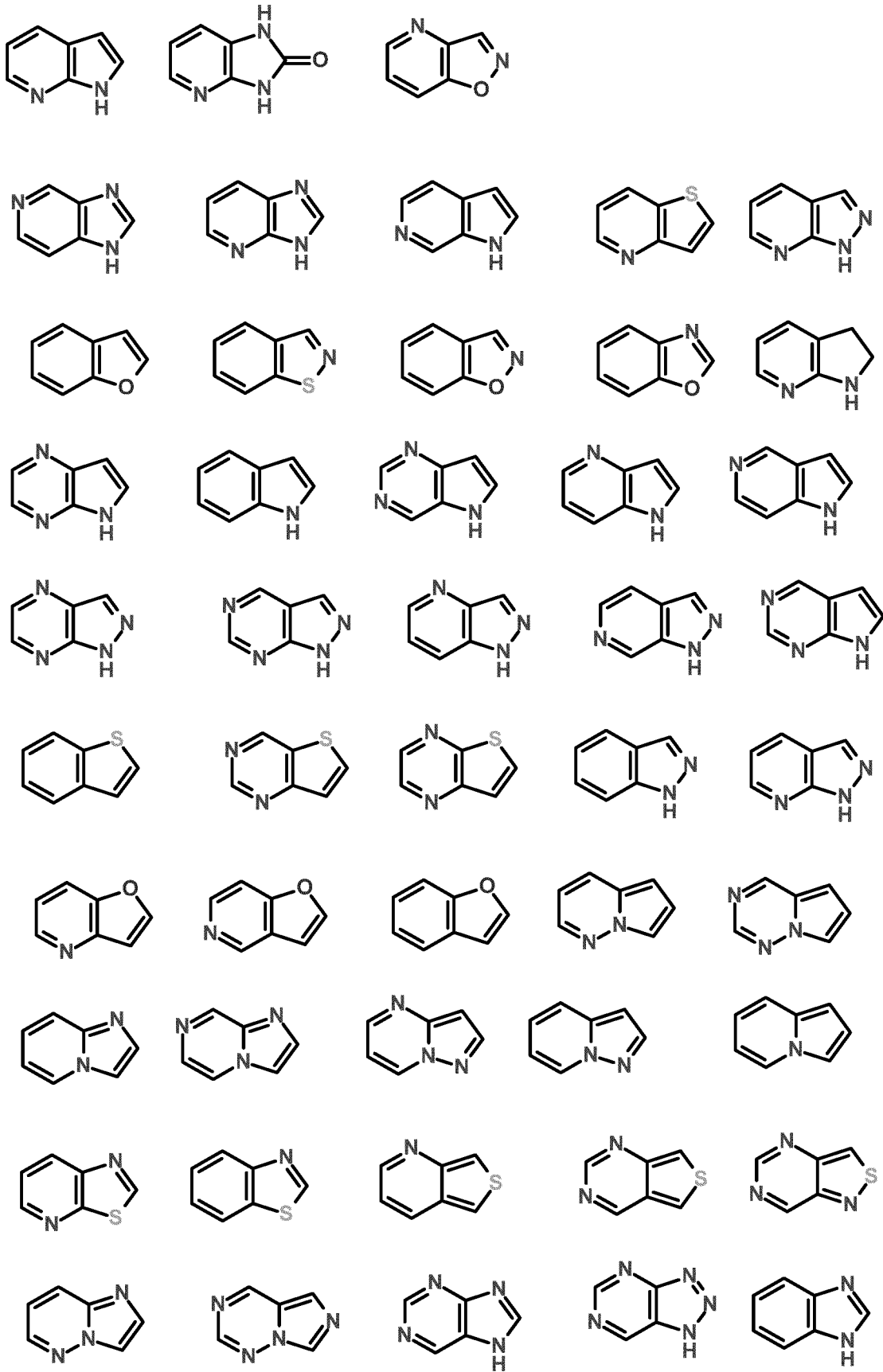
In one aspect, the present invention relates to compounds of general formula I, or a pharmaceutically acceptable acid addition salt, a racemic mixture or its corresponding enantiomer and/or optical isomers thereof,



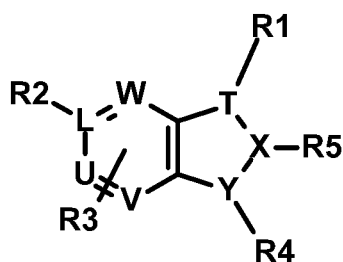
(I)

wherein

- the central core A which is the 6,5 heterobicyclic rings contains at least one heteroatom from O,N,S and C atoms can be optionally substituted by halogen, cyano, C1-6 alkyl, trifluoromethyl, difluoromethyl, (C2-6) alkenyl, hydroxy, (C1-6) alkoxy, difluoromethoxy, trifluoromethoxy, trifluoroethoxy, (C1-6) alkylthio, (C1-6) alkylsulphonyl, amino, (C1-6) alkylamino, di(C1-6)alkylamino, (C1-6)alkoxy(C1-6)alkyl-amino, N-[(C1-6)alkyl]-N-[hydroxy(C1-6)alkyl]amino, (C2-6) alkylcarbonylamino, (C2-6) alkoxy carbonylamino, (C1-6) alkylsulphonylamino, formyl, (C2-6) alkylcarbonyl, carboxy, (C2-6) alkoxy carbonyl, aminocarbonyl, (C1-6) alkylaminocarbonyl, di(C1-6)alkylaminocarbonyl, aminosulphonyl, (C1-6) alkylaminosulphonyl or di(C1-6)alkylaminosulphonyl; (C3-7)heterocycloalkyl or (C3-7)spiroheterocycloalkyl, either of which groups may be optionally substituted by one or more substituents;
- R1 represents alkyl or cycloalkyl amines including fused and spirocycloalkyl amines optionally substituted including (C1-3) aminoalkyl, (C3-7) aminocycloalkyl, (C1-3)alkylimidazole, (C1-3)alkyl isoindoline, (C1-3)alkylpiperazine, (C1-3)alkylpiperidine, (C1-3)alkyl imidazopiperazine, (C1-3)alkyl(C4-7)aminocycloalkyl, (C1-3)alkyl(C4-7)aminodicycloalkyl; and
- R2 represents aryl, heteroaryl, heterobicyclic, (C4-7) aminocycloalkyl, cycloalkyl, heterocycloalkyl, (C6-8) diaminocycloalkyl, morpholino, (C4-7)cycloalkylmethyl, piperziny, piperdiny. R2 is optionally substituted with groups including hydroxyl, (C1-6)alkyl, acetyl, halogen, cyano, C1-6 alkyl, trifluoromethyl, difluoromethyl, (C2-6) alkenyl, hydroxy, (C1-6) alkoxy, difluoromethoxy, trifluoromethoxy, trifluoroethoxy, (C1-6) alkylthio, (C1-6) alkylsulphonyl, amino, (C1-6) alkylamino, di(C1-6)alkylamino, (C1-6)alkoxy(C1-6)alkyl-amino, N-[(C1-6)alkyl]-N-[hydroxy(C1-6)alkyl]amino, (C2-6) alkylcarbonylamino, (C2-6) alkoxy carbonylamino, (C1-6) alkylsulphonylamino, formyl, (C2-6) alkylcarbonyl, carboxy, (C2-6) alkoxy carbonyl, aminocarbonyl, (C1-6) alkylaminocarbonyl, di(C1-6)alkylaminocarbonyl, aminosulphonyl, (C1-6) alkylaminosulphonyl or di(C1-6)alkylaminosulphonyl; (C3-7)heterocycloalkyl or (C3-7)spiroheterocycloalkyl, either of which groups may be optionally substituted by one or more substituents.
- Examples of the central core A is selected from the group consisting of



According to another embodiment of the invention, the central core A is selected amongst:



Wherein

- 5 L, U, V, W, is C or N;
 X, T is C, N or O;
 Y is C, N or S;
- R1 represents (C4-7)cycloalkyl; (4-9-membered)-heterocycloalkyl; fused cycloalkylamine; fused
 10 heterocycloalkylamine; spirocycloalkylamine; spiro-heterocycloalkylamine; (C1-3) aminoalkyl;
 (C3-7) aminocycloalkyl; (C1-3)alkylimidazole; (C1-3)alkyl isoindoline; (C1-3)alkylpiperazine; (C1-
 3)alkylpiperidine; (C1-3)alkyl imidazopiperazine; (C1-3)alkyl(C4-7)aminocycloalkyl; (C1-
 3)alkyl(C4-7)aminodicycloalkyl; a (C1-3)alkyl group substituted with one or more groups chosen
 15 amongst (C4-7)cycloalkyl, (4-9-membered)-heterocycloalkyl, fused cycloalkylamine, fused
 heterocycloalkylamine, spirocycloalkylamine, spiro-heterocycloalkylamine, (C1-C3) aminoalkyl,
 (C3-C7) aminocycloalkyl, (C1-C3)alkylimidazole, (C1-C3)alkyl isoindoline, (C1-
 C3)alkylpiperazine, (C1-C3)alkylpiperidine, (C1-C3)alkyl imidazopiperazine, (C1-C3)alkyl(C4-
 C7)aminocycloalkyl, (C1-C3)alkyl(C4-C7)aminodicycloalkyl ;
- 20 R1 is optionally substituted with Halogen, hydroxyl, (C1-C3)alkyl, (C1-C3)alkylcarboxy, (C1-
 C3)alkylamino, (C5-C6)heteroaryl optionally substituted with (C1-C3)alkyl, Halogen, (C3-C7)
 aminocycloalkyl substituted with halogen, aryl, aryl(C1-C3)alkyl, aryl(C1-C3)alkyl(C1-
 C3)dialkylamine, aryloxy ;
- 25 - R2 represents H; Halogen; aryl; heteroaryl; heterobicyclic; (C4-C7)aminocycloalkyl; cycloalkyl;
 heterocycloalkyl; (C6-C8) diaminocycloalkyl; morpholino; (C4-C7)cycloalkylmethyl; piperzinyll;
 piperdinyll;
- R2 is optionally substituted with groups including aryl; heteroaryl; hydroxyl; (C1-C6)alkyl; acetyl;
 30 halogen; cyano; (C1-C6) alkyl; trifluoromethyl; difluoromethyl; (C2-C6) alkenyl; hydroxy; (C1-
 C6)alkoxy; difluoromethoxy; trifluoromethoxy; trifluoroethoxy; (C1-C6)alkylthio; (C1-
 6)alkylsulphonyl; amino; (C1-C6)alkylamino; di(C1-6)alkylamino; (C1-C6)alkoxy(C1-6)alkyl-

amino; N-[(C1-6)alkyl]-N-[hydroxy(C1-C6)alkyl]amino; (C2-C6)alkylcarbonylamino; (C2-C6)alkoxycarbonylamino; (C1-C6)alkylsulphonylamino; formyl; (C2-C6)alkylcarbonyl; carboxy; (C2-C6)alkoxycarbonyl; aminocarbonyl; (C1-C6)alkylaminocarbonyl; di(C1-C6)alkylaminocarbonyl; aminosulphonyl, (C1-6) alkylaminosulphonyl or di(C1-6)alkylaminosulphonyl; (C3-7)heterocycloalkyl or (C3-7)spiroheterocycloalkyl; either of which groups may be optionally substituted by one or more substituents chosen amongst hydroxyl, halogen, amino, methylamino, dimethylamino, (C1-3)alkyl, (C1-3)alkoxy, sulphonyl, (C1-3)carbonyl, (C1-4)alkylcarboxy, cyano, oxo, (C1-6)alkyl(C5-10)heteroaryl(C1-3)carbonyl, sulphonyl, methylsulphonyl, pyridinyl;

10 - R3 is selected independently from each other amongst H; halogen; cyano; (C4-7)heterocycloalkyl optionally substituted with (methylsulphonyl)aryl, acetyl, (C1-C3)alkylcarbonyl;

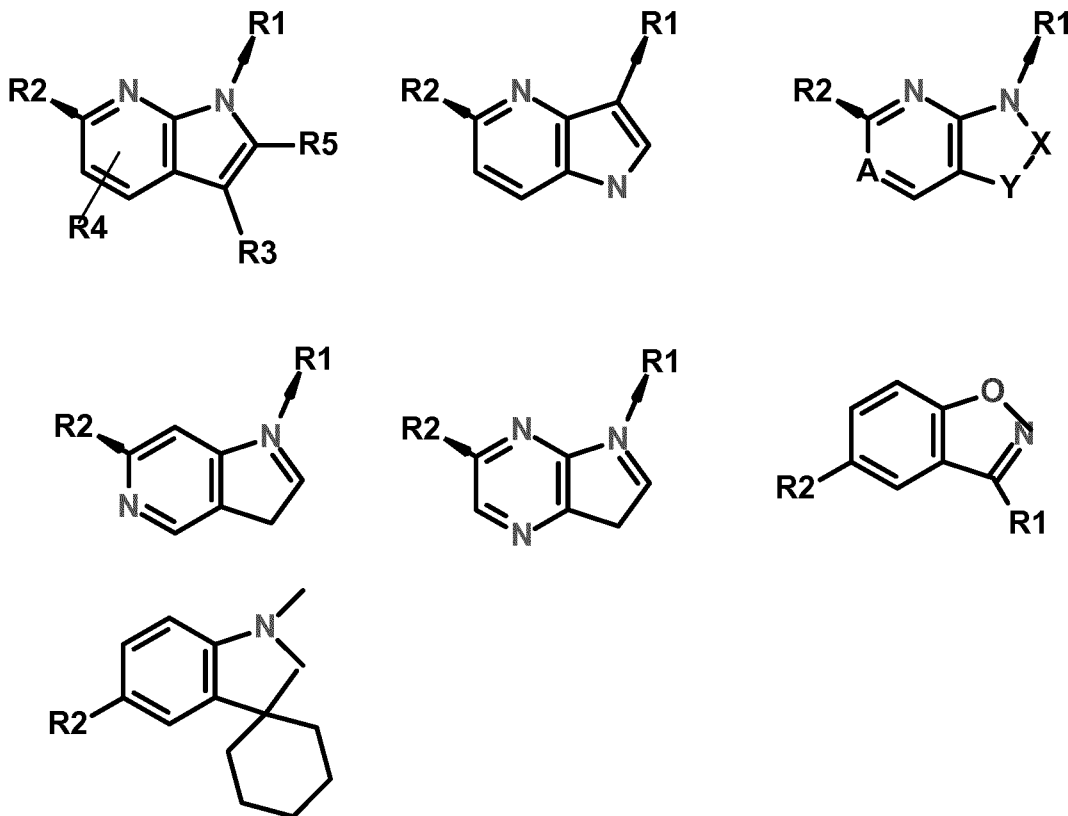
15 - R4 is selected amongst H; Halogen; difluoromethyl; trifluoromethyl; phenyl; cyano; (C1-3)alkyl; amino(C1-3)alkyl; (C4-C7)heterocycloalkyl; (C4-C7)heteroaryl wherein the heteroaryl group is optionally substituted with a (C1-C3)alkyl group; (C4-C7)heteroaryl-(C1-C3)alkyl wherein the heteroaryl group is optionally substituted with a (C1-C3)alkyl group; (C4-C7)heteroaryl group optionally substituted with (C1-C3)alkyl, amino-carbonyl, (C1-C3)-alkylamino-carbonyl; (C1-C3)-alkoxycarbonyl; (C1-C3)alkyl-sulfonyl; (C4-C7)heteroalkyl-carbonyl; (C1-C3)alkylamino-carbonyl; di(C1-C3)alkylamino-carbonyl;

20 R5 is selected amongst H; oxo; (C1-C3)alkyl; (C4-C7)heterocycloalkyl-(C1-C3)alkyl; methoxycarbonyl ;

25 Wherein
 When T is O, X is N then L, U, V, W are C;
 When W and T are N, then X, Y, V, U, L are C;
 When W and Y are N, then L, T, X, V, U are C;
 30 When W, T, X are N then Y, V, U, L is C;
 When W, T, Y are N, L, X, V, U is C;
 When V, W, T are N, L, X, Y, U is C;
 When U, T are N, then L, X, Y, V, W are C;
 When L, T, X are N, then Y, V, U are C;
 35 When W is N, Y is N or S, then T, X, V, U, L are C;
 When T is N and W, X, Y, V, U are C then R4 forms a 6-membered carbocyclic ring; and R1, R3 is methyl, R2, R5 is H;

When Y is N and L, U, V, W, T is C, then R1 and R5 form together a 6-membered heterocyclic ring, R3, R4, is hydrogen.

According to a further embodiment, the central core A is selected amongst the following:



5

Wherein

X is O, C, or N, wherein C is optionally substituted with an oxo moiety,

10 Y is C, S or N,

A is C or N, optionally substituted with 1-C₍₁₋₄₎-4-aryl-piperazine or 1-C₍₁₋₄₎-4-heteroaryl-piperazine or 1-(4-C₍₁₋₄₎-aryl)piperazine or 1-(4-C₍₁₋₄₎-heteroaryl)piperazine or 1-C₍₁₋₄₎-4-aryl-piperidine or 1-C₍₁₋₄₎-4-heteroaryl-piperidine or 1-(4-C₍₁₋₄₎-aryl)piperidine or 1-(4-C₍₁₋₄₎-heteroaryl)piperidine with optional substitution on aryl, heteroaryl, piperazine or piperidine groups;

15

R1 is selected amongst H, ethyl-azabicyclo[3.2.0]heptane; or 2-substituted-5-azaspiro[3.4]octane; or ethyl-2-pyrrolidine optionally substituted with one or more (C1-3)alkyl, or (C4-7) cycloalkylamines including 3-substituted-N-methyl-cyclobutanamine and piperidine;

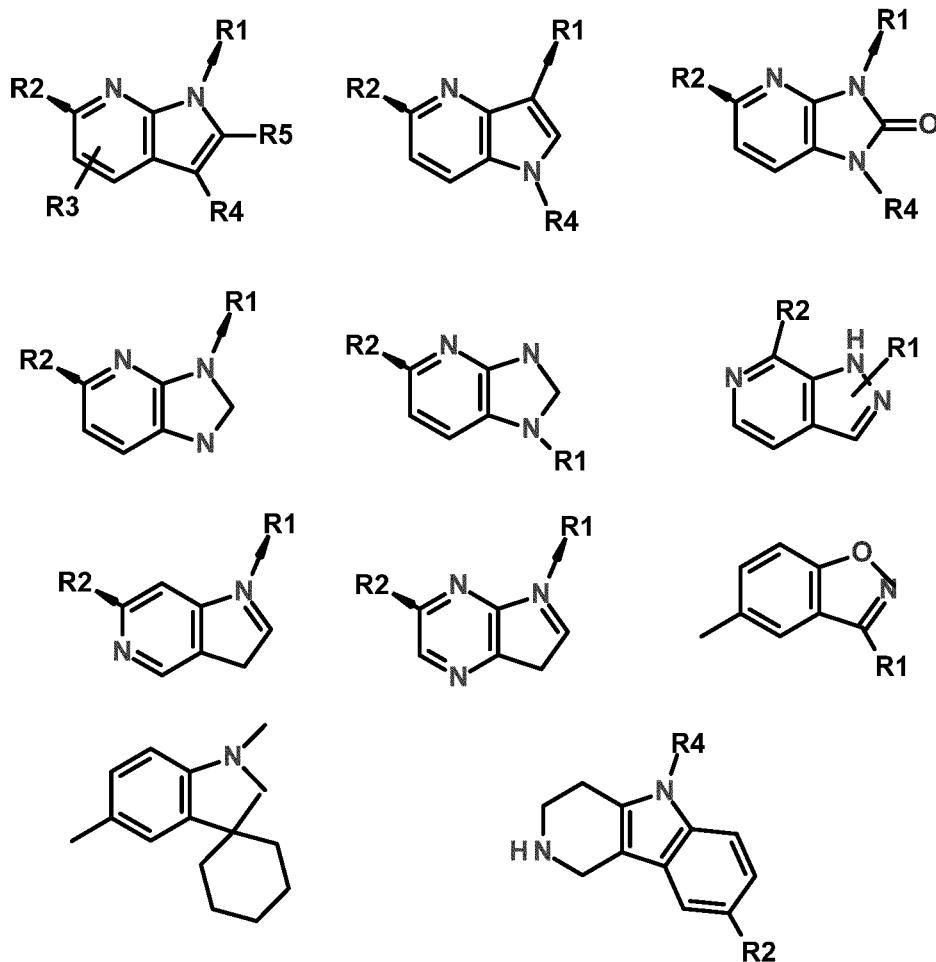
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5 R2 is selected amongst 1-C₍₁₋₄₎-4-aryl-piperazine or 1-C₍₁₋₄₎-4-heteroaryl-piperazine or 1-(4-C₍₁₋₄₎-aryl)piperazine or 1-(4-C₍₁₋₄₎-heteroaryl)piperazine or 1-C₍₁₋₄₎-4-aryl-piperidine or 1-C₍₁₋₄₎-4-heteroaryl-piperidine or 1-(4-C₍₁₋₄₎-aryl)piperidine or 1-(4-C₍₁₋₄₎-heteroaryl)piperidine with optional substitution on aryl, heteroaryl, piperazine or piperidine groups;

10 R3, R4 is selected independently from each other amongst H, halogen, cyano, C1-6 alkyl, trifluoromethyl, difluoromethyl, (C2-6) alkenyl, hydroxy, (C1-6) alkoxy, difluoromethoxy, trifluoromethoxy, trifluoroethoxy, (C1-6) alkylthio, (C1-6) alkylsulphonyl, amino, (C1-6) alkylamino, di(C1-6)alkylamino, (C1-6)alkoxy(C1-6)alkyl-amino, N-[(C1-6)alkyl]-N-[hydroxy(C1-6)alkyl]amino, (C2-6) alkylcarbonylamino, (C2-6) alkoxy carbonylamino, (C1-6) alkylsulphonylamino, formyl, (C2-6) alkylcarbonyl, carboxy, (C2-6) alkoxy carbonyl, aminocarbonyl, (C1-6) alkylaminocarbonyl, di(C1-6)alkylaminocarbonyl, aminosulphonyl, (C1-6) alkylaminosulphonyl or di(C1-6)alkylaminosulphonyl; (C3-7)heterocycloalkyl or (C3-7)spiroheterocycloalkyl

20 R5 is selected amongst H, 2-(Pyrrolidin-1-yl)ethyl.

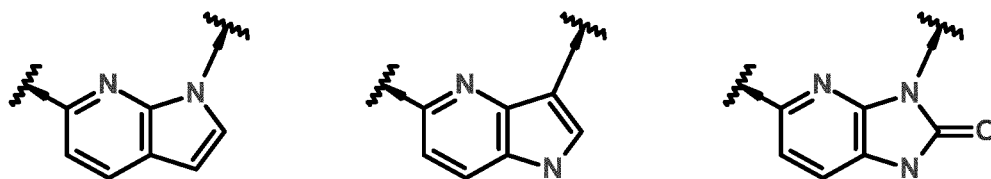
According to a further embodiment, the core A is selected amongst the following:



Wherein R1, R2 R3, R4 and R5 are defined as herein.

In a specific embodiment, the central core A is

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Usually, R1 is ethyl-azabicyclo[3.2.0]heptane; or 2-substituted-5-azaspiro[3.4.]octane; or ethyl-2-methyl-pyrrolidine or (C4-7) cycloalkylamines including 3-substituted-N-methyl-cyclobutanamine and piperidine.

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Preferrably, R1 is 3-substituted-N-methyl-cyclobutanamine.

In another preferred embodiment, R1 is 2-substituted-5-azaspiro[3.4.]octane.

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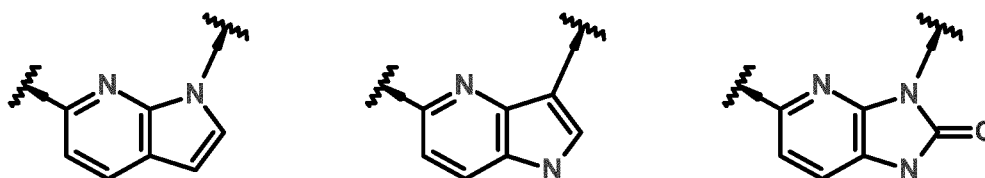
In another preferred embodiment, R1 is (C4-7) cycloalkylamines including 3-substituted-N-methyl-cyclobutanamine and piperidine.

Usually, R2 is 1-substituted-4-aryl-piperazine or 1-substituted-4-heteroaryl-piperazine or 1-(4-substituted-aryl)piperazine or 1-(4-substituted-heteroaryl)piperazine or 1-substituted-4-aryl-piperidine or 1-substituted-4-heteroaryl-piperidine or 1-(4-substituted-aryl)piperidine or 1-(4-substituted-heteroaryl)piperidine with optional substitution on aryl, heteroaryl, piperazine or piperidine groups.

Preferrably, R2 is 1-substituted-4-aryl-piperazine or 1-substituted-4-heteroaryl-piperazine, 1-substituted-4-aryl-piperidine or 1-substituted-4-heteroaryl-piperidine.

In a further specific embodiment, compounds of formula I are those wherein

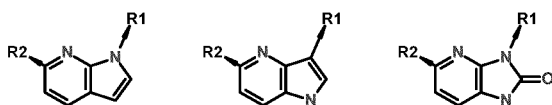
- the central core A is



- R1 is ethyl-azabicyclo[3.2.0]heptane ; or 2 -substituted-5-azaspiro[3.4.]octane; or ethyl-2-methyl-pyrrolidine or (C4-7) cycloalkylamines including 3-substituted-N-methyl-cyclobutanamine and piperidine ;
- R2 is 1-substituted-4-aryl-piperazine or 1-substituted-4-heteroaryl-piperazine or 1-(4-substituted-aryl)piperazine or 1-(4-substituted-heteroaryl)piperazine or 1-substituted-4-aryl-piperidine or 1-substituted-4-heteroaryl-piperidine or 1-(4-substituted-aryl)piperidine or 1-(4-substituted-heteroaryl)piperidine with optional substitution on aryl, heteroaryl, piperazine or piperidine groups.

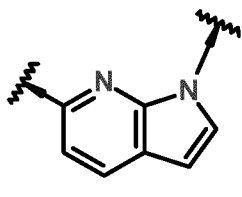
In a further embodiment, compounds of formula are those wherein

- The central core A is



In a further preferred specific embodiment, compounds of formula I are those wherein

- the central core A is



;

- 5
- R1 is 2-substituted-5-azaspiro[3.4.]octane or 3-substituted-N-methyl-cyclobutanamine or 4-substituted piperidine;
 - R2 is 1-substituted-4-aryl-piperazine or 1-substituted-4-heteroaryl-piperazine, 1-substituted-4-aryl-piperidine or 1-substituted-4-heteroaryl-piperidine.

- 10 According to a further embodiment, compounds of the invention are those wherein the core A is as defined above and

R1 is selected amongst:

- 2-(pyrrolidin-1-yl)ethyl,
- 15 1-(methyl)pyrrolidin-3-yl,
- 3-(methylamino)-cyclobut-1-yl,
- piperid-3-yl,
- 2-[(4-methyl)piperazin-1-yl]ethyl,
- N-(isopropyl)-eth-2-yl,
- 20 2-[(N,N-dimethyl)amino]pyrrolidin-3-yl,
- 2-(2-methylmethoxy-pyrrolidin-1-yl)ethyl,
- 3-methoxy-pyrrolidin-1-yl-ethyl,
- 2-(azabicyclo[3.1.0]hex-2-yl)ethyl,
- 2-(octahydro-1H-pyrrolo[2,3-c]pyrid-1-yl)ethyl,
- 25 2-[(6-methyl)-octahydro-1H-pyrrolo[3,4-b]pyrid-1-yl]ethyl,
- 2-(5-methylhexahydropyrrolo[3,4-b]pyrrol-1(2H)-yl)ethyl,
- 2-(3-methoxyazetid-1-yl)ethyl,
- 2-[(2R)-2-methylpyrrolidin-1-yl]ethyl,
- 2-[3-(pyridin-2-yl)pyrrolidin-1-yl]ethyl,

- 2-[3-(N,N-dimethylamino)-pyrrolidin-1-yl]ethyl,
2-(6-azabicyclo[3.2.0]hept-6-yl)ethyl,
2-amino[N-benzyl-N-methyl]ethyl,
2-(3-phenoxy-pyrrolidin-1-yl)ethyl,
5 2-(2-phenylazetid-1-yl)ethyl,
2-[(fluorophenyl)azetid-1-yl]ethyl,
2-(3-phenoxyazetid-1-yl)ethyl,
2-[(3-hydroxy,3-phenyl)azetid-1-yl]ethyl,
3-(methylamino)cyclobut-1-yl,
10 2-[1-(methyl)pyrrolidin-3-yl]ethyl,
3-dimethylamino-cyclobut-1-yl,
(3S)-1-(methyl)pyrrolidin-3-yl,
(3R)-1-(methyl)pyrrolidin-3-yl,
cis-N-benzyl-N-methyl-amnio-cyclobut-3-yl,
15 *trans*-N-benzyl-N-methyl-amnio-cyclobut-3-yl,
2-(1-benzylpyrrolidin-3-yl)ethyl,
(3S)-1-benzylpyrrolidin-3-yl,
(3R)-1-benzylpyrrolidin-3-yl,
2-(N,N,dimethylamino)-ethyl,
20 2-(1-oxa-6-azaspiro[3.4]oct-6-yl)ethyl,
2-(2-oxa-7-azaspiro[3.5]non-7-yl)ethyl
2-(pyrrolidin-3-yl)ethyl
trans-(3-methylamino)-but-1-yl,
3-piperazin-1-yl,
25 2-(oxolan-3-yl)ethyl,
2-[(*tert*-butyl-acetate)pyrrolidin-3-yl]-ethyl,
2-(pyrrolidin-2-on-1-yl)ethyl,
(3R)-pyrrolidin-3-yl,

- (3S)-pyrrolidin-3-yl,
2-(5-azaspiro[3.4]oct-5-yl)ethyl,
piperidin-4-yl,
(3R,4R)-3-fluoropiperidin-4-yl,
5 1-(methyl)piperidin-4-yl,
trans-3-amino-cyclobut-1-yl,
trans-N-methyl-3 amino-cyclobut-1-yl,
2-azaspiro[3.3]heptan-6-yl
cis-1-(N-methylamino)cyclohex-4-yl
10 *trans*-1-(N-methylamino)cyclohex-4-yl
quinuclidin-3-yl,
1-methyl-piperid-3-yl,
1-methyl-piperid-4-yl,
3-(N,N-dimethylamino-carboxamide)azetidine-1-yl,
15 2-(3-imidazol-1-ylpyrrolidin-1-yl)ethyl,
3-(methanesulfonamido)azetid-1-yl,
2-(3-fluoro-3-methyl-pyrrolidin-1-yl)ethyl,
2-[4-(2-methylpyrazol-3-yl)-piperid-1-yl]ethyl,
2-[4-(oxetan-3-yl)-piperid-1-yl]ethyl,
20 2-(3,4-dihydro-1H-isoquinol-1-yl)ethyl,
N-methylaminocyclobut-3-yl,
5-azaspiro[3.4]octan-2-yl,
1,2,3,6-tetrahydropyridin-4-yl
4-(methyl)piperid-4-yl,
25 piperidin-4-yl,
piperazyn-3-yl;

R2 is selected amongst:

H,

Chlorine,

(3S)-3-methyl-4-(2-methylphenyl)piperazin-1-yl,

(2S)-2-methyl-4-(2-methylphenyl)piperazin-1-yl,

5 4-[2-(methylsulfonyl)phenyl]piperazin-1-yl,

(2R)-2-methyl-4-(2-methylphenyl)piperazin-1-yl,

4-phenylpiperazin-1-yl,

4-[4-(methylsulfonyl)phenyl]piperazin-1-yl,

4-[3-(methylsulfonyl)phenyl]piperazin-1-yl,

10 4-(ethylbenzoate)piperazin-1-yl,

4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl,

4-(pyridin-2-yl)piperazin-1-yl,

4-(pyridin-3-yl)piperazin-1-yl,

4-(pyridin-4-yl)piperazin-1-yl,

15 pyrrolidin-1-yl,

4-[4-(methylsulfonyl)phenyl]piperazin-1-yl,

4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl,

4-(4-acetylphenyl)piperazin-1-yl,

4-(6-cyanopyridin-2-yl)piperazin-1-yl,

20 4-(acetylphenyl)piperazin-1-yl,

4-(methylsulfonyl)phenyl]piperazin-1yl,

4-hydroxy-4-phenyl-piperidin-1yl,

4-phenylpiperidin-1-yl

4-phenyl-4-cyano-piperidin-1-yl,

25 4-(3-methoxyphenyl)piperazin-1-yl,

4-(3-chlorophenyl)piperazin-1-yl,

4-(3-benzonitrile)piperazin-1-yl,

4-(thiophen-2-yl)piperazin-1-yl,

- 4-(3-methylphenyl)piperazin-1-yl,
4-(4-methylpyridin-3-yl)piperazin-1-yl,
4-(4-methoxyphenyl)piperazin-1-yl,
4-(2-methoxyphenyl)piperazin-1-yl,
5 4-(4-benzonitrile)piperazin-1-yl,
4-(4-chlorophenyl)piperazin-1-yl,
4-(4-methylphenyl)piperazin-1-yl,
4-(3-methylpyridin-4-yl)piperazin-1-yl,
4-isoquinol-1-yl- piperazin-1-yl,
10 imidazo[1,2-a]pyrid-6-yl,
imidazo[1,2-a]pyrid-5-yl,
4-(3-methylpyridin-2-yl)piperazin-1-yl,
4-(5-methylpyridin-2-yl)piperazin-1-yl,
4-(1-acetyl)piperazin-1-yl,
15 4-[(1-methylpiperidin-3-yl)-1-acetyl]piperazin-1-yl,
4-[(1-methylpiperidin-2-yl)-1-acetyl]piperazin-1-yl,
4-(2-methylphenyl)piperazin-1-yl,
4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl,
4-[4-(methylsulfonyl)phenyl]piperazin-1-yl,
20 4-methylpiperazin-1-yl,
4-(1-oxoethyl
4-(phenylethanone),
piperazin-1-yl,
4-(3-thienyl)piperazin-1-yl,
25 4-(6-acetyl-3-pyridyl)piperazin-1-yl,
4-(1-methyl-2-oxo-4-pyridyl)piperazin-1-yl,
4-(4-formylphenyl)piperazin-1-yl,
4-(4-hydroxyphenyl)piperazin-1-yl,

- 4-(4-oxochroman-7-yl)piperazin-1-yl,
4-[4-[(R)-methylsulfinyl]phenyl]piperazin-1-yl,
4-(2-methyl-4-methylsulfonylphenyl)piperazin-1-yl,
4-(2-methyl-1-oxo-3H-isoindol-5-yl)piperazin-1-yl,
5 5-(methyl-acetyl)-pyrid-3-yl-piperazin-1-yl,
4-(methyl-acetyl)-pirazin-5-yl-piperazin-1-yl,
4-(N,N-dimethylbenzylamide)piperazin-1-yl,
4-[4-(2-oxopyrrolidin-1-yl)phenyl]piperazin-1-yl,
4-(5-methylsulfonylpyridin-2-yl)piperazin-1-yl,
10 4-(3-methylsulfonylphenyl)piperazin-1-yl,
4-(4-pyridin-2-ylphenyl)piperazin-1-yl,
4-(4-acetyl-pyridin-2-ylphenyl)piperazin-1-yl,
4-[4-(1-methylimidazol-2-yl)phenyl]piperazin-1-yl,
(3S)-4-(4-acetylphenyl)-3-methylpiperazin-1-yl,
15 (2R)-4-(4-acetylphenyl)-2-methylpiperazin-1-y,
(2S)-4-(4-acetylphenyl)-2-methylpiperazin-1-y,
(3R)-4-(4-acetylphenyl)-3-methylpiperazin-1-yl,
(2S)-4-(4-acetylphenyl)-2-methylpiperazin-1-yl,
4-(4-methylsulfonylphenyl)piperazin-1-yl,
20 4-(4-acetyl-3-hydroxy-phenyl)piperazin-1-yl,
4-(4-acetyl-3-fluoro-phenyl)piperazin-1-yl,
4-(2-acetyl-5-fluoro-phenyl)piperazin-1-yl,
4-(4-acetyl-pyrimidin-2-yl)piperazin-1-yl,
4-[(N,N-dimethylaminocarbonyl)pyridin-6-yl]piperazin-1-yl,
25 4-[4-(2-methylpropanoyl)phenyl]piperazin-1-yl,
4-(1-oxotetralin-6-yl)piperazin-1-yl,
4-[4-(1,4-dioxobut-1-yl)phenyl]-piperazin-1-yl,
4-[4-(tert-butylacetyl)phenyl]-piperazin-1-yl,

- 4-[4-(1,4-dioxoethyl)phenyl]-piperazin-1-yl,
4-[4-(3-(methyl)1,4-dioxobut-1-yl)phenyl]-piperazin-1-yl,
4-(1-oxoindan-5-yl)piperazin-1-yl,
4-(5-acetylpyridin-2-yl)piperazin-1-yl,
5 4-(5-acetylpyrimidin-2-yl)piperazin-1-yl,
4-(5-acetylpyrazin-2-yl)piperazin-1-yl,
4-(6-acetylpyridazin-3-yl)piperazin-1-yl,
4-(4-methylsulfonylcyclohexyl)piperazin-1-yl,
4-(1-methylsulfonyl-4-piperidyl)piperazin-1-yl,
10 4-ethylpiperazin-1-yl,
4-[4-(2,2,2-trifluoroacetyl)phenyl]piperazin-1-yl,
4-(o-tolyl)piperazin-1-yl,
4-(imidazo[1,2-a]pyridin-5-yl)-piperazin-1-yl
4-(cyclopentane-carbonyl)piperazin-1-yl,
15 4-[2-(pyridinyl)-ethanoyl]piperazin-1-yl,
4-[(azetidiny)-carbonyl]piperazin-1-yl,
4-[(phenyl)-carbonyl]piperazin-1-yl
4-[(pyridyl)-carbonyl]piperazin-1-yl,
4-[(piperidyl)-carbonyl]piperazin-1-yl,
20 4-(3-methoxy-2-pyridyl)piperazin-1-yl,
6-(4-acetylphenyl)-3-pyridyl,
4-(4-methylsulfonylphenyl)phenyl,
4-[4-[(E)-N-methoxy-C-methyl-carbonimidoyl]phenyl]piperazin-1-yl
methylcarbonylpiperazin-1-yl,
25 4-[4-(1,1-dimethoxyethyl)phenyl]piperazin-1-yl,
4-(4-acetylphenyl)phenyl,
4-(4-acetyl-2-methylphenyl)piperazin-1-yl,
4-[4-(methoxycarbonyl)phenyl]piperazin-1-yl,

4-[4-(azetidine-1-carbonyl)phenyl]piperazin-1-yl;

R3 is selected amongst:

H,

5 Chlorine,

Fluorine,

4-[(4-methylsulfonylphenyl)]piperazin-1-yl

piperazin-1-yl,

cyano,

10 4-acetylpiperazin-1-yl;

R4 is selected amongst:

H,

methyl,

15 Bromine,

trifluoromethyl,

cyano,

2-(pyrrolidin-1-yl)ethyl,

1-methylpyrazol-4-yl,

20 4-(4-methylsulfonylphenyl)piperazin-1-yl

3-piperazin-1-yl,

phenyl,

dimethylaminocarbonyl,

methoxycarbonyl,

25 methylsulfonyl,

2-methylpyridin-3-yl

1-methylpyrazol-3-yl,

1-methylpyrazol-4-yl,

- 2-methylpyrimidin-5-yl,
morpholino-carbonyl,
methylaminocarbonyl,
4-piperidyl
- 5 1-methylpyrazol-5-yl
1H-pyrazol-5-yl
pyrid-3-yl,
oxetan-3-yl;
- 10 R5 is selected amongst:
H,
oxo,
methyl,
2-(pyrrolidin-1-yl)ethyl,
- 15 methoxycarbonyl.

Specific compounds of the present invention are those notably selected from the group consisting of :

- 20 6-[(3S)-3-methyl-4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
6-[(2S)-2-methyl-4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 25 6-[4-[2-(methylsulfonyl)phenyl]piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
6-[(2R)-2-methyl-4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
6-(4-phenylpiperazin-1-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 30 6-[4-[4-(methylsulfonyl)phenyl]piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
6-[4-[3-(methylsulfonyl)phenyl]piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;

- ethyl 4-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)benzoate ;
- 5-(4-{1-[2-(piperidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 5 N,N-diethyl-2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethanamine ;
- 6-[4-(pyridin-2-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(pyridin-3-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(pyridin-4-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-(pyrrolidin-1-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 10 1-(1-methylpyrrolidin-3-yl)-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine ;
- 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[3,2-c]pyridine ;
- 15 cis-N-methyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine ;
- trans-N-methyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine ;
- 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[(3R)-pyrrolidin-3-yl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[(3S)-pyrrolidin-3-yl]-1H-pyrrolo[2,3-b]pyridine ;
- 20 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-(piperidin-4-yl)-1H-pyrrolo[3,2-c]pyridine ;
- cis-3-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}-N-methylcyclobutanamine ;
- trans-3-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}-N-methylcyclobutanamine ;
- 25 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[trans-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[cis-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 30 6-[4-(6-cyanopyridin-2-yl)piperazin-1-yl]-1-[trans-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(6-cyanopyridin-2-yl)piperazin-1-yl]-1-[cis-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 1-[4-(4-{5-fluoro-1-[trans-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)phenyl]ethenone ;

- trans-3-(5-fluoro-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-methylcyclobutanamine ;
- 1-(4-phenyl-1-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperidin-4-yl)ethenone ;
- 4-phenyl-1-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperidin-4-ol ;
- 5 6-(4-phenylpiperidin-1-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 4-phenyl-1-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperidine-4-carbonitrile ;
- 6-[4-(3-methoxyphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(3-chlorophenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 3-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)benzotrile ;
- 10 1-[2-(pyrrolidin-1-yl)ethyl]-6-[4-(thiophen-2-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(3-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(4-methylpyridin-3-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(4-methoxyphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(2-methoxyphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 15 4-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)benzotrile ;
- 6-[4-(4-chlorophenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(4-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(3-methylpyridin-4-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 2-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)quinoline ;
- 20 1-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)isoquinoline ;
- 6-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 25 6-[4-(3-methylpyridin-2-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(5-methylpyridin-2-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 1-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)ethenone ;
- (1-methylpiperidin-3-yl)(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)methanone ;

- (1-methylpiperidin-2-yl)(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)methanone ;
- 6-[4-(2-methylphenyl)piperazin-1-yl]-1-[2-(4-methylpiperazin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 5 N-(2-{6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)propan-2-amine ;
N,N-dimethyl-1-(2-{6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)pyrrolidin-3-amine ;
1-{2-[2-(methoxymethyl)pyrrolidin-1-yl]ethyl}-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine ;
- 10 1-[2-(3-methoxypyrrolidin-1-yl)ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine ;
1-[2-(2-azabicyclo[3.1.0]hex-2-yl)ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine
- 15 6-methyl-1-(2-{6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)octahydro-1H-pyrrolo[2,3-c]pyridine ;
6-methyl-1-(2-{6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)octahydro-1H-pyrrolo[3,4-b]pyridine ;
1-[2-(5-methylhexahydropyrrolo[3,4-b]pyrrol-1(2H)-yl)ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine ;
- 20 1-[2-(3-methoxyazetidid-1-yl)ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine ;
6-[4-(2-methylphenyl)piperazin-1-yl]-1-{2-[(2R)-2-methylpyrrolidin-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridine ;
- 25 6-[4-(2-methylphenyl)piperazin-1-yl]-1-{2-[3-(pyridin-2-yl)pyrrolidin-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridine ;
1-(2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)-N,N-dimethylpyrrolidin-3-amine ;
5-(4-{1-[2-(6-azabicyclo[3.2.0]hept-6-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 30 5-[4-(1-{2-[3-(1-methyl-1H-imidazol-2-yl)pyrrolidin-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine ;
5-[4-(1-{2-[2-(1-methyl-1H-pyrazol-4-yl)pyrrolidin-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine ;
- 35 5-[4-(1-{2-[3-(4,4-difluoropiperidin-1-yl)azetidid-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine ;

- 5-[4-(1-{2-[3-(pyrrolidin-1-yl)azetid-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(2-oxa-7-azaspiro[3.5]non-7-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 5 5-(4-{1-[2-(5-azaspiro[3.4]oct-5-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(6-azaspiro[3.5]non-6-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 10 N-benzyl-2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}-N-methylethanamine ;
- 5-(4-{1-[2-(3-phenoxyprolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(2-phenylazetid-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 15 5-[4-(1-{2-[3-(2-fluorophenyl)azetid-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(3-phenoxyazetid-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 20 1-(2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)-3-phenylazetid-3-ol ;
- trans*-N-methyl-3-[3-(1-methyl-1H-pyrazol-4-yl)-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- trans*-N-methyl-3-[3-(1-methyl-1H-pyrazol-5-yl)-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- 25 *trans*-N-methyl-3-[6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-3-(1H-pyrazol-5-yl)-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- trans*-N-methyl-3-[3-(1-methyl-1H-pyrazol-3-yl)-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- 30 5-(4-{1-[2-(1-methylpyrrolidin-3-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- cis*-N,N-dimethyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine ;
- trans*-N,N-dimethyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine ;
- 35 1-[(3*S*)-1-methylpyrrolidin-3-yl]-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine ;

- 1-[(3R)-1-methylpyrrolidin-3-yl]-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine ;
- cis-N-benzyl-N-methyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine ;
- 5 trans-N-benzyl-N-methyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine ;
- 5-(4-{1-[2-(1-benzylpyrrolidin-3-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 10 1-[(3S)-1-benzylpyrrolidin-3-yl]-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine ;
- 1-[(3R)-1-benzylpyrrolidin-3-yl]-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine ;
- 6-(4-methylpiperazin-1-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 15 2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}-N,N-dimethylethanamine ;
- 5-(4-{1-[2-(1-oxa-6-azaspiro[3.4]oct-6-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 20 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile ;
- 3-methyl-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 25 trans-3-(3-bromo-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-methylcyclobutanamine ;
- 6-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)pyridine-2-carbonitrile ;
- 2-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)pyridine-3-carbonitrile ;
- 30 6-[4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[3,2-c]pyridine ;
- cis-3-(4-chloro-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-methylcyclobutanamine ;

- cis-N-methyl-3-[6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-3-(trifluoromethyl)-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrazolo[3,4-b]pyridine;
- 5 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-2-[2-(pyrrolidin-1-yl)ethyl]-2H-pyrazolo[3,4-b]pyridine;
- 5-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[3,2-c]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 10 2-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-7-[2-(pyrrolidin-1-yl)ethyl]-7H-pyrrolo[2,3-d]pyrimidine ;
- 6-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[3,2-c]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(piperazin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 15 5-(4-{1-[2-(2-methyl-1H-imidazol-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(pyrrolidin-3-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethanamine ;
- 20 4-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenol ;
- 6-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyridine-3-carbonitrile ;
- 5-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-3-[2-(pyrrolidin-1-yl)ethyl]-3H-imidazo[4,5-b]pyridine ;
- 5-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-imidazo[4,5-b]pyridine ;
- 25 1-(4-{1-[trans-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}phenyl)ethenone ;
- 6-piperazin-1-yl-1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridine ;
- trans-N-methyl-3-[6-[4-(3-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutan-1-amine ;

- 5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-3-piperazin-1-yl-thieno[3,2-b]pyridine ;
- 1-(2-pyrrolidin-1-ylethyl)-6-[4-(3-thienyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine ;
- cis-N,N-dimethyl-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carboxamide ;
- 5 cis-methyl 1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carboxylate ;
- trans-6-[4-(6-acetyl-3-pyridyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl)-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 10 trans-1-[3-(methylamino)cyclobutyl]-6-[4-(1-methyl-2-oxo-4-pyridyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-[4-(4-formylphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 15 cis-N-methyl-3-[3-methylsulfonyl-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- trans-N-methyl-3-[7-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-c]pyridin-1-yl]cyclobutanamine ;
- trans-6-[4-(4-hydroxyphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 20 trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-oxochroman-7-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-[(R)-methylsulfinyl]phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile;
- 25 trans-1-[3-(methylamino)cyclobutyl]-6-[4-(2-methyl-4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-(2-methyl-1-oxo-3H-isoindol-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-methyl 5-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyridine-3-carboxylate ;
- 30

- trans-methyl 2-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyridine-4-carboxylate ;
- trans-methyl 5-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyrazine-2-carboxylate ;
- 5 trans-4-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]-N,N-dimethylbenzamide ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-(2-oxopyrrolidin-1-yl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-(5-methylsulfonylpyridin-2-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 10 6-[4-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1-[2-(oxolan-3-yl)ethyl]pyrrolo[2,3-b]pyridine ;
- tert-butyl 3-[2-[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethylpyrrolidine-1-carboxylate ;
- 1-2-[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethylpyrrolidin-2-one ;
- 15 ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-(3-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 20 trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-pyridin-2-ylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-N-methyl-3-[6-[4-(4-pyridin-2-ylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutan-1-amine ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-(1-methylimidazol-2-yl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 25 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3R)-pyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3S)-pyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-piperidin-4-ylpyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-piperidin-4-ylpyrrolo[3,2-c]pyridine-3-carbonitrile ;

- 6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-[(3S)-pyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[rel-(3R,4R)-3-fluoropiperidin-4-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 5 trans-6-[(3S)-4-(4-acetylphenyl)-3-methylpiperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- Trans-6-[(3R)-4-(4-acetylphenyl)-3-methylpiperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-[(2R)-4-(4-acetylphenyl)-2-methylpiperazin-1-yl]-1-[3-
- 10 (methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-[(2S)-4-(4-acetylphenyl)-2-methylpiperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- cis-1-[4-[4-[1-[3-(methylamino)cyclobutyl]-3-(1-methylpyrazol-4-yl)]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- 15 trans-1-[4-[4-[1-[3-(methylamino)cyclobutyl]-3-(1-methylpyrazol-4-yl)]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- trans-N-methyl-3-[3-(1-methylpyrazol-4-yl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutan-1-amine ;
- 1-[4-[4-[3-(2-methylpyridin-3-yl)-1-piperidin-4-yl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-
- 20 yl]phenyl]ethenone ;
- 1-[4-[4-[3-(1-methylpyrazol-3-yl)-1-piperidin-4-yl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- 1-[4-[4-[3-(2-methylpyrimidin-5-yl)-1-piperidin-4-yl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- 25 1-[4-[4-[1-[3-(methylamino)cyclobutyl]-3-(1-methylpyrazol-4-yl)]pyrrolo[3,2-c]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- trans-6-[4-(4-acetyl-3-hydroxy-phenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-[4-(4-acetyl-3-fluoro-phenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-
- 30 b]pyridine-3-carbonitrile ;

- trans-6-[4-(2-acetyl-5-fluoro-phenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-2-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyrimidine-4-carboxamide ;
- 5 trans-6-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]-N,N-dimethylpyridine-2-carboxamide ;
- trans-6-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]-N-methylpyridazine-3-carboxamide ;
- trans-6-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]-N,N-dimethylpyridine-3-carboxamide ;
- 10 Trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-(2-methylpropanoyl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- Trans-1-[3-(methylamino)cyclobutyl]-6-[4-(1-oxotetralin-6-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 15 Trans-4-[4-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]-4-oxo-butanoic acid;
- Trans-6-[4-[4-(2,2-dimethylpropanoyl)phenyl]piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- Trans-4-[4-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]-2-methyl-4-oxo-butanoic acid ;
- 20 Trans-1-[3-(methylamino)cyclobutyl]-6-[4-(1-oxoindan-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- Trans-6-[4-(5-acetylpyridin-2-yl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 25 Trans-6-[4-(5-acetylpyrimidin-2-yl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- Trans-6-[4-(5-acetylpyrazin-2-yl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- Trans-6-[4-(6-acetylpyridazin-3-yl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 30

- cis-[1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-3-yl]-morpholino-methanone ;
- cis-N-methyl-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carboxamide ;
- 5 trans-3-[6-chloro-4-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]-N-methyl-cyclobutanamine ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylcyclohexyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylcyclohexyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 10 trans-1-[3-(methylamino)cyclobutyl]-6-[4-(1-methylsulfonyl-4-piperidyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-[4-(1-acetyl-4-piperidyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 15 trans-6-(4-ethylpiperazin-1-yl)-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpiperidin-4-yl)pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3S)-1-methylpyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 20 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3R)-1-methylpyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 1-[(3S)-1-methylpyrrolidin-3-yl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-(dimethylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 25 trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-(2,2,2-trifluoroacetyl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-[4-(4-acetylphenyl)piperazin-1-yl]-2-methyl-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 30 trans-3-[5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;

- trans-N-methyl-3-[3-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyrazin-5-yl]cyclobutanamine ;
- trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate ;
- 5 trans-1-[4-[4-[2-methyl-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- trans-5-[4-(4-acetylphenyl)piperazin-1-yl]-3-[3-(methylamino)cyclobutyl]-1-(1-methylpyrazol-4-yl)imidazo[4,5-b]pyridin-2-one ;
- 10 5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpyrazol-4-yl)-3-(4-piperidyl)imidazo[4,5-b]pyridin-2-one ;
- 1-(1-methylpyrazol-4-yl)-5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-3-(4-piperidyl)imidazo[4,5-b]pyridin-2-one ;
- 5-[4-(4-acetylphenyl)piperazin-1-yl]-3-(4-methyl-4-piperidyl)-1-(1-methylpyrazol-4-yl)imidazo[4,5-b]pyridin-2-one ;
- 15 trans-5-[4-(4-acetylphenyl)piperazin-1-yl]-3-[3-(methylamino)cyclobutyl]-1-phenyl-imidazo[4,5-b]pyridin-2-one ;
- 5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpyrazol-3-yl)-3-(4-piperidyl)imidazo[4,5-b]pyridin-2-one ;
- 6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-(4-piperidyl)pyrrolo[2,3-b]pyridine ;
- 20 (1R,3R)-3-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclopentanamine ;
- 1-(2-azaspiro[3.3]heptan-6-yl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine ;
- (1R,3S)-3-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclopentanamine ;
- 25 cis-N-methyl-4-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclohexanamine ;
- trans-N-methyl-4-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclohexanamine ;
- 30 6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-quinuclidin-3-yl-pyrrolo[2,3-b]pyridine ;

- 1-(1-methyl-3-piperidyl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine ;
- 1-(1-methyl-4-piperidyl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine ;
- N,N-dimethyl-1-[2-[6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]azetidine-3-carboxamide ;
- 5 1-[2-(3-imidazol-1-ylpyrrolidin-1-yl)ethyl]-6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine ;
- N-[1-[2-[6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]azetidin-3-yl]methanesulfonamide ;
- 1-[2-(3-fluoro-3-methyl-pyrrolidin-1-yl)ethyl]-6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine ;
- 6-(4-imidazo[1,2-a]pyridin-5-ylpiperazin-1-yl)-1-[2-[4-(2-methylpyrazol-3-yl)-1-piperidyl]ethyl]pyrrolo[2,3-b]pyridine ;
- 10 6-(4-imidazo[1,2-a]pyridin-5-ylpiperazin-1-yl)-1-[2-[4-(oxetan-3-yl)-1-piperidyl]ethyl]pyrrolo[2,3-b]pyridine ;
- 2-[2-[6-(4-imidazo[1,2-a]pyridin-5-ylpiperazin-1-yl)pyrrolo[2,3-b]pyridin-1-yl]ethyl]-3,4-dihydro-1H-isoquinoline ;
- 15 cyclopentyl-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]methanone ;
- 2-(2-pyridyl)-1-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]ethenone ;
- cyclobutyl-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]methanone ;
- phenyl-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]methanone ;
- 4-pyridyl-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]methanone ;
- 20 4-piperidyl-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]methanone ;
- 6-[4-(3-methoxy-2-pyridyl)piperazin-1-yl]-1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridine;
- trans-N-methyl-3-[5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- 3-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-5-piperazin-1-yl-1,2-benzoxazole ;
- 25 5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-3-piperazin-1-yl-1,2-benzoxazole ;
- trans-6-[6-(4-acetylphenyl)-3-pyridyl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

- trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)phenyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-[4-[4-[(E)-N-methoxy-C-methyl-carbonimidoyl]phenyl]piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile;
- 5 1-methyl-5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]spiro[indoline-3,4'-piperidine] ;
- N-methyl-3-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-2,3-dihydropyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- trans-1-[4-[1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-4-yl]piperazin-1-yl]ethenone ;
- 10 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-(5-azaspiro[3.4]octan-2-yl)pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-1-(5-azaspiro[3.4]octan-2-yl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-1-[4-[3-bromo-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]ethenone ;
- 15 5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpyrazol-4-yl)-3-(4-piperidyl)benzimidazol-2-one ;
- 5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(oxetan-3-yl)-3-(4-piperidyl)imidazo[4,5-b]pyridin-2-one ;
- trans-1-[4-[4-[3-bromo-2-methyl-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- 20 trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate ;
- Trans-6-[4-(4-acetylphenyl)piperazin-1-yl]-5-fluoro-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-[4-(1,1-dimethoxyethyl)phenyl]piperazin-1-yl]-5-fluoro-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 25 (methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 1-methyl-5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-3-(1,2,3,6-tetrahydropyridin-4-yl)pyrrolo[2,3-c]pyridine ;
- trans-1-[4-[4-[1-[3-(methylamino)cyclobutyl]-3-(3-pyridyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone trifluoroacetate ;
- 30 7-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-2-piperidin-4-ylpyrazolo[3,4-c]pyridine ;

7-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-(4-piperidyl)pyrazolo[3,4-c]pyridine

6-[4-(4-acetylpiperazin-1-yl)phenyl]-1-[trans-3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

5 1-[4-[4-[5-(1-methylpyrazol-4-yl)-1,2,3,4-tetrahydropyrido[4,3-b]indol-8-yl]piperazin-1-yl]phenyl]ethanone ;

trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-3-bromo-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate ;

5-[4-(4-acetylphenyl)piperazin-1-yl]-3-(4-methyl-4-piperidyl)-1-(oxetan-3-yl)imidazo[4,5-b]pyridin-2-one ;

10 trans-5-[4-(4-acetylphenyl)piperazin-1-yl]-3-[3-(methylamino)cyclobutyl]-1-(oxetan-3-yl)imidazo[4,5-b]pyridin-2-one ;

6-[4-(4-Acetylphenyl)phenyl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

6-[4-(4-acetyl-2-methylphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

15 trans-methyl 4-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]benzoate ;

6-[4-[4-(azetidine-1-carbonyl)phenyl]piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

20 1-[4-[4-[3-(1-methylpyrazol-4-yl)-1-piperidin-4-yl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone ;

1-[4-[4-[1-(1-methylpyrazol-4-yl)-3-piperazin-1-yl]pyrrolo[3,2-b]pyridin-5-yl]piperazin-1-yl]phenyl]ethanone ;

1-[4-[4-[1-(1-methylpyrazol-4-yl)-3-piperidin-4-yl]pyrrolo[3,2-b]pyridin-5-yl]piperazin-1-yl]phenyl]ethanone.

25 Specific compounds of the present invention are those notably selected from the group consisting of :

30 1-[4-[4-[3-(1-methylpyrazol-4-yl)-1-(4-piperidyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone,

1-[4-[4-[3-(2-methyl-3-pyridyl)-1-(4-piperidyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone,

6-[(2S)-2-methyl-4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine,
1-[4-[4-[1-(1-methylpyrazol-4-yl)-3-(4-piperidyl)pyrrolo[3,2-b]pyridin-5-yl]piperazin-1-yl]phenyl]ethanone,
5 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-(5-azaspiro[3.4]octan-2-yl)pyrrolo[2,3-b]pyridine-3-carbonitrile,
1-[3-(methylamino)cyclobutyl]-6-[4-[4-(2,2,2-trifluoroacetyl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile,
6-[4-(4-acetylphenyl)piperazin-1-yl]-1-(4-piperidyl)pyrrolo[2,3-b]pyridine-3-carbonitrile, 6-
10 [4-(4-acetyl-3-hydroxy-phenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile,
6-[4-(4-acetyl-3-fluoro-phenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile,
6-[(4-(4-acetylphenyl)-2-methyl-piperazin-1-yl)-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-
15 b]pyridine-3-carbonitrile,
6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile,
5-[4-(4-acetylphenyl)piperazin-1-yl]-3-[3-(methylamino)cyclobutyl]-1-(1-methylpyrazol-4-yl)imidazo[4,5-b]pyridin-2-one,
20 6-[4-(4-acetylphenyl)-3-methyl-piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile,
6-[4-(4-acetylphenyl)piperazin-1-yl]-2-methyl-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile,
6-[4-(5-acetyl-2-pyridyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-
25 3-carbonitrile.

The following paragraphs provide definitions of the various chemical moieties that make up the compounds according to the invention and are intended to apply uniformly throughout the specification and claims unless an otherwise expressly set out definition provides a broader
30 definition.

As used herein, the term "C1-C6 alkyl" refers to a saturated, aliphatic hydrocarbon group including a straight or branched carbon chain with 1 - 6 carbon atoms. Examples for "alkyl" are methyl, ethyl, n-propyl, and isopropyl.

The term "C1-C6 alkoxy" refers to a group -O-R' wherein R' is C1-C6 alkyl as defined above.

35 The term "halogen" refers to fluorine, chlorine, bromine or iodine.

The term "C1-C6 alkyl substituted by halogens or hydroxy or C1-C6 alkoxy" refers to an alkyl group as defined above, wherein at least one hydrogen atom is replaced by a halogen atom, a hydroxyl or a C1-C6 alkoxy.

The term "C1-C6 alkoxy substituted by halogens or hydroxy or C1-C6 alkoxy" refers to an alkoxy group as defined above, wherein at least one hydrogen atom is replaced by a halogen atom, a hydroxyl or a C1-C6 alkoxy.

The term "heterocyclyl" refers to a saturated ring, containing 1-3 heteroatoms, selected from N, O or S, for example morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl or azetidiny.

The term heteroaryl refers to an unsaturated aromatic ring, containing from 1 to 3 heteroatoms, selected from N, O, S, for example pyrrole, imidazolul,pyrimidinyl.

The term "pharmaceutically acceptable salt" or "pharmaceutically acceptable acid addition salt" according to the invention embraces therapeutically active, non-toxic acid or base salt forms which the compounds of formula I are able to form.

The acid addition salt form of a compound of formula I that occurs in its free form as a base can be obtained by treating the free base with an appropriate acid such as an inorganic acid, for example, a hydrohalic such as hydrochloric or hydrobromic, sulfuric, nitric, phosphoric and the like; or an organic acid, such as, for example, acetic, trifluoroacetic, oxalic, hydroxyacetic, propanoic, lactic, pyruvic, malonic, succinic, maleic, fumaric, malic, tartaric, citric, methanesulfonic, ethanesulfonic, benzenesulfonic, p-toluenesulfonic, cyclamic, salicylic, p-aminosalicylic, pamoic and the like.

The invention also relates to all stereoisomeric forms such as enantiomeric and diastereoisomeric forms of the compounds of formula I or mixtures thereof (including all possible mixtures of stereoisomers).

With respect to the present invention reference to a compound or compounds is intended to encompass that compound in each of its possible isomeric forms and mixtures thereof, unless the particular isomeric form is referred to specifically.

Some of the compounds of formula I may also exist in tautomeric forms. Such forms although not explicitly indicated in the above formula are intended to be included within the scope of the present invention.

It is to be understood that each individual atom present in formula (I), or in the formulae depicted hereinafter, may in fact be present in the form of any of its naturally occurring isotopes, with the most abundant isotope(s) being preferred. Thus, by way of example, each individual hydrogen atom present in formula (I), or in the formulae depicted hereinafter, may be present as a 1H, 2H (deuterium) or 3H (tritium) atom, preferably 1H. Similarly, by way of example, each individual carbon atom present in formula (I), or in the formulae depicted hereinafter, may be present as a 12C, 13C or 14C atom, preferably 12C.

Another embodiment of the present invention concerns a pharmaceutical composition comprising a detectable amount of a compound of formula I or a pharmaceutically acceptable salt thereof in combination with a pharmaceutically acceptable diluent or carrier.

In another embodiment, the present invention concerns a compound as listed above for use as a medicament.

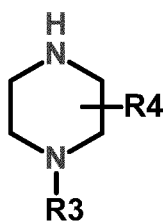
In a specific embodiment, the present invention concerns a compound as listed above for use as a medicament in the treatment of inflammatory conditions driven by STING, such as SLE (Systemic lupus erythematosus) and geographic atrophy.

The invention concerns the compounds for use in the treatment of inflammatory conditions
5 driven by STING activation.

In another embodiment, the present invention concerns a pharmaceutical composition containing a compound as listed above as well as pharmaceutically acceptable excipients.

In another embodiment, the invention concerns the synthesis of intermediates, acid addition salt,
10 a racemic mixture or its corresponding enantiomer and/or optical isomers thereof.

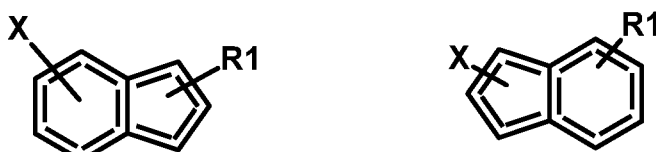
In another embodiment, the present invention concerns synthesis intermediates of general formula II



15 (II)

wherein R4 represents (C1-6)alkyl, (C1-6)alkoxy or oxo and R3 represents optionally substituted aryl or heteroaryl.

In another embodiment, the present invention concerns synthesis intermediates of general
20 formula III

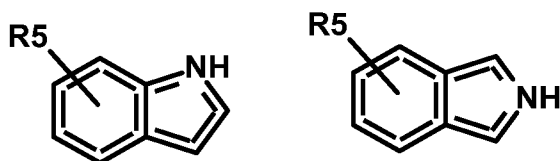


(III)

wherein

- 25
- X represents a halogen (Br, Cl, I) suitable for cross-coupling with intermediates of formula (II) or cross-coupling with an aryl or heteroaryl boronic acid derivative ; and
 - R1 represents alkyl or cycloalkyl amines optionally substituted including (C1-3) aminoalkyl, (C3-7) aminocycloalkyl, (C1-3)alkylimidazole, (C1-3)alkyl isoindoline, (C1-3)alkylpiperazine, (C1-3)alkylpiperidine, (C1-3)alkyl imidazopiperazine, (C1-3)alkyl(C4-7)aminocycloalkyl,
30 (C1-3)alkyl(C4-7)aminodicycloalkyl.

In another embodiment, the present invention concerns synthesis intermediates of general formula IV

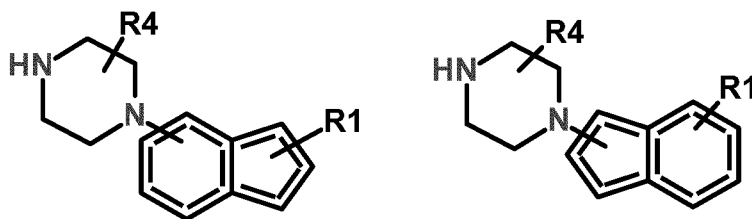


(IV)

5

wherein R5 can be either X or R2.

In another embodiment, the present invention concerns synthesis intermediates of general formula V



(V)

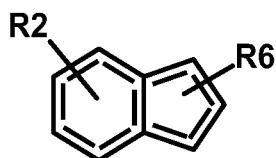
10

wherein

- R4 represents (C1-6)alkyl, (C1-6)alkoxy or oxo ; and
- R1 represents alkyl or cycloalkyl amines optionally substituted including (C1-3) aminoalkyl, (C3-7) aminocycloalkyl, (C1-3)alkylimidazole, (C1-3)alkyl isoindoline, (C1-3)alkylpiperazine, (C1-3)alkylpiperidine, (C1-3)alkyl imidazopiperazine, (C1-3)alkyl(C4-7)aminocycloalkyl, (C1-3)alkyl(C4-7)aminodicycloalkyl.

15

In another embodiment, the present invention concerns synthesis intermediates of general formula VI



(VI)

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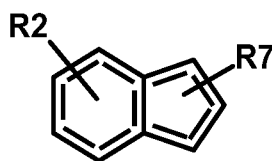
wherein

- R6 represents an alkyl or cycloalkyl substituent bearing a functional group suitable for displacement by an amine, for example 4-methylbenzenesulfonate; and
- R2 represents aryl, heteroaryl, heterobicyclic, (C4-7) aminocycloalkyl, cycloalkyl, heterocycloalkyl, (C6-8) diaminocycloalkyl, morpholino, (C4-7)cylcoalkylmethyl, piperzinyll,

25

piperdiny]. R2 is optionally substituted with groups including hydroxyl, (C1-6)alkyl, acetyl, halogen, cyano, C1-6 alkyl, trifluoromethyl, difluoromethyl, (C2-6) alkenyl, hydroxy, (C1-6) alkoxy, difluoromethoxy, trifluoromethoxy, trifluoroethoxy, (C1-6) alkylthio, (C1-6) alkylsulphonyl, amino, (C1-6) alkylamino, di(C1-6)alkylamino, (C1-6)alkoxy(C1-6)alkyl-
5 amino, N-[(C1-6)alkyl]-N-[hydroxy(C1-6)alkyl]amino, (C2-6) alkylcarbonylamino, (C2-6) alkoxy carbonylamino, (C1-6) alkylsulphonylamino, formyl, (C2-6) alkylcarbonyl, carboxy, (C2-6) alkoxy carbonyl, aminocarbonyl, (C1-6) alkylaminocarbonyl, di(C1-6)alkylaminocarbonyl, aminosulphonyl, (C1-6) alkylaminosulphonyl or di(C1-6)alkylaminosulphonyl; (C3-7)heterocycloalkyl or (C3-7)spiroheterocycloalkyl, either of which
10 groups may be optionally substituted by one or more substituents.

In another embodiment, the present invention concerns synthesis intermediates of general formula VII



(VII)

15 wherein

- R7 represents an primary or secondary amine ; and
- R2 represents aryl, heteroaryl, heterobicyclic, (C4-7) aminocycloalkyl, cycloalkyl, heterocycloalkyl, (C6-8) diaminocycloalkyl, morpholino, (C4-7)cylcoalkylmethyl, piperziny], piperdiny]. R2 is optionally substituted with groups including hydroxyl, (C1-6)alkyl, acetyl, halogen, cyano, C1-6 alkyl, trifluoromethyl, difluoromethyl, (C2-6) alkenyl, hydroxy, (C1-6) alkoxy, difluoromethoxy, trifluoromethoxy, trifluoroethoxy, (C1-6) alkylthio, (C1-6) alkylsulphonyl, amino, (C1-6) alkylamino, di(C1-6)alkylamino, (C1-6)alkoxy(C1-6)alkyl-
20 amino, N-[(C1-6)alkyl]-N-[hydroxy(C1-6)alkyl]amino, (C2-6) alkylcarbonylamino, (C2-6) alkoxy carbonylamino, (C1-6) alkylsulphonylamino, formyl, (C2-6) alkylcarbonyl, carboxy, (C2-6) alkoxy carbonyl, aminocarbonyl, (C1-6) alkylaminocarbonyl, di(C1-6)alkylaminocarbonyl, aminosulphonyl, (C1-6) alkylaminosulphonyl or di(C1-6)alkylaminosulphonyl; (C3-7)heterocycloalkyl or (C3-7)spiroheterocycloalkyl, either of which
25 groups may be optionally substituted by one or more substituents.

30

SYNTHETIC METHODS

The compounds of formula I according to the invention can be prepared analogously to conventional methods as understood by the person skilled in the art of synthetic organic chemistry.

According to one embodiment, some compounds of general formula I may be prepared by reacting intermediate (II) with intermediate (III) under Buchwald cross-coupling conditions with a suitable transition metal catalyst and base. Compounds of general formula (I) may also be prepared by reacting intermediate (III) with an appropriate aryl or heteroaryl boronic acid or boronic ester under Suzuki cross-coupling conditions. Alternatively, some compounds of general formula (I) may be prepared by reacting intermediate (IV) with a suitable R1 group bearing either a halogen (Cl, Br, I) for direct alkylation or an alcohol for Mitsunobu coupling. In this instance if R5 is a halogen in intermediate (IV), Buchwald or Suzuki cross-coupling with a suitable R2 group bearing either an amine, boronic acid or boronic ester will also be required to yield compounds of formula (I).

Compounds of general formula (I) may also be prepared from intermediate (V) by Buchwald cross-coupling with a suitable arylhalide or heteroaryl halide.

Compounds of general formula (I) may also be prepared from intermediate (V) by amide bond formation or urea formation by reaction with a suitable acid, acid chloride or isocyanate under appropriate coupling conditions.

Alternatively, compounds of general formula (I) may also be prepared from intermediate (VI) by amine displacement of a leaving group on the R6 substituent.

Compounds of general formula (I) may also be prepared from intermediate (VII) by reductive amination involving condensation with an aldehyde or ketone followed by reduction of the resulting imine.

EXAMPLES

The following examples illustrate how the compounds covered by formulas I and II may be synthesized. They are provided for illustrative purposes only and are not intended, nor should they be construed, as limiting the invention in any manner. Those skilled in the art will appreciate that routine variations and modifications of the following examples can be made without exceeding the spirit or scope of the invention.

All reactions involving air- or moisture-sensitive reagents were performed under a nitrogen atmosphere using dried solvents and glassware unless otherwise noted.

Abbreviations

BOC: tert-butyloxycarbonyl	
DCM: dichloromethane	EtOAc: ethyl acetate
DMF: <i>N,N</i> -dimethylformamide	MeOH: methanol
DMSO: dimethylsulfoxide	EtOH: ethanol
Et ₂ O: diethyl ether	MeCN: acetonitrile
THF: tetrahydrofuran	DIPEA: <i>N,N</i> -diisopropylethylamine

	H ₂ O: water	LDA: lithium diisopropylamide
	NH ₃ : ammonia	Pd(OAc) ₂ : palladium(II) acetate
	MgSO ₄ : magnesium sulphate	Na ₂ SO ₄ : sodium sulphate
	K ₂ CO ₃ : potassium carbonate	NBS: N-bromosuccinimide
5	NIS: N-iodosuccinimide	DBU: 1,8-diazabicyclo[5.4.0]undec-7-ene
	eq.: equivalents	SM: starting material
	TFA: trifluoroacetic acid	DME: 1,2-dimethoxyethane
	pTSA: <i>p</i> -toluenesulfonic acid	TBAF: tetra- <i>n</i> -butylammonium fluoride
	min.: minutes	h: hour
10	r.t.: room temperature	RT: retention time
	br: broad	M: molar
	N: Normal	ES+: Electrospray Positive Ionisation
	SCX: solid phase cation exchange	N ₂ : nitrogen
	HPLC: High Performance Liquid Chromatography	
15	LCMS: Liquid Chromatography Mass Spectrometry	
	brine: saturated aqueous sodium chloride solution	
	PdCl ₂ (dppf)-DCM: [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II)	
	Pd-Ruphos G3: (2-Dicyclohexylphosphino-2',6'-diisopropoxy-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)]palladium(II) methanesulfonate	
20	BINAP: (2,2'-bis(diphenylphosphino)-1,1'-binaphthyl)	
	Pd ₂ dba ₃ : Tris(dibenzylideneacetone)dipalladium(0)	
	HATU: 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium	3-oxid
	hexafluorophosphate	
	FCC: flash column chromatography	
25	CMBP: (Cyanomethylene)trimethylphosphorane	
	CDI: 1,1'-carbonyldiimidazole	

Nomenclature

Compounds were named with the aid of ACD-ConsoleVersion 14.03 and/or Biovia Draw 2016.

30

Analytical Conditions

All reactions involving air- or moisture-sensitive reagents were performed under a nitrogen atmosphere using dried solvents and glassware unless otherwise noted.

Except where otherwise stated, analytical LCMS data were obtained by using the below methods.

35

All quoted LCMS Retention Time (RT) values are in minutes.

Method 1:

pH 10

Gradient:

Time (mins)	A%	B%
0.00	95.00	5.00
4.00	5.00	95.00
5.00	5.00	95.00
5.10	95.00	5.00

Flow: 1 mL/min

Solvent A: 10 mM Ammonium Formate in water + 0.1 % Ammonia Solution

5

Solvent B: Acetonitrile + 5 % water + 0.1 % Ammonia Solution

Column: XBridge C18, 2.1 x 20 mm, 2.5 μ mMethod 2:

pH 10

10

Gradient:

Time (mins)	A%	B%
0.00	95.00	5.00
1.50	5.00	95.00
2.25	5.00	95.00
2.50	95.00	5.00

Flow 1 mL/min

Solvent A: 10 mM Ammonium Formate in water + 0.1% Ammonia Solution

Solvent B: Acetonitrile + 5 % water + 0.1% Ammonia Solution

Column: XBridge C18, 2.1 x 20 mm, 2.5 μ m

15

Method 3:

pH 3

Gradient:

Time (mins)	A%	B%
0.00	98.00	2.00
0.3	98.00	2.00
3.00	5.00	95.00
4.00	5.00	95.00
4.10	98.00	2.00
5.10	98.00	2.00

Flow 0.8 mL/min

Solvent A: Water + Acetonitrile + Formic Acid (95/5/750 μ L)

Solvent B: Water + Acetonitrile + Formic Acid (5/95/500 μ L)

Column: Acquity UPLC HSS T3 C18 column (1.8 μ m, 2.1 x 50 mm)

5

Method 4:

pH 10

Gradient:

Time (mins)	A%	B%
0.0	95	5
0.1	95	5
2.6	5	95
2.75	5	95
2.8	95	5
3.0	95	5

Flow: 1 mL/min

Solvent A = 10 mM Ammonium formate + 0.1 % Ammonia Solution (pH10)

Solvent B = MeCN + 5 % H₂O + 0.1 % Ammonia Solution (pH10)

Column: Waters XBridge BEH C18 XP 2.5 μ m 2.1 x 50 mm

10

Method 5:

pH 3

Gradient:

Time (mins)	A%	B%
0.0	94	6
1.5	5	95
2.25	5	95
2.5	94	6

Flow: 1 mL/min

5 Solvent A = 10 mM Ammonium formate in water + 0.1% Formic acid

Solvent B = MeCN + 5 % H₂O + 0.1% Formic acid

Column: X-Bridge C18 Waters 2.1 x 20 mm, 2.5 μM column

Method 6:

10 pH 10

Gradient:

Time (mins)	A%	B%
0.0	94	6
1.5	5	95
2.25	5	95
2.5	94	6

Flow: 1 mL/min

Solvent A = 10 mM Ammonium formate in water + 0.1% ammonia solution

15 Solvent B = MeCN + 5 % H₂O + 0.1% Formic acid

Column: X-Bridge C18 Waters 2.1 x 20 mm, 2.5 μM column

Method 7:

Gradient:

Time (mins)	A%	B%
0.0	100	0
2.0	2	98
3.0	2	98
3.2	100	0
4.0	100	0

Flow: 1.2 mL/min

Solvent A = 5 mM Ammonium Bicarbonate Solution

Solvent B = MeCN

Column: Waters XBridge BEH C18 2.5 µm 3.0 x 50 mm

5

Method 8:

Gradient:

Time (mins)	A%	B%
0.0	100	0
2.0	2	98
3.0	2	98
3.2	100	0
4.0	100	0

Flow: 1.2 mL/min

Solvent A = 0.05% Formic acid in water/MeCN (95:5)

Solvent B = 0.05% Formic acid in MeCN

Column: Waters X-Select CSH 2.5 µm 3.0 x 50 mm

10

15

Method 9:

pH 10

Gradient:

Time (mins)	A%	B%
0.0	95	5
4.0	5	95
5.0	5	95
5.1	95	5
6.5	95	5

Flow: 1 mL/min

Solvent A = 5 mM Ammonium formate + 0.1% Ammonia Solution

5

Solvent B = MeCN + 5% Solvent A + 0.1% Ammonia Solution

Column: Waters XBridge BEH C18 2.5 μ m 2.1 x 50 mmMethod 10:

pH 3

10 Gradient

Time (mins)	A%	B%
0.0	95	5
1.2	0	100
1.30	0	100
1.31	95	5

Flow: 1.2 mL/min

Solvent A = Water + 0.1% Formic acid

Solvent B = MeCN + 0.1% Formic acid

15

Column: Kinetex Core-Shell C18, 2.1 x 50mm, 5 μ m columnMethod 11:

pH 3

Gradient

Time (mins)	A%	B%
0.0	95	5
5.3	0	100
5.80	0	100
5.82	95	5
7.00	95	5

Flow: 0.6 mL/min

5 Solvent A = Water + 0.1% Formic acid

Solvent B = MeCN + 0.1% Formic acid

Column: Phenomenex Kinetix-XB C18, 2.1 x 100mm, 1.7µm column

Method 12:

10 pH 3

Gradient

Time (mins)	A%	B%
0.0	95	5
1.83	0	100
2.25	0	100
2.26	95	5

Flow: 1.2 ml/min

15 Solvent A = Water + 0.1% Formic acid

Solvent B = MeCN + 0.1% Formic acid

Column: Kinetex Core-Shell C8, 2.1 x 50mm, 5µm column

Method 13:

pH 3

Gradient

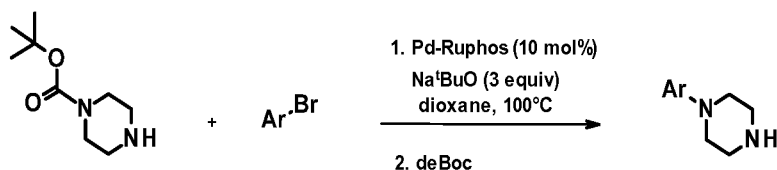
Time (mins)	A%	B%
0.0	95	5
5.00	0	100
5.40	0	100
5.42	95	5
7.00	95	5

Flow: 0.6 ml/min

Solvent A= Water + 0.1% Formic acid

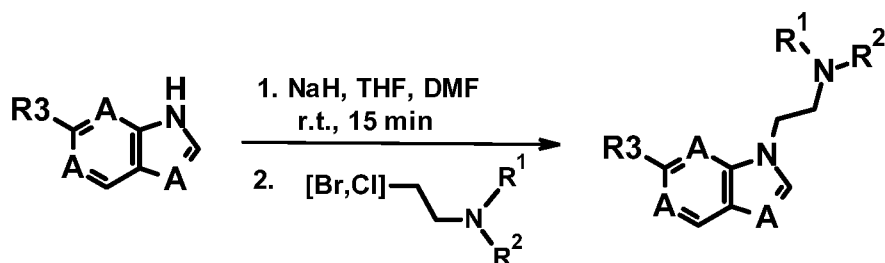
5 Solvent B =: MeCN + 0.1% Formic acid

Column: Waters Atlantis dC18, 2.1 x 100mm, 3 μ m column

General Procedure 1

A mixture of 1-BOC-piperazine (1 equiv.), sodium tert-butoxide (1.5 - 3 equiv.), arylhalide (1.2 equiv.) and Pd-Ruphos G3 (0.1 equiv.) were dissolved in pre-degassed 1,4-dioxane (0.15 - 0.3 M). The reaction mixture was then heated at 100 °C until complete. The reaction mixture was cooled to ambient temperature and then either treated with an aqueous work up or with filtration through celite. The solvent was dried (using either MgSO₄, Na₂SO₄ or a phase separator) and subsequently removed under vacuum. The residue was purified by flash silica chromatography to give the product or used directly in the next step. The product was then dissolved in DCM (4-5 mL) and TFA (0.5 - 1 ml) added (either at 0 °C or at room temperature). The reaction mixture was stirred at ambient temperature until complete (LCMS monitoring). Then, the reaction was filtered through an SCX cartridge eluting first with methanol then with ammonia (2-7 M) in methanol. The ammonia in methanol solution was concentrated under reduced pressure to give the desired product.

15

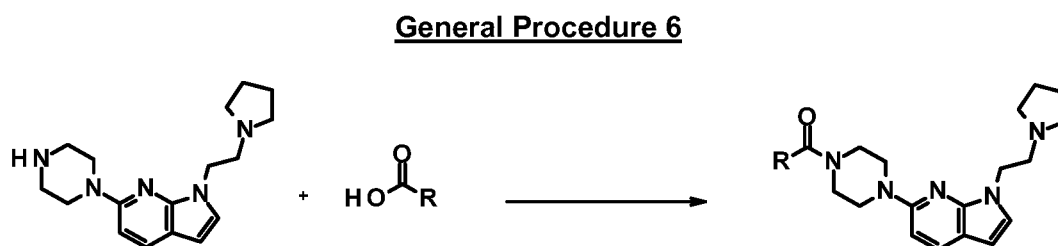
General Procedure 2

The appropriate heterocycle (1 equiv.) was dissolved in a mixture of DMF and THF (1:1 or 1:1.5). The solution was cooled to 0 °C and sodium hydride (1.2 or 2.2 equiv.) carefully added portion-wise. After approximately 5 min. the alkyl halide (1.2 equiv.) was added portion-wise. The reaction mixture was stirred at 0 °C or at rt for 15 min. to an hour then heated at 80 °C for a period ranging between 30 min to 6 h. The reaction mixture was cooled to 0 °C and quenched with water and treated with EtOAc and the organic layer separated. The organic solvent was dried (using either MgSO₄, Na₂SO₄ or a phase separator) and subsequently removed under vacuum. The residue was purified by flash silica column chromatography or reverse phase column chromatography to give the product.

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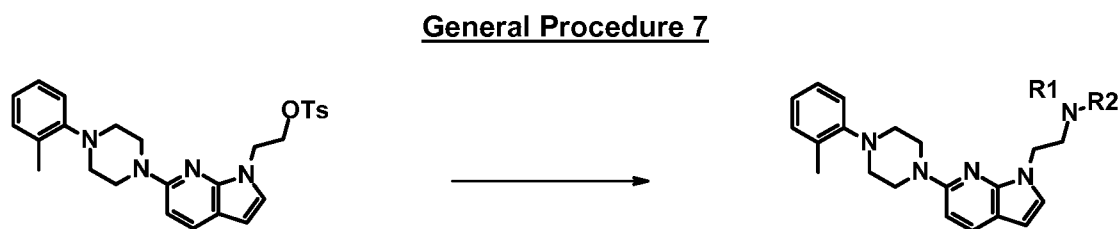
and then either treated with an aqueous work up or with filtration through Celite. The solvent was dried (using either $MgSO_4$, Na_2SO_4 or a phase separator) and subsequently removed under vacuum. The residue was purified by flash silica chromatography to give the product or used directly in the next step.

5



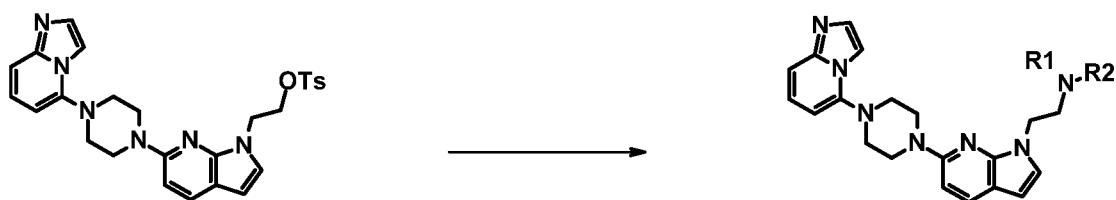
The appropriate carboxylic acid (0.05 mmol, 1 eq.) was added to a solution of Intermediate 7 (15 mg, 0.05 mmol, 1 eq.) and 2,4,6-tripropyl-1,3,5,2,4,6-trioxatriphosphorinane-2,4,6-trioxide (38 mg, 0.06 mmol, 1.2 eq) in DCM (0.5 mL). The reaction mixture was stirred at r.t. overnight. Reaction mixture filtered and diluted with DMF (0.45 mL) and purified by reverse phase column chromatography to yield the desired product.

15



The appropriate amine (1.4 eq.), potassium carbonate (6 eq.) and Intermediate 17 (1.0 eq.) in 1,4-dioxane were stirred at 100 °C over a period of 6-12 hours. Small scale reactions (0.05 mmol) were filtered and purified by preparative HPLC to yield the desired product. Larger scale reactions (> 0.08 mmol) were passed through an SCX cartridge washing first with MeOH then eluting with approx. 2 M NH_3 in MeOH. The ammonia in methanol solution was concentrated under reduced pressure and the crude residue purified by reverse phase HPLC to yield the desired product.

25

General Procedure 8

5 A mixture of the appropriate amine (1.5 eq.) and Intermediate 15 (20 mg, 0.03 mmol, 1 eq.) in acetonitrile and triethylamine (0.02 mL, 0.14 mmol, 4 eq.) were stirred at 80 °C overnight. The reaction mixture was filtered and purified by HPLC to yield the desired product.

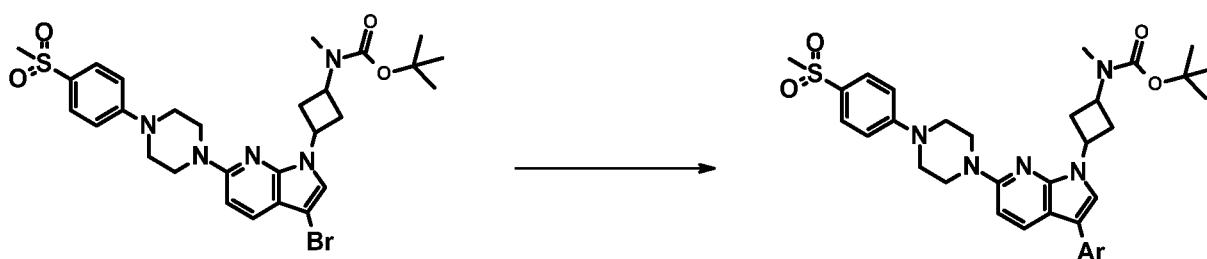
General Procedure 9

10 A mixture of the alcohol (1.5 eq.) and heterocycle (1 eq.) was dissolved in toluene (0.25 M). Cyanomethylenetributylphosphorane (1.5 eq) was then added and the reaction mixture heated at 90-110 °C for 3-12 hours. The crude reaction mixture was loaded onto a silica column and eluted with a gradient of ethyl acetate in hexane to give the desired product.

General Procedure 10

15 The corresponding arylbromide (1 eq.), boronic acid (1.5 eq.) and K₂CO₃ (2 eq.) were dissolved in 1,4-dioxane (0.1 M). H₂O (1 M) was added and the mixture degassed before PdCl₂(dppf)-DCM (0.01 eq.) was added and heated at 90 °C until the starting material was consumed. The reaction mixture was cooled to ambient temperature and EtOAc and H₂O were added. The layers were separated and the organic layer dried over Na₂SO₄. The solvent was removed under vacuum and the residue purified by flash silica column chromatography using hexane to EtOAc as eluent to afford the desired product.

20

General Procedure 11

25 Intermediate 23 (70 mg, 0.11 mmol), boronic ester (2 eq., 0.22 mmol), K₂CO₃ (2 eq., 0.22 mmol) and PdCl₂(dppf)-DCM complex (0.1 equiv., 0.01 mmol) were dissolved in 1,4-dioxane (0.1 M, 1

mL). H₂O (0.1 mL) was added and the mixture was degassed for 1 min. The mixture was stirred overnight at 100°C. The mixture was then cooled to ambient temperature and DCM (3 mL) and H₂O (2 mL) were added and the layers separated. TFA (1 mL) was added to the DCM layer and the reaction mixture was stirred at room temperature for 2 h. reaction mixture was filtered through an SCX column, rinsed with MeOH and DCM, and the product eluted with NH₃ (7N in MeOH). The volatiles were removed under vacuum and the residue was purified by reverse phase HPLC to afford the desired product.

General Procedure 12

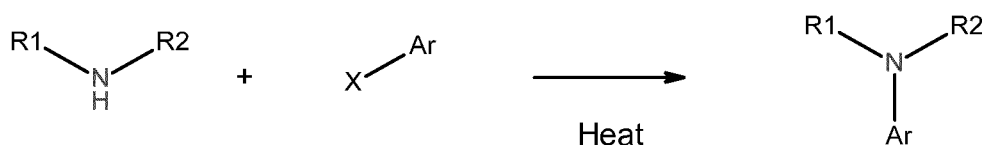
The amine (1 eq.) was dissolved in a 1:1 mixture of tetrahydrofuran and ethanol (2 ml) or DCM (2 ml) or DMF (0.13 M). The carbonyl compound (1-10 eq.) was then added, followed by acetic acid (1-10 eq.) and sodium triacetoxyborohydride (3 - 4 eq.). The reaction mixture was stirred at room temperature until complete. The reaction mixture was then concentrated under reduced pressure, dissolved in DCM and washed with aq. sodium hydroxide (2 M). The organic solvent was separated, dried (Na₂SO₄) and concentrated under reduced pressure. Alternatively, the reaction mixture was diluted in EtOAc and the organic phase washed with water, brine, dried over Na₂SO₄ and concentrated to dryness in vacuo. The residue was optionally purified by reverse phase column chromatography to give the desired product as a free base or formic acid salt.

General Procedure 13

Boc-protected amine (1 eq.) was treated according to Method A or Method B:

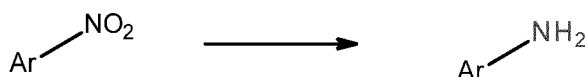
Method A: Amine was dissolved in DCM (4-5 mL) and TFA (0.5 - 1 mL or 20 eq.) added. The reaction mixture was stirred until completion. The reaction was diluted in DCM and washed with 2 M aqueous Na₂CO₃. The organic phase was then dried over Na₂SO₄ and concentrated to dryness in vacuo. Alternatively, the crude reaction mixture was purified by filtration through an SCX cartridge washing first with methanol then eluting with approx. 2 M ammonia in methanol. The ammonia in methanol solution was concentrated under reduced pressure to give the desired product. The product was optionally further purified by prep HPLC.

Method B: 4N HCl (10-50 eq.) in dioxane was added to a solution of Boc-protected amine (1 eq.) in DCM at room temperature. The reaction mixture was stirred for 1-16 h at room temperature. The reaction mixture was concentrated to dryness and the desired product was used as such in the next step as a HCl salt or purified by prep HPLC to afford the desired product as a formic acid salt or free base.

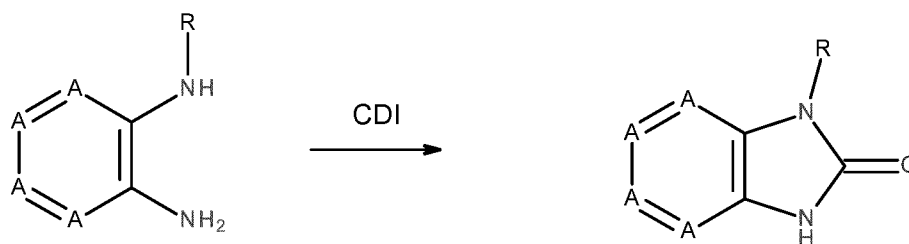
General Procedure 14

5 A solution of amine (1 eq.) and the corresponding halogen-substituted heterocycle (1 eq.) were heated (80-140 °C) with or without potassium carbonate (1.4 eq) in DMSO until reaction was complete. The mixture was diluted with EtOAc, washed with brine (5 times), dried (Na₂SO₄) and concentrated in vacuo. The product was optionally further purified by column chromatography or via trituration with an appropriate solvent.

10

General Procedure 15

15 To a solution of nitroarene in MeOH was added zinc (6 equiv) and ammonium formate (5 equiv) at 0°C. After complete addition the resulting reaction mixture was stirred at rt. After complete consumption of starting material (~15 mins), the methanol was evaporated under reduced pressure, the residue was then dissolved in ethyl acetate and filtered through Celite. The Celite was washed with ethyl acetate. The collected filtrate was washed with water (x 2), dried over sodium sulphate and evaporated under reduced pressure. The crude material was optionally
20 purified by column chromatography.

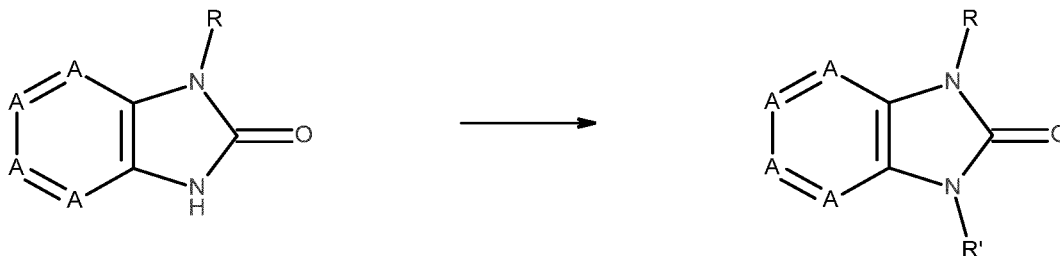
General Procedure 16

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To a stirred solution of diamine in toluene was added CDI (2 equiv) at room temperature in a sealed tube. The reaction mixture was allowed to stir at 100 °C for 16 h. The reaction mixture was diluted with water and extracted with ethyl acetate (x 2). The organic layer was washed with brine,

dried (Na_2SO_4) and concentrated under reduced pressure. The crude compound was optionally purified by column chromatography.

General Procedure 17

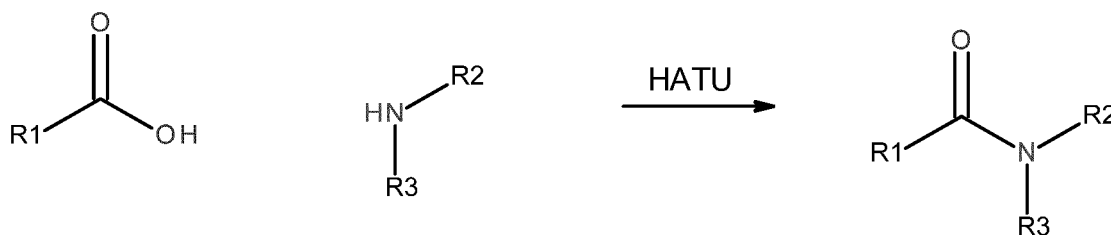


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To a stirred solution of arylimidazol-2-one in MeCN was added aryl iodide (1.5 equiv), K_2CO_3 (3 equiv) and N,N'-dimethylethylenediamine (5 equiv) at rt. The mixture was degassed by using argon gas for 15 min. CuI (1.5 equiv) was then added and the reaction mixture was degassed for 15 min. The reaction was stirred at $100\text{ }^\circ\text{C}$ for 16h. After cooling to rt, the mixture was diluted with water and extracted with ethyl acetate (x 3). The organic layer was washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was optionally purified by column chromatography.

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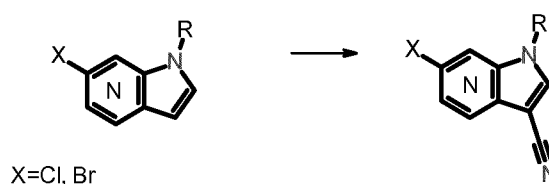
General Procedure 18



Carboxylic acid (1 equiv), amine (1.5 equiv) and HATU (1.3 equiv mmol) were dissolved in N,N-dimethylformamide and N,N-diisopropylethylamine. The mixture was then stirred at rt under N_2 for 1 hour. The mixture was diluted with EtOAc, water and brine then the layers were separated and the aqueous was further extracted with EtOAc. The combined organics were washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was optionally purified by column chromatography

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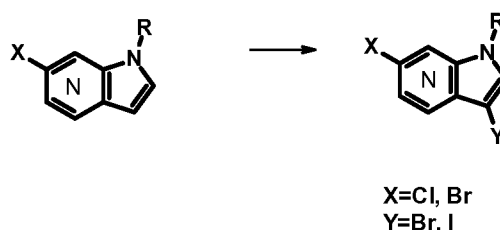
General Procedure 19



25

A 1-substituted -{6-bromo-1H-pyrrolo[2,3-b]pyridine (1 eq) was dissolved in anhydrous DMF (0.5 M) and anhydrous MeCN (0.5M) and cooled to 0 °C under nitrogen. Chlorosulfonyl isocyanate (1.15 eq.) was added and the reaction mixture was stirred at 0 °C under nitrogen for 10 min. The reaction mixture was allowed to warm to rt and stirred at rt for 30 min. The reaction was cooled to 0 °C and 1M NaOH aq. was added dropwise until the aqueous phase was at pH 10. The reaction suspension was extracted with EtOAc and the combined organic phase was washed with brine and dried over Na₂SO₄. The crude product was purified by FCC (Biotage Isolera, SNAP Ultra, gradient elution 10-100% EtOAc:Heptanes) to afford the desired 3-cyano product.

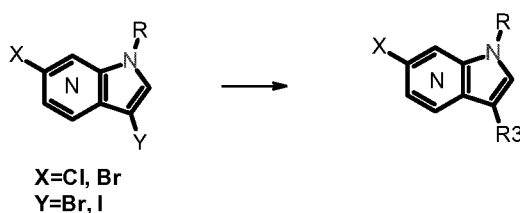
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General Procedure 20

15

NIS or NBS (1 eq.) was added to a solution of 1-substituted -{6-halo-1H-pyrrolo[2,3-b]pyridine (1 eq) in anhydrous DMF (0.05M) at rt. The reaction mixture was stirred under nitrogen for 20 min. Water was added and the reaction mixture was extracted with EtOAc. The organic phase was washed successively with water, brine, dried over Na₂SO₄ and concentrated to dryness in vacuo to afford the desired 3-halogenated product.

20

General Procedure 21

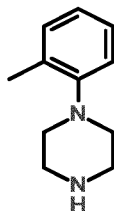
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A mixture of aryl halide (1 eq.), aryl boronic acid (1 eq.) and 2M sodium carbonate (3 eq.) in dioxane (0.12M) was degassed by N₂ bubbling for 10 min, then Tetrakis(triphenylphosphine)palladium(0) (0.05 - 0.1 eq) was added and the reaction was heated at 80-100 °C for 30 min in the CEM microwave 200W or thermally for 1-16 h. The reaction mixture was diluted in EtOAc and washed successively with water and brine. The aqueous phase was extracted with EtOAc, the combined organic phase was dried over Na₂SO₄ and concentrated to dryness in vacuo. The residue was purified by FCC (Biotage isolera, SNAP Ultra, gradient

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elution 10-100% EtOAc:Heptane to afford the desired product.

INTERMEDIATE 1

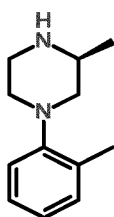


5 1-(o-tolyl)piperazine

1-(o-tolyl)piperazine was prepared following General Procedure 1 using 1-BOC-piperazine (6 g, 32 mmol) and 2-bromotoluene (5 mL, 41 mmol) to afford intermediate 1 (7.2 g, 82% yield) LCMS (Method 2, ES⁺) 1.56 min, 177 *m/z* (M+H)⁺.

10

INTERMEDIATE 2



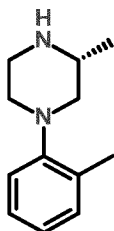
(3S)-3-methyl-1-(o-tolyl)piperazine

(3S)-3-methyl-1-(o-tolyl)piperazine was prepared following General Procedure 1 using 2-bromotoluene (170 mg, 1 mmol) and (S)-4-N-Boc-2-methylpiperazine (240 mg, 1.2 eq., 1.2 mmol) to afford intermediate 2 (110 mg, 47% yield).

15

LCMS (Method 2, ES⁺) 1.1 min, 191 *m/z* (M+H)⁺.

INTERMEDIATE 3



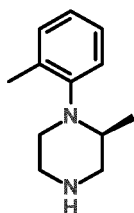
20 (3R)-3-methyl-1-(o-tolyl)piperazine

(3R)-3-methyl-1-(o-tolyl)piperazine was prepared following General Procedure 1 using 2-bromotoluene (170 mg, 1 mmol) and (R)-4-N-Boc-2-methylpiperazine (240 mg, 1.2 eq., 1.2 mmol) to afford intermediate 3 (122 mg, 52% yield).

LCMS (Method 2, ES⁺) 1.1 min, 191 *m/z* (M+H)⁺.

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INTERMEDIATE 4

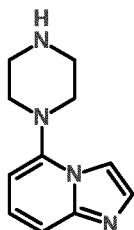


(2S)-2-methyl-1-(o-tolyl)piperazine

(2S)-2-methyl-1-(o-tolyl)piperazine was prepared following General Procedure 1 using 2-bromotoluene (170 mg, 1 mmol) and (S)-1-N-Boc-2-methylpiperazine (240 mg, 1.2 eq., 1.2 mmol) to afford intermediate 4 (180 mg, 77% yield).

LCMS (Method 2, ES⁺) 1.08 min, 191 *m/z* (M+H)⁺.

INTERMEDIATE 5



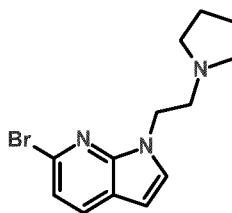
15

5-piperazin-1-ylimidazo[1,2-a]pyridine

5-piperazin-1-ylimidazo[1,2-a]pyridine was prepared following General Procedure 1 using 5-bromoimidazo[1,2-A]pyridine (5 g, 25 mmol) and 1-boc-piperazine (4.7 g, 25 mmol) to afford intermediate 5 (1.1 g, 55% yield).

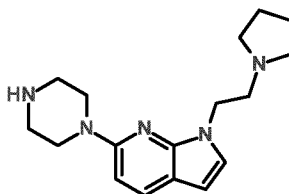
LCMS (Method 2, ES⁺) 0.35 min, 203 *m/z* (M+H)⁺.

20

INTERMEDIATE 6**6-bromo-1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridine**

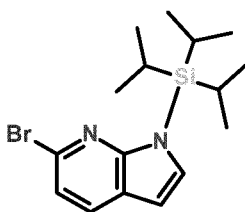
5 6-bromo-1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridine was prepared following General Procedure 2 using 6-bromo-1H-pyrrolo[2,3-b]pyridine (10 g, 50 mmol) and 1-(2-chloroethyl)pyrrolidine hydrochloride (11 g, 63.4 mmol). The reaction was heated to 80 °C for 2 hours. The residue was purified by flash silica column chromatography using gradient elution from hexane to 1:1 hexane:EtOAc to afford the intermediate 6 (12 g, 82% yield).

10 LCMS (Method 2, ES⁺) 1.30 min, 295 & 297 *m/z* (M+H)⁺.

INTERMEDIATE 7**6-piperazin-1-yl-1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridine**

15 Intermediate 6 (7 g, 23.8 mmol) was treated according to General Procedure 1 followed by General Procedure 13 to afford Intermediate 7 (4.5 g, 67% yield).

LCMS (Method 2, ES⁺) 1.02 min, 300 *m/z* (M+H)⁺.

INTERMEDIATE 8

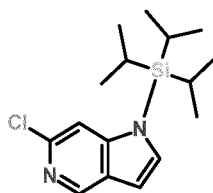
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(6-bromopyrrolo[2,3-b]pyridin-1-yl)-triisopropyl-silane

6-Bromo-1H-pyrrolo[2,3-b]pyridine (4 g, 20.3 mmol) was dissolved in 1,4-dioxane (100 mL) and DIPEA (11 mL, 63.1 mmol) was added followed by triisopropylsilyl trifluoromethanesulfonate (6.5 mL, 24 mmol). The reaction mixture was then stirred at r.t. for 30 min. before it was heated at 80°C overnight. Triisopropylsilyl trifluoromethanesulfonate (1.2 equiv., 24.4 mmol) was added and stirred at 80°C for an additional 3 hours. The reaction was cooled down to ambient temperature and NH₄Cl aq. solution and EtOAc were added. The layers were separated and the aq. phase was extracted with EtOAc. The combined organic layers were dried over MgSO₄ and the solvent was removed under vacuum. The residue was purified by flash chromatography using gradient elution from hexane to a 1:1 mixture hexane:EtOAc to yield Intermediate 8 (5.2 g, 72% yield).

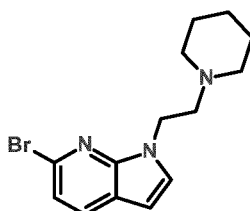
LCMS (Method 2, ES⁺) 1.96 min, 353 & 355 *m/z* (M+H)⁺.

15

INTERMEDIATE 9(6-chloropyrrolo[3,2-c]pyridin-1-yl)-triisopropyl-silane

6-Chloro-5-azaindole (1 g, 6.42 mmol) was partially suspended in 1,4-dioxane (30 mL). DIPEA (3.5 mL, 20 mmol) was then added followed by triisopropylsilyl trifluoromethanesulfonate (2.5 mL, 9.3 mmol). The reaction mixture was stirred at room temperature for 5 h 30 min and then treated with an aq. work up. The organic solvent was dried (Na₂SO₄) and concentrated under reduced pressure to give a residue that was purified by flash silica column chromatography to give the title compound (1.68 g, 84%).

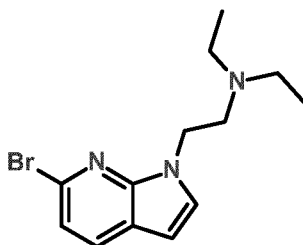
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INTERMEDIATE 10

6-bromo-1-[2-(1-piperidyl)ethyl]pyrrolo[2,3-b]pyridine

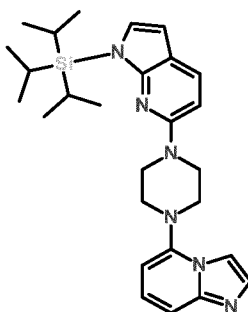
6-bromo-1-[2-(1-piperidyl)ethyl]pyrrolo[2,3-b]pyridine was prepared following General Procedure 2 using 6-bromo-1H-pyrrolo[2,3-b]pyridine (400 mg, 2 mmol) and 1-(2-bromoethyl)piperidine hydrobromide (1.2 equiv., 2.39 mmol). The product was purified by flash silica column chromatography using gradient elution from hexane to hexane:EtOAc 1:1 to give intermediate 10 (420 mg, 69% yield).

LCMS (Method 2, ES⁺) 1.45 min, 308 & 310 *m/z* (M+H)⁺.

INTERMEDIATE 112-(6-bromopyrrolo[2,3-b]pyridin-1-yl)-N,N-diethyl-ethanamine

2-(6-bromopyrrolo[2,3-b]pyridin-1-yl)-N,N-diethyl-ethanamine was prepared following General Procedure 2 using 6-bromo-1H-pyrrolo[2,3-b]pyridine (400 mg, 2 mmol) and 2-bromo-N,N-diethylamine hydrobromide (1.2 equiv., 2.4 mmol). The crude product was purified by flash silica column chromatography using gradient elution from hexane to EtOAc to afford Intermediate 11 (360 mg, 61% yield).

LCMS (Method 2, ES⁺) 1.42 min, 296 & 298 *m/z* (M+H)⁺.

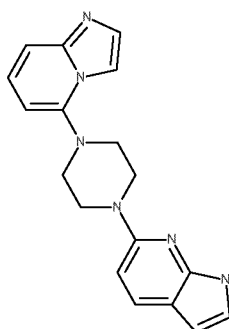
INTERMEDIATE 12[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]-triisopropyl-silane

[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]-triisopropyl-silane was prepared following General Procedure 3 using Intermediate 8 (1.2 eq., 13 mmol) and Intermediate 5 (2.2 g, 11 mmol). The residue was purified by flash silica column chromatography with gradient elution from hexane to EtOAc to yield Intermediate 12 (3.2 g, 61% yield).

5

LCMS (Method 2, ES⁺) 1.90 min, 475 *m/z* (M+H)⁺.

INTERMEDIATE 13



10 5-[4-(1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine

Intermediate 12 (3.15 g, 6.64 mmol) was dissolved in THF (0.25 M, 26 mL) and TBAF (8 mL, 1.2 eq., 7.96 mmol, 1 mmol/mL) added. The reaction mixture was stirred at ambient temperature for 3 hours and then H₂O and Et₂O were added. The layers were separated and the aqueous phase extracted with Et₂O. The solvent was removed under vacuum and the residue was re-

15

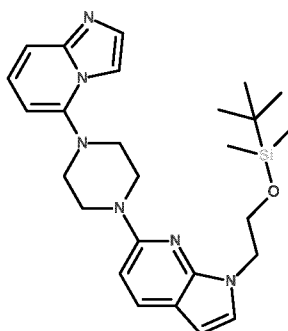
dissolved in MeOH and filtered through an SCX column and washed with MeOH and then eluted

with NH₃ (7N in MeOH) to give Intermediate 13 (1.0 g, 44%).

LCMS (Method 2, ES⁺) 1.13 min, 319 *m/z* (M+H)⁺.

INTERMEDIATE 14

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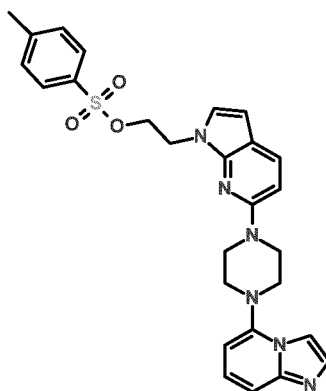


tert-butyl-[2-[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethoxy]-dimethyl-silane

Intermediate 13 (2 g, 6.3 mmol) was dissolved in a mixture of THF (0.25 M) and DMF (0.25 M) and cooled at 0 °C before sodium hydride (1.5 eq., 400 mg, 9.95 mmol) was added in portions. The mixture was stirred at ambient temperature for 30 min. before (2-bromoethoxy)-tert-butyl dimethylsilane (1.2 eq., 8 mmol) was added. The mixture was warmed to 60 °C and stirred until the reaction was complete. The reaction mixture was quenched with H₂O and EtOAc added. The layers were separated and the aq. phase extracted with EtOAc. The combined organic layers were dried over Na₂SO₄ and the solvent removed under vacuum. The residue was purified by column chromatography, gradient elution from EtOAc to 1:1 MeOH:EtOAc to afford Intermediate 14 as a white solid (1 g, 44% yield).

LCMS (Method 2, ES⁺) 1.78 min, 477 *m/z* (M+H)⁺.

INTERMEDIATE 15



15

2-[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl ethyl 4-methylbenzenesulfonate

Intermediate 14 (1 g, 2.098 mmol) was dissolved in THF (0.25 M, 102.3 mmol) and TBAF (3.1 mL, 3.15 mmol, 1 mmol/mL) was added. The reaction mixture was stirred at ambient temperature for 3 hours and then H₂O and Et₂O added. The layers were separated and the aqueous phase was extracted with Et₂O. The combined organic layers were dried over Na₂SO₄. The solvent was removed under vacuum and the residue was dissolved in MeOH and filtered through an SCX column and washed with MeOH and then eluted with NH₃ (7 N) in MeOH. The resulting residue was dissolved in DCM (0.25 M) and triethylamine (1.5 eq., 3 mmol) added. The solution was cooled to 0 °C, and *p*-toluenesulfonyl chloride (1.2 eq., 2 mmol) was added and the reaction mixture stirred at ambient temperature overnight. The reaction mixture was quenched with H₂O and DCM and the layers separated. The solvent was removed under vacuum and the

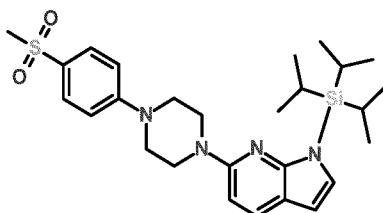
25

residue purified by flash silica column chromatography using gradient elution from hexane to EtOAc, and then to 20% MeOH in EtOAc to afford Intermediate 15 (900 mg, 69% yield)

LCMS (Method 2, ES⁺) 1.50 min, 517 *m/z* (M+H)⁺.

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INTERMEDIATE 16



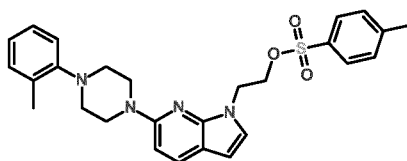
triisopropyl-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]silane

10 Triisopropyl-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]silane was prepared following General Procedure 3 using Intermediate 8 (5 g, 14.2 mmol) and 1-[4-(methylsulfonyl)phenyl]piperazine (1.2 eq., 17 mmol). The residue was purified by flash column chromatography with gradient elution from hexane to EtOAc and then until 30% MeOH in EtOAc to give Intermediate 16 (5.3 g, 73% yield).

LCMS (Method 2, ES⁺) 1.98 min, 513 *m/z* (M+H)⁺

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INTERMEDIATE 17

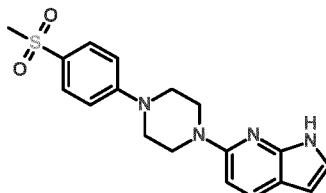


2-[6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl 4-methylbenzenesulfonate

20 Intermediate 21 (0.3 g, 0.89 mmol) was dissolved in dichloromethane (5 mL) and triethylamine (0.2 mL, 1 mmol) was added followed by *p*-toluenesulfonylchloride (171 mg, 0.88 mmol). After 2 h a second portion of triethylamine (0.2 mL, 1 mmol) was added followed by a second portion of intermediate 21 (0.3 g, 0.89 mmol) in dichloromethane (5 mL) and a second portion of *p*-toluenesulfonylchloride (171 mg, 0.88 mmol). The reaction mixture was then stirred at rt overnight and treated with an aqueous work up. The organic solvent was dried (Na₂SO₄) and
25 concentrated under reduced pressure. The crude residue was then purified by flash silica column chromatography to give the title compound (0.51 g, quant.)

LCMS (Method 2, ES⁺) 1.63 min, 491 *m/z* (M+H)⁺.

INTERMEDIATE 18



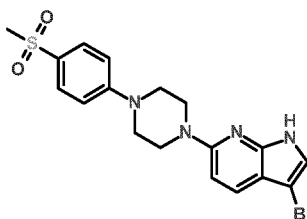
5 6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine

Intermediate 16 (3 g, 5.9 mmol) was dissolved in THF (0.5 M) and TBAF (8.8 mL, 1.5 eq., 8.8 mmol, 1 mmol/mL) was added at ambient temperature. The mixture was stirred for 1 hour then H₂O and Et₂O were added. The layers were separated and the aq. phase was extracted with Et₂O. The solvent was removed under vacuum and the residue purified by flash
10 chromatography gradient elution from hexane to EtOAc and then to a mixture of 1:1 EtOAc:MeOH to yield intermediate 18 (950 mg, 46% yield).

LCMS (Method 2, ES⁺) 1.20 min, 357 *m/z* (M+H)⁺.

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INTERMEDIATE 19



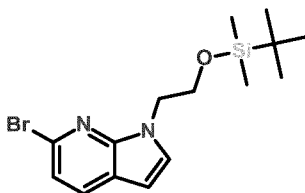
3-bromo-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine

Intermediate 16 (730 mg, 1.4 mmol) was dissolved in DCM (30 mL) and cooled to 0 °C. N-bromosuccinimide (165 mg, 0.92 mmol) was added portion-wise over 20 min. The reaction was
20 stirred at that temperature for an additional 10 minutes before it was quenched with saturated NaHCO₃ and the layers separated. The aqueous phase was then extracted with DCM. The solvent was removed under vacuum and the residue directly dissolved in THF (10 mL). TBAF (1.6 mL, 1.2 eq., 1.6 mmol, 1 mmol/mL) was added and the mixture was stirred at ambient
25 temperature for 20 minutes. The crude reaction mixture was quenched with saturated aq. NH₄Cl solution and EtOAc added. The layers were separated. The aq. phase was then extracted with EtOAc. The combined organic layers were combined, dried over Na₂SO₄ and the solvent

removed under vacuum. The residue was purified by chromatography gradient elution from DCM to 30% MeOH in DCM to yield Intermediate 19 (500 mg, 32% yield).

LCMS (Method 2, ES⁺) 1.34 min, 434 & 436 *m/z* (M+H)⁺.

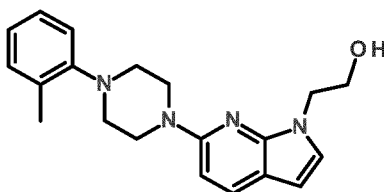
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INTERMEDIATE 20**2-(6-bromopyrrolo[2,3-b]pyridin-1-yl)ethoxy-tert-butyl-dimethyl-silane**

2-(6-bromopyrrolo[2,3-b]pyridin-1-yl)ethoxy-tert-butyl-dimethyl-silane was prepared following General Procedure 2 using 6-bromo-1H-pyrrolo[2,3-b]pyridine (2 g, 9.9 mmol) and (2-bromoethoxy)-tert-butyl-dimethylsilane (2.7 mL, 12 mmol) to afford intermediate 20 (3.13 g, 88% yield).

10

LCMS (Method 2, ES⁺) 1.78 min, 355 & 357 *m/z* (M+H)⁺.

INTERMEDIATE 21

15

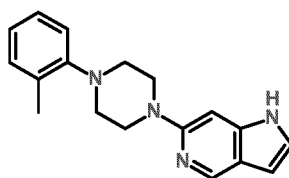
2-[6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethanol

Using general procedure 3, intermediate 1 (1.2 g, 6.8 mmol), intermediate 20 (2.7 g, 7.6 mmol) gave tert-butyl-dimethyl-[2-[6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethoxy]silane, which was then dissolved in THF (20 mL). TBAF (14 mL, 14 mmol) was then added and the reaction mixture stirred at room temperature for 5 days. The reaction mixture was concentrated under reduced pressure and loaded onto an SCX cartridge washing first with methanol then eluting with 2 M (approx.) ammonia in methanol. The ammonia in methanol solution was concentrated under reduced pressure and the residue purified by flash silica column chromatography to give the title compound (1.37 g, 60% yield).

20

LCMS (Method 2, ES⁺) 1.47 min, 337 *m/z* (M+H)⁺.

INTERMEDIATE 22



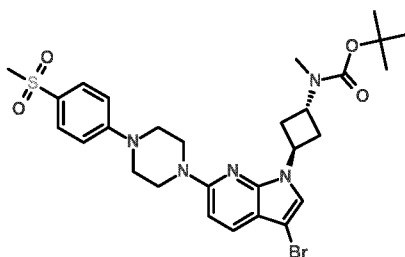
5

6-[4-(o-tolyl)piperazin-1-yl]-1H-pyrrolo[3,2-c]pyridine

Using general procedure 3, intermediate 9 (455 mg, 1.47 mmol) and intermediate 1 (236 mg, 1.33 mmol) gave triisopropyl-[6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[3,2-c]pyridin-1-yl]silane, which was dissolved in THF (5 mL). TBAF (4 mL, 4 mmol) was then added and the reaction mixture stirred at r.t. overnight. The reaction mixture was treated with an aqueous work up and the organic layer dried (Na₂SO₄) and concentrated under reduced pressure. The resulting residue was passed through an SCX cartridge washing first with methanol then eluting with approx. 2 M ammonia in methanol. The solution was concentrated under reduced pressure to give the title compound (46 mg, 12% yield over two steps).

15 LCMS (Method 2, ES⁺) 1.31 min, 293 *m/z* (M+H)⁺.

INTERMEDIATE 23

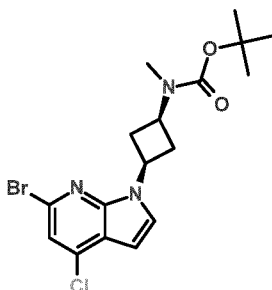


20 Trans-tert-butyl N-[3-[3-bromo-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]-N-methyl-carbamate

Intermediate 19 (500 mg, 1.15 mmol) and cis-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate (1.5 eq., 1.7 mmol) were reacted following General Procedure 9 and purified by flash column chromatography eluting from hexane to 70% EtOAc in hexane to give intermediate 23 (410 mg, 78% yield).

LCMS (Method 2, ES⁺) 1.73 min, 618 & 620 *m/z* (M+H)⁺.

INTERMEDIATE 24



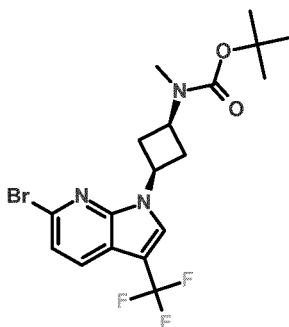
5 Cis-tert-butyl N-[3-(6-bromo-4-chloro-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate

6-Bromo-4-chloro-1H-pyrrolo[2,3-b]pyridine (250 mg, 1.08 mmol, 100 mass%) and trans-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate (1.5 eq., 1.62 mmol) were reacted following General Procedure 9 to yield Intermediate 24 (430 mg, 96% yield).

LCMS (Method 2, ES⁺) 1.84 min, 414 & 416 *m/z* (M+H)⁺.

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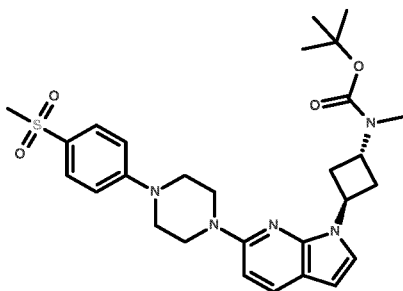
INTERMEDIATE 25



Cis-tert-butyl N-[3-[6-bromo-3-(trifluoromethyl)pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]-N-methyl-carbamate

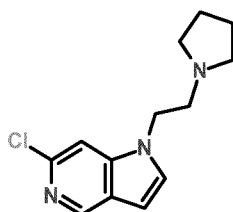
15 6-Bromo-3-(trifluoromethyl)-1H-pyrrolo[2,3-b]pyridine (100 mg, 0.38 mmol) and trans-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate (1.5 eq., 0.6 mmol) were reacted following General Procedure 9 to yield intermediate 25 (160 mg, 86% yield).

LCMS (Method 2, ES⁺) 1.84 min, 448 & 450 *m/z* (M+H)⁺.

INTERMEDIATE 26

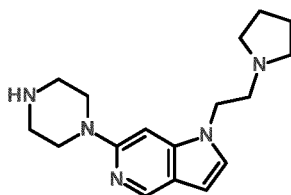
Trans-tert-butyl N-methyl-N-[3-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]carbamate

- 5 6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine (Intermediate 18, 650 mg, 1.8 mmol) and cis-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate (1.5 eq., 2.7 mmol) were reacted following the General Procedure 9. The reaction mixture was concentrated and the residue was directly purified by flash chromatography gradient elution from hexane to EtOAc to afford Intermediate 26 (610 mg, 62% yield).
- 10 LCMS (Method 2, ES⁺) 1.61 min, 640 *m/z* (M+H)⁺.

INTERMEDIATE 27

6-chloro-1-(2-pyrrolidin-1-ylethyl)pyrrolo[3,2-c]pyridine

- 15 6-Chloro-5-azaindole (750 mg, 4.8 mmol) and 1-(2-chloroethyl)pyrrolidine hydrochloride (1 g, 5.76 mmol) were reacted using general procedure 2 to give the title compound (860 mg, 71%).
- LCMS (Method 2, ES⁺) 1.06 min, 250 *m/z* (M+H)⁺.

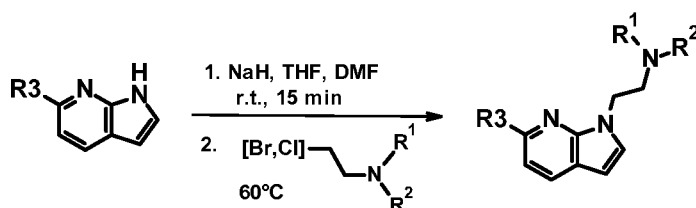
INTERMEDIATE 28

6-piperazin-1-yl-1-(2-pyrrolidin-1-ylethyl)pyrrolo[3,2-c]pyridine

- 5 Using general procedure 1 and intermediate 27 (250 mg, 1.00 mmol) the title compound was obtained (250 mg, 83%).

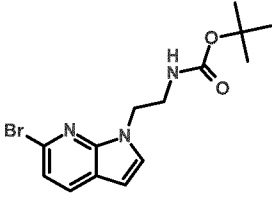
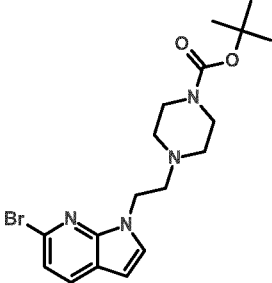
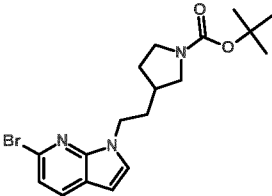
LCMS (Method 2, ES⁺) 0.94 min, 300 *m/z* (M+H)⁺.

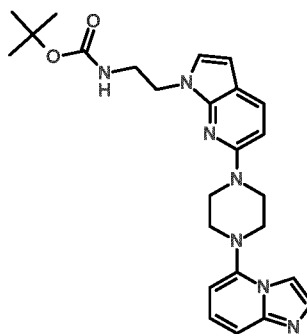
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INTERMEDIATE 29-32

- 15 Intermediates 29-32 can be synthesized from commercially available 6-bromo-1H-pyrrolo[2,3-b]pyridine and the appropriate alkyl halide using General Procedure 2. Intermediates 29-32 analysed by LCMS Method 2.

Interm. Number	Structure	Alkyl halide	Compound Name	LCMS (Method 2) RT (min)	<i>m/z</i> (M+H) ⁺
29		1-(2-Chloroethyl)-2-methyl-1H-imidazole hydrochloride	6-bromo-1-[2-(2-methylimidazol-1-yl)ethyl]pyrrolo[2,3-b]pyridine	1.07	305 & 307

30		N-Boc-2-chloroethylamine	tert-butyl N-[2-(6-bromopyrrolo[2,3-b]pyridin-1-yl)ethyl]carbamate	1.40	340 & 242
31		tert-butyl 4-(2-bromoethyl)piperazine-1-carboxylate	tert-butyl 4-[2-(6-bromopyrrolo[2,3-b]pyridin-1-yl)ethyl]piperazine-1-carboxylate	1.50	409 & 411
32		tert-butyl 3-(2-bromoethyl)pyrrolidine-1-carboxylate	tert-butyl 3-[2-(6-bromopyrrolo[2,3-b]pyridin-1-yl)ethyl]pyrrolidine-1-carboxylate	1.54	338 & 340 [M-tBu+H]

INTERMEDIATE 33

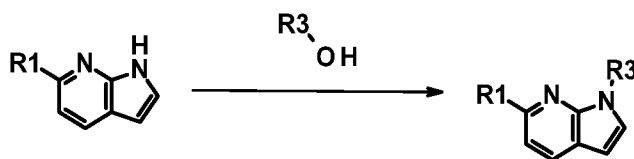
tert-butyl N-[2-[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]carbamate

5

General Procedure 3, using intermediate 30 (384 mg, 1.13 mmol) and intermediate 5 (240 mg, 1.18 mmol) gave the title compound (252 mg, 48%).

LCMS (Method 2, ES⁺) 1.41 min, 462 *m/z* (M+H)⁺.

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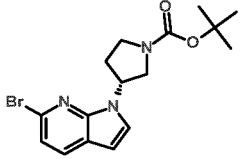
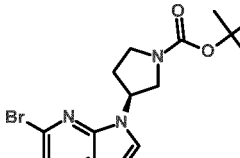
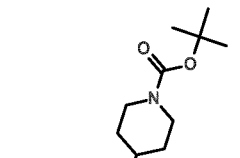
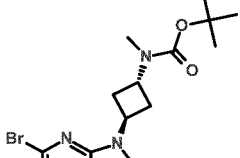
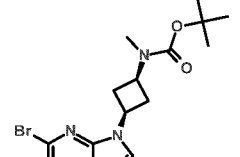
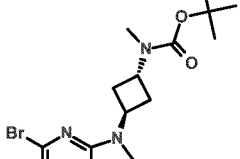
INTERMEDIATE 34-42

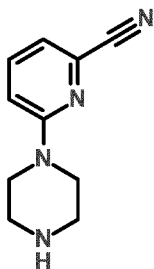
Intermediates 34-42 were synthesized according to General Procedure 9 from an appropriate heterocycle and alcohol tabulated below.

- 5 Intermediate 33 was purified by filtration through an SCX cartridge washing first with methanol then eluting with approx. 2 M ammonia in methanol. The ammonia in methanol solution was concentrated under reduced pressure to give the desired product.

Intermediates 34-42 were analysed by LCMS Method 2.

Intermediate	Structure	Pyrrolo-pyrimidine	Alcohol	Compound Name	LCMS RT (min)	Mass Ion
34		6-bromo-1H-pyrrolo[2,3-b]pyridine	<i>trans</i> -tert-butyl N-(3-hydroxycyclobutyl)-N-methylcarbamate	<i>cis</i> -tert-butyl N-[3-(6-bromopyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methylcarbamate	1.65	380 & 382
35		6-bromo-1H-pyrrolo[2,3-b]pyridine	<i>cis</i> -tert-butyl N-(3-hydroxycyclobutyl)-N-methylcarbamate	<i>trans</i> -tert-butyl N-[3-(6-bromopyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methylcarbamate	1.62	380 & 382
36		6-bromo-1H-pyrrolo[2,3-b]pyridine	1-methyl-3-pyrrolidinol	6-bromo-1-(1-methylpyrrolidin-3-yl)pyrrolo[2,3-b]pyridine	1.31	280 & 282

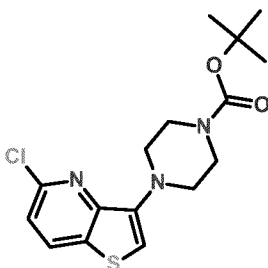
37		6-bromo-1H-pyrrolo[2,3-b]pyridine	tert-butyl (1S)-3-hydroxypyrrolidine-1-carboxylate	tert-butyl (3R)-3-(6-bromopyrrolo[2,3-b]pyridin-1-yl)pyrrolidine-1-carboxylate	1.57	310 & 312 [M-tBu+H] ⁺
38		6-bromo-1H-pyrrolo[2,3-b]pyridine	tert-butyl (1R)-3-hydroxypyrrolidine-1-carboxylate	tert-butyl (3S)-3-(6-bromopyrrolo[2,3-b]pyridin-1-yl)pyrrolidine-1-carboxylate	1.54	310 & 312 [M-tBu+H] ⁺
39		6-chloro-1H-pyrrolo[3,2-c]pyridine	tert-butyl 4-hydroxypiperidine-1-carboxylate	tert-butyl 4-(6-chloropyrrolo[3,2-c]pyridin-1-yl)piperidine-1-carboxylate	1.37	336
40		6-bromo-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile	<i>cis</i> -tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate	<i>trans</i> -tert-butyl N-[3-(6-bromo-3-cyano-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate	1.56	349 & 351 [M-tBu+H] ⁺
41		6-bromo-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile	<i>trans</i> -tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamates	<i>cis</i> -tert-butyl N-[3-(6-bromo-3-cyano-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate	1.59	405 & 407
42		6-bromo-5-fluoro-7-azaindol	<i>cis</i> -tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate	<i>trans</i> -tert-butyl N-[3-(6-bromo-5-fluoro-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate	1.62	342 & 344 [M-tBu+H] ⁺

INTERMEDIATE 43**6-Piperazin-1-ylpyridine-2-carbonitrile**

Intermediate 43 was prepared using General Procedure 1, from 6-bromo-2-pyridinecarbonitrile
5 (500 mg, 2.7 mmol) and tert-butyl piperazine-1-carboxylate (610 mg, 3.2 mmol), followed by
General Procedure 13 to give the title compound after reverse phase chromatography (120 mg,
23%)

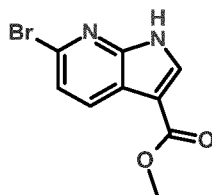
LCMS (Method 2, ES+) 0.51 min, 189 m/z (M+H)⁺.

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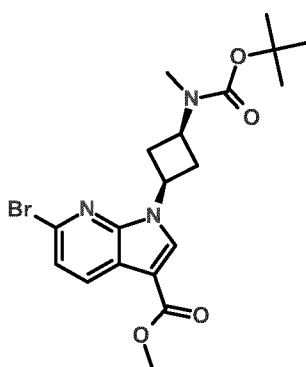
INTERMEDIATE 44**tert-butyl 4-(5-Chlorothieno[3,2-b]pyridin-3-yl)piperazine-1-carboxylate**

General Procedure 5, using 3-bromo-5-chlorothieno[3,2-B]pyridine (200 mg, 0.79 mmol) and 1-
15 boc-piperazine (180 mg, 0.95 mmol) at 80 °C gave the title compound (24 mg, 9%).

LCMS (Method 2, ES+) 1.53 min, 354 & 356 m/z (M+H)⁺.

INTERMEDIATE 45**Methyl 6-bromo-1H-pyrrolo[2,3-b]pyridine-3-carboxylate**

- 6-bromo-1H-pyrrolo[2,3-b]pyridine (1 g, 5.1 mmol) was dissolved in DCM (40 mL) and AlCl₃ (3.5 equiv., 17.8 mmol) was added at r.t. portion-wise. The mixture was stirred for 30 minutes before trichloroacetyl chloride (1 equiv., 5.1 mmol) was added drop-wise. The mixture was stirred at r.t. for 2 hours. H₂O and DCM were added and the layers were separated. The solvent was removed under vacuum. The solid was dissolved in MeOH (20 mL) and KOH (200 mg, 3.6 mmol) was added. The mixture was stirred at 60°C for 3 hours until complete consumption of the starting material. Then the reaction was cooled to r.t. and EtOAc and HCl (2 M) aq. solution was added. The layers were separated and the organic layer was dried over Na₂SO₄. The volatiles were removed under vacuum and the residue purified by flash chromatography with gradient elution from hexane to EtOAc, and then 10% MeOH in EtOAc to yield Intermediate 45 (420 mg, 24% yield).
- LCMS (Method 2, ES+) 1.01 min, 255 & 257 m/z.

INTERMEDIATE 46

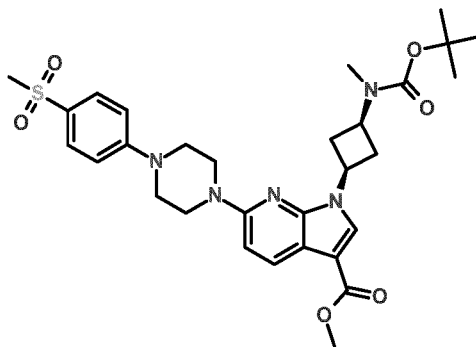
- cis-Methyl 6-bromo-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]pyrrolo[2,3-b]pyridine-3-carboxylate**

Intermediate 45 (400 mg, 1.6 mmol) was reacted with trans-tert-butyl-N-(trans-3-hydroxycyclobutyl)-N-methylcarbamate (1.5 equiv., 2.3 mmol) following the General Procedure

9. The product was purified by flash column chromatography gradient elution from hexane to 70% EtOAc in hexane to yield Intermediate 46 (550 mg, 80% yield).

LCMS (Method 2, ES⁺) 1.66 min, 438 & 440 m/z (M+H)⁺.

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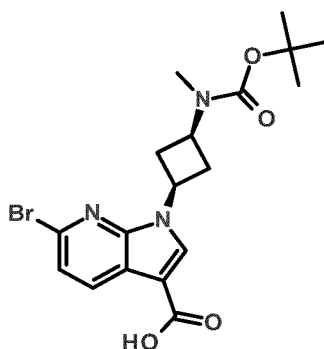
INTERMEDIATE 47

cis-Methyl 1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl] pyrrolo[2,3-b]pyridine-3-carboxylate

10 Intermediate 46 (315 mg, 0.7 mmol) and 1-[4-(4-methylsulfonyl)phenyl]piperazine were reacted following the General Procedure 3 at 60 °C. The mixture was cooled to r.t. and H₂O and EtOAc added. The layers were separated and the aq. phase was extracted with EtOAc. The combined organic layers were dried over Na₂SO₄ and the volatiles were removed under vacuum. The residue was purified by flash column chromatography using gradient elution from hexane to EtOAc and then EtOAc to 30% of MeOH in EtOAc to afford Intermediate 47 (140 mg, 19% yield) and Intermediate 48.

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LCMS (Method 2, ES⁺) 1.54 min, 598 m/z (M+H)⁺.

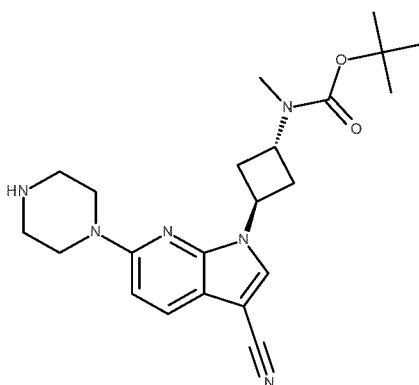
INTERMEDIATE 48

cis-6-bromo-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]pyrrolo[2,3-b]pyridine-3-carboxylic acid

Intermediate 48 was obtained (180 mg, 34% yield) as a by-product from the synthesis of Intermediate 47.

- 5 LCMS (Method 2, ES+) 1.14 min, 424 & 426 m/z

INTERMEDIATE 49



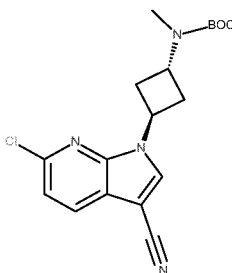
- 10 trans-tert-butyl N-[3-(3-cyano-6-piperazin-1-yl-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate

A solution of Intermediate 50 (3.4 g, 9.3 mmol) and piperazine (4.0 g, 46.0 mmol) was dissolved in a mixture of dimethyl sulfoxide (15 mL), 2-propanol (5 mL) and ethanol (3 mL). The mixture was heated at 120 °C overnight. After cooling to rt, the reaction mixture was diluted with diethyl ether (200 mL) and 50% saturated bicarbonate solution (200 mL). The organic layer was washed with water (100 mL) and brine (200 mL), dried (Na₂SO₄) and concentrated under reduced pressure to give an oil which solidified on standing to give the product as a yellow solid (3.4 g, 89%).

LCMS (Method 2, ES⁺) 1.23 min, 411 m/z (M+H)⁺

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INTERMEDIATE 50



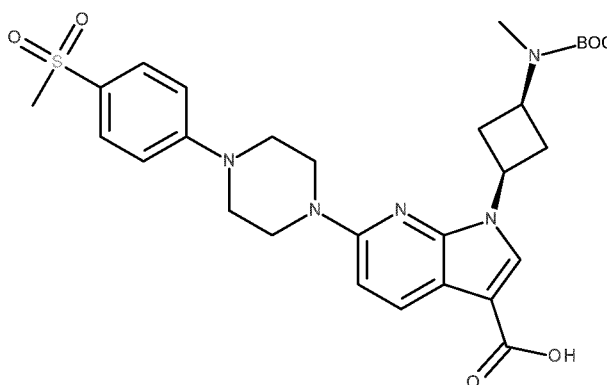
trans-tert-butyl N-[3-(6-chloro-3-cyano-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate

6-chloro-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile (2.0 g, 10.7 mmol) and cis-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate (2.6 g, 13.0 mmol) were used in General Procedure 9 to give the product (3.4 g, 9.3 mmol, 86%).

LCMS (Method 2, ES⁺) 1.46 min, 305 & 307 *m/z* (M⁺Bu+H)⁺

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INTERMEDIATE 51



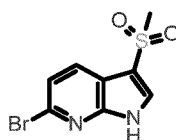
10 trans-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carboxylic acid

General procedure 3 with Intermediate 46 and 1-[4-(methylsulfonyl)phenyl]piperazine gave the product in 15% yield.

LCMS (Method 2, ES⁺) 1.19 min, 584 *m/z* (M+H)⁺

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INTERMEDIATE 52



6-bromo-3-methylsulfonyl-1H-pyrrolo[2,3-b]pyridine

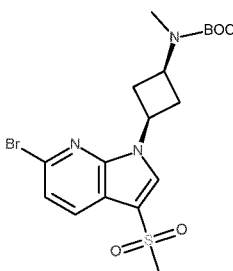
6-Bromo-1H-pyrrolo[2,3-b]pyridine (1 g, 5.1 mmol, 1 equiv.) was dissolved in THF (0.05 M, 100 mL), and cooled at -10 °C before potassium *tert*-butoxide (626 mg, 1.1 equiv., 5.6 mmol) was added. The reaction mixture was stirred at that temperature for 30 min before triethylborane (5.6 mL, 1.1 equiv., 5.6 mmol, 1 mol/L) was added. The reaction was stirred at that temperature for an additional 30 minutes. Then, methanesulfonyl chloride (0.45 mL, 1.2 equiv., 5.8 mmol) was added dropwise at -10°C and was stirred over the weekend at room temperature. The reaction was quenched by addition of NH₄Cl aq. sat solution and EtOAc. The layers were separated, and the aqueous phase was extracted again with EtOAc. The combined organic layers were dried

25

over Na₂SO₄. The volatiles were removed under vacuum and the residue was purified from hexane to 1:1 hexane:EtOAc to give Intermediate 52 as a white solid (180 mg, 13% yield).

LCMS (Method 2, ES⁺) 0.86 min, 275 & 277 *m/z* (M+H)⁺

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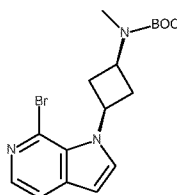
INTERMEDIATE 53

cis-tert-butyl N-[3-(6-bromo-3-methylsulfonyl-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate

- 10 Intermediate 52 (180 mg, 0.7 mmol) was reacted with trans-tert-butyl-N-(trans-3-hydroxycyclobutyl)-N-carbamate (208 mg, 1.5 equiv., 1 mmol) following General Procedure 9 to give Intermediate 53 as a yellowish oil (220 mg, 69% yield).

LCMS (Method 2, ES⁺) 1.50 min, 458 & 460 *m/z* (M+H)⁺.

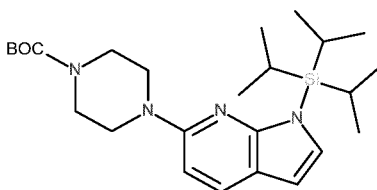
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INTERMEDIATE 54

cis-tert-butyl N-[3-(7-bromopyrrolo[2,3-c]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate

- 20 7-Bromo-1H-pyrrolo[2,3-c]pyridine (200 mg, 1 mmol) and trans-tert-butyl-N-(trans-3-hydroxycyclobutyl)-N-methylcarbamate (306 mg, 1.5 equiv., 1.45 mmol) were reacted following General Procedure 9 to give Intermediate 54 as a yellow syrup (330 mg, 90% yield).

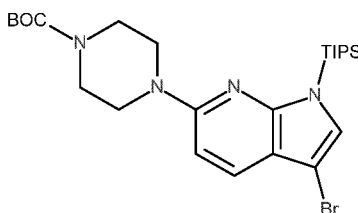
LCMS (Method 2, ES⁺) 1.45 min, 380 & 382 *m/z* (M+H)⁺.

INTERMEDIATE 55tert-butyl 4-(1-triisopropylsilylpyrrolo[2,3-b]pyridin-6-yl)piperazine-1-carboxylate

5 Intermediate 8 (8.5 g, 24 mmol), 1-boc-piperazine (1.8 equiv., 43 mmol), sodium tert-butoxide (3 equiv., 72 mmol) and (2-dicyclohexylphosphino-2',6'-diisopropoxy-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)]palladium(II) methanesulfonate (0.1 equiv., 2.4 mmol) were dissolved in degassed 1,4-dioxane (0.5 M). The mixture was heated to 80°C overnight and then cooled down to ambient temperature. EtOAc and H₂O were added and the layers were separated. The aqueous phase
10 was then further extracted with EtOAc. The combined organic layers were dried over Na₂SO₄ and the solvent was removed under vacuum. The residue was purified by column chromatography from DCM to 20% MeOH in DCM to afford Intermediate 55 as yellowish solid (11 g, 94% yield).

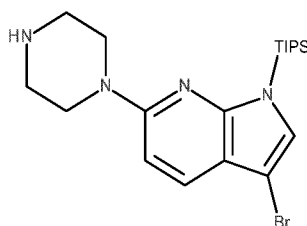
LCMS (Method 2, ES⁺) 2.12 min, 459 *m/z* (M+H)⁺.

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INTERMEDIATE 56tert-butyl 4-(3-bromo-1-triisopropylsilylpyrrolo[2,3-b]pyridin-6-yl)piperazine-1-carboxylate

Intermediate 55 (4 g, 8.7 mmol) was dissolved in DCM (30 mL) and cooled to 0 °C. NBS (1.1 g, 0.75 equiv.) was added portionwise over 30 minutes. The reaction mixture was stirred in the presence of the cooling bath for an additional 10 mins before it was quenched with saturated bicarb (20 mL) and diluted with DCM (20 mL). The aqueous layer was extracted with DCM, the combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified from hexane to EtOAc affording a syrup (4.1 g, 87% yield).

25 LCMS (Method 2, ES⁺) 2.27 min, 537 & 539 *m/z* (M+H)⁺.

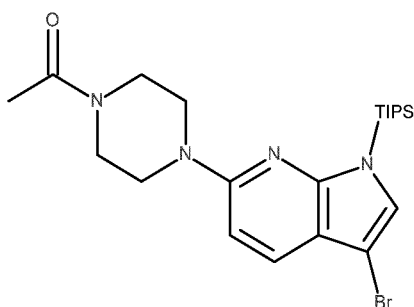
INTERMEDIATE 57

(3-bromo-6-piperazin-1-yl-pyrrolo[2,3-b]pyridin-1-yl)-triisopropyl-silane

- 5 Intermediate 56 (800 mg, 1.5 mmol) was reacted following the General Procedure 13 to give Intermediate 57 (420 mg, 65% yield).

LCMS (Method 2, ES⁺) 1.63 min, 437 & 439 *m/z* (M+H)⁺.

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INTERMEDIATE 58

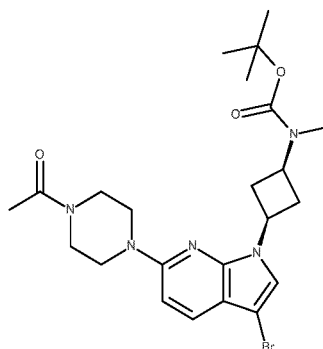
1-[4-(3-bromo-1-triisopropylsilyl-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]ethanone

- 15 Intermediate 57 (300 mg, 0.7 mmol) were reacted with acetic acid (1.5 equiv., 1 mmol) analogously to General Procedure 6. H₂O was added and the layers were separated. The aq. phase was washed again with DCM. The combined organic layers were dried under vacuum and the residue was purified by flash chromatography from hexane to EtOAc to give Intermediate 58 as a white solid (220 mg, 67% yield)

LCMS (Method 2, ES⁺) 1.88 min, 479 & 481 *m/z* (M+H)⁺.

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INTERMEDIATE 59

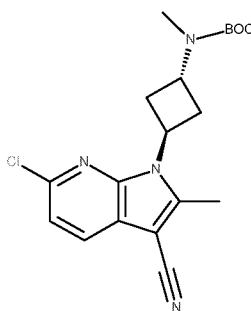


trans-tert-butyl N-[3-[6-(4-acetylpiperazin-1-yl)-3-bromo-pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]-N-methyl-carbamate

Intermediate 58 (200 mg, 0.42 mmol) was dissolved in THF (0.1 M) and TBAF (1.3 equiv., 0.5 mmol, 1 mmol/mL in THF) was added. The mixture was stirred at ambient temperature for 30 minutes until starting material was consumed. EtOAc and H₂O were added to the reaction mixture and the layers were separated. The organic phase was dried over Na₂SO₄ and the solvent was removed under vacuum. The residue was then reacted with tert-butyl-N-(3-hydroxycyclobutyl)-N-methyl-carbamate following General Procedure 9 to give Intermediate 59 as a brownish solid (100 mg, 47% yield over two steps).

LCMS (Method 2, ES⁺) 1.54 min, 506 & 508 *m/z* (M+H)⁺.

INTERMEDIATE 60

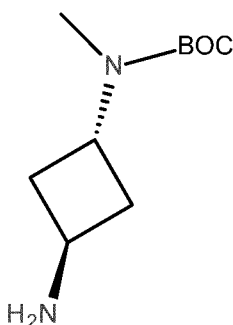


trans-tert-butyl N-[3-(6-chloro-3-cyano-2-methyl-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate

6-chloro-2-methyl-1H-pyrrolo[2,3-b]pyridine was reacted with cis-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate using General Procedure 9. The resulting trans-tert-butyl N-[3-(6-chloro-2-methyl-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate was dissolved in 1:1 MeCN/DMF, cooled to 0 °C, then chlorosulphonyl isocyanate (5 equiv) was added. The mixture was stirred at 40 °C for 2 hours. After cooling to rt, the mixture was diluted with water, extracted with EtOAc (2 x), washed with brine, dried (Na₂SO₄) and concentrated in vacuo. The residue was then purified by column chromatography (10% EtOAc/hexane) to give the product (35% over 2 steps).

LCMS (Method 7, ES⁺) 2.34 min, 319 & 321 *m/z* (M-^tBu+H)⁺

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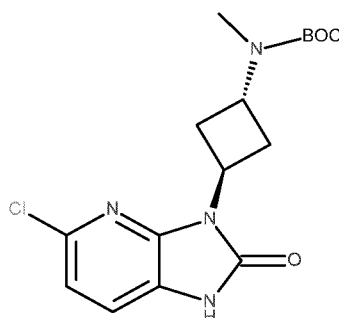
INTERMEDIATE 61**trans-tert-butyl N-(3-aminocyclobutyl)-N-methyl-carbamate**

To a stirred solution of cis-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate (3.00 g, 14.9 mmol) in DCM (50 mL) was added triethylamine (5.02 mL, 44.7 mmol) and methanesulfonyl chloride (1.50 mL, 19.4 mmol) at 0°C, and maintained for 30 min for 0°C. After complete addition, the resulting reaction mixture was stirred at rt for 1 h. After complete consumption of starting material, reaction mixture was quenched by ice cold water (100 mL). Aqueous layer extracted with DCM (100 mL x 2). The collected organic layer was dried over sodium sulphate and evaporated under reduced pressure to give crude cis-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl] methanesulfonate (crude weight: 4.2 g).

To a stirred solution of cis-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl] methanesulfonate (4.20 g, 14.2 mmol) in DMF (30 mL), was added NaN₃ (4.61 g, 70.9 mmol) at 0 °C. After complete addition, the resulting reaction mixture was stirred at 70 °C for 16 h. After complete consumption of starting material, the reaction mixture was quenched by ice cold water (100 mL) and extracted with ethyl acetate (100 mL x 2). The organic layer washed with saturated sodium bicarbonate solution (100 mL), and brine (100 mL), the organic layer was collected and dried over sodium sulphate, then filtered and evaporated under reduced pressure to get crude trans-tert-butyl N-(3-azidocyclobutyl)-N-methyl-carbamate (crude weight: 4.3 g)

To a stirred solution of trans-tert-butyl N-(3-azidocyclobutyl)-N-methyl-carbamate (4.30 g, 17.6 mmol) in methanolic ammonia (30 mL) was added 20% palladium on carbon (1 g). The reaction mixture was stirred under hydrogen atmosphere for 36 hour at room temperature. After complete consumption of starting material, the reaction mixture was filtered on celite and washed with methanol (100 mL). The filtrate was concentrated under reduced pressure and purified by column chromatography (15% methanol in DCM) to obtain the product (2.0 g, 9.57 mmol, 64 % over 3 steps).

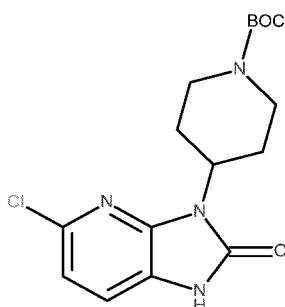
LCMS (Method 7, ES⁺) 1.36 min, 201 *m/z* (M+H)⁺

INTERMEDIATE 62trans-tert-butyl N-[3-(5-chloro-2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)cyclobutyl]-N-methyl-carbamate

5 To a stirred solution of 2,6-dichloro-3-nitro-pyridine (1.00 g, 5.18 mmol) in ethanol (20 mL) was added Intermediate 61 (1.30 g, 6.22 mmol) followed by sodium carbonate (1.63 g, 15.5 mmol) at rt. The mixture was stirred at rt for 16 hours, then diluted with water (50 mL) and extracted with EtOAc (50 mL x 2). The collected organic layer was washed with brine (50 mL), dried (Na₂SO₄) and concentrated under reduced pressure. The crude compound was purified by column chromatography (1:1 EtOAc/hexane) to give trans-tert-butyl N-[3-[(6-chloro-3-nitro-2-pyridyl)amino]cyclobutyl]-N-methyl-carbamate (1.30 g, 3.61 mmol, 70%).

trans-tert-butyl N-[3-[(6-chloro-3-nitro-2-pyridyl)amino]cyclobutyl]-N-methyl-carbamate (1.30 g, 3.61 mmol) was submitted to General Procedure 15, followed by General Procedure 16 to give the product trans-tert-butyl N-[3-(5-chloro-2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)cyclobutyl]-N-methyl-carbamate (0.65 g, 1.84 mmol, 51% over two steps).

LCMS (Method 8, ES⁺) 1.87 min, 297 & 299 *m/z* (M^{-t}Bu+H)⁺

INTERMEDIATE 63tert-butyl 4-(5-chloro-2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)piperidine-1-carboxylate

20 To a stirred solution of 2,6-dichloro-3-nitro-pyridine (5.00 g, 25.9 mmol) in ethanol (50 mL) was added tert-butyl 4-aminopiperidine-1-carboxylate (7.78 g, 38.9 mmol) followed by sodium carbonate (8.16 g, 77.7 mmol) at rt. The mixture was stirred at rt for 16 hours then diluted with

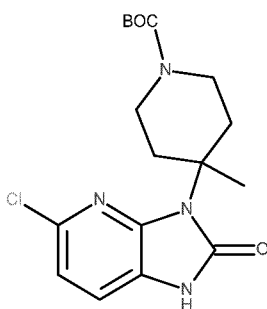
ethyl acetate (300 mL) and washed with water (300 mL x 2). The organic layer was separated, washed with brine (500 mL), dried over sodium sulfate and concentrated under reduced pressure. The crude compound was purified by column chromatography (70% EtOAc in hexane) to give tert-butyl 4-[(6-chloro-3-nitro-2-pyridyl)amino]piperidine-1-carboxylate (6.50 g, 18.2 mmol, 70%).

5 tert-butyl 4-[(6-chloro-3-nitro-2-pyridyl)amino]piperidine-1-carboxylate (4.0 g, 11.2 mmol) was submitted to General Procedure 15, followed by General Procedure 16 to give the product tert-butyl 4-(5-chloro-2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)piperidine-1-carboxylate (1.0 g, 2.71 mmol, 24% over two steps).

LCMS (Method 7, ES⁺) 1.85 min, 297 & 299 [55%] *m/z* (M-^tBu+H)⁺, 253 & 255 [100%] *m/z* (M-^tBuCO₂+H)⁺

10

INTERMEDIATE 64



tert-butyl 4-(5-chloro-2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)-4-methyl-piperidine-1-carboxylate

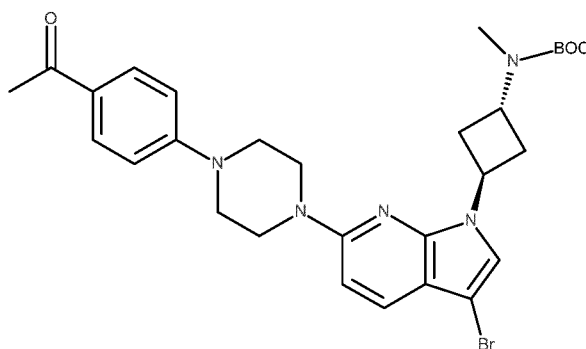
15 Sodium carbonate (3.26 g, 31.1 mmol) and tert-butyl 4-amino-4-methyl-piperidine-1-carboxylate (2.67 g, 12.4 mmol) were added to a stirred solution of 2,6-dichloro-3-nitro-pyridine (2 g, 10.4 mmol) in ethanol (35 mL) at rt under argon. The resulting reaction mixture was heated at 70 °C for 24 h. The reaction mixture was diluted with ethyl acetate (100 mL) and washed with water (100 mL X 2). The organic layer was separated, washed with brine (100 mL), dried over sodium

20 sulfate and concentrated under reduced pressure. The crude material was purified by column chromatography using 50% ethyl acetate in hexane to give tert-butyl 4-[(6-chloro-3-nitro-2-pyridyl)amino]-4-methyl-piperidine-1-carboxylate (2.50 g, 5.76 mmol, 56%).

tert-butyl 4-[(6-chloro-3-nitro-2-pyridyl)amino]-4-methyl-piperidine-1-carboxylate (2.50 g, 5.76 mmol) was submitted to General Procedure 15 then General Procedure 16 to give tert-butyl 4-(5-chloro-2-oxo-1H-imidazo[4,5-b]pyridin-3-yl)-4-methyl-piperidine-1-carboxylate (0.70 g, 1.84

25 mmol, 32% over 2 steps).

LCMS (Method 7, ES⁺) 2.07 min, 311 & 313 *m/z* (M-^tBu+H)⁺

INTERMEDIATE 65

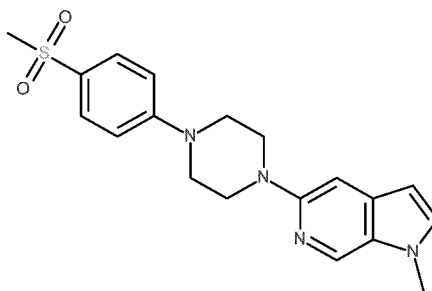
5 trans-tert-butyl N-[3-[6-[4-(4-acetylphenyl)piperazin-1-yl]-3-bromo-pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]-N-methyl-carbamate

3-Bromo-6-chloro-7-azaindole (4.0 g, 16.8 mmol) and cis-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate (4.1 g, 20.1 mmol) were reacted according to General Procedure 9 to give trans-tert-butyl N-[3-(3-bromo-6-chloro-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate (7.6 g, quant).

10 tert-butyl N-[3-(3-bromo-6-chloro-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate (3.0 g, 7.2 mmol) and 1-(4-acetylphenyl)piperazine (7.4 g, 36 mmol) were reacted according to General Procedure 14 to give 0.6 g product (14%).

LCMS (Method 2, ES⁺) 1.52 min, 582 & 584 m/z (M+H)⁺.

15

INTERMEDIATE 66

20 1-methyl-5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-c]pyridine

A solution of 5-bromo-1h-pyrrolo[2,3-c]pyridine (2.5 g, 13 mmol) in tetrahydrofuran (25 mL) was degassed (3 x evacuate for 5 minutes then backfill with N₂) then cooled with an ice/brine bath. sodium hydride (760 mg, 19 mmol) was then added in three portions and the mixture stirred for 30 minutes. Iodomethane (1.04 mL, 16.5 mmol) was then added, the mixture stirred for 5 minutes then removed from the ice bath and allowed to warm to rt. After 1 hour, the reaction was quenched

with water (30 ml) and the product was extracted with EtOAc (2 x 30 ml). The combined organics were washed with brine (20 ml), dried (Na₂SO₄) and concentrated in vacuo. The product was then purified by column chromatography to give 5-bromo-1-methyl-1h-pyrrolo[2,3-c]pyridine (2.5 g, 11.3 mmol, 89%) as an orange oil which crystallised on standing.

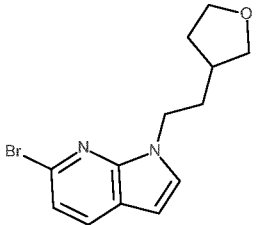
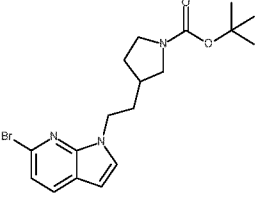
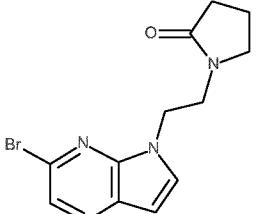
- 5 5-Bromo-1-methyl-1h-pyrrolo[2,3-c]pyridine (1.0 g, 4.5 mmol) was reacted with 1-[4-(methylsulfonyl)phenyl]piperazine (1.2 g, 5.0 mmol) according to General Procedure 5 to give the product (1.3 g, 3.6 mmol, 80%).

LCMS (Method 2, ES⁺) 1.12 min, 371 m/z (M+H)⁺.

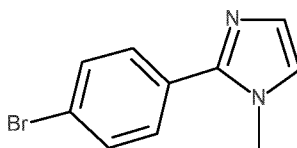
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INTERMEDIATES 67-69

Intermediates 67-69 can be synthesised from commercially available 6-bromo-1H-pyrrolo[2,3-b]pyridine and the appropriate alkyl halide using General Procedure 2

Interm. Number	Structure	Alkyl halide	Compound Name	LCMS (Method 2) RT (min)	m/z (M+H) ⁺
67		3-(2-bromoethyl)tetrahydrofuran	6-bromo-1-(2-(2-bromoethyl)tetrahydrofuran-3-ylethyl)pyrrolo[2,3-b]pyridine	1.29	295 & 297
68		tert-butyl 3-(2-bromoethyl)pyrrolidine-1-carboxylate	tert-butyl 3-[2-(6-bromopyrrolo[2,3-b]pyridin-1-yl)ethyl]pyrrolidine-1-carboxylate	1.54	338 & 340
69		1-(2-bromoethyl)pyrrolidin-2-one	1-[2-(6-bromopyrrolo[2,3-b]pyridin-1-yl)ethyl]pyrrolidin-2-one	1.07	308 & 310

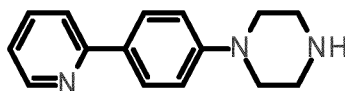
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INTERMEDIATE 70**2-(4-bromophenyl)-1-methyl-imidazole**

2-(4-Bromo-phenyl)-1H-imidazole (215 mg, 0.94 mmol) was dissolved in a mixture of tetrahydrofuran (5 mL) and N,N-dimethylformamide (1 mL). The solution was cooled to 0 °C and sodium hydride (45 mg, 1.12 mmol, 60 mass%) added. After approx. 5 mins iodomethane (0.1 mL, 2 mmol) was added and the reaction mixture (suspension) stirred at RT for approx. 3 hours. The suspension was cooled to 0 °C and water added. The clear solution was stirred in the presence of the cooling bath for 1 h then diluted with 50% saturated ammonium chloride (20 mL) and diethyl ether (20 mL). The organic layer was washed with water (2 x 20 mL), dried (Na₂SO₄) and concentrated under reduced pressure to give the title intermediate (215 mg, 96%).
LCMS (Method 2, ES⁺) 1.02 min, 239 *m/z* (M+H)⁺.

INTERMEDIATE 71

15

**1-[4-(2-pyridyl)phenyl]piperazine**

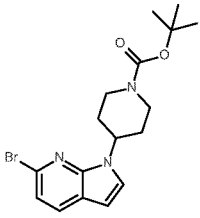
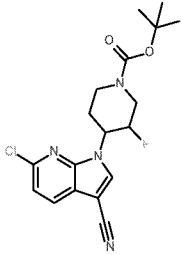
2-(4-Bromophenyl)pyridine (529 mg, 2.15 mmol) and (S)-4-N-boc-2-methylpiperazine (400 mg, 2.15 mmol) were used in general procedure 3 to afford tert-butyl 4-[4-(2-pyridyl)phenyl]piperazine-1-carboxylate (736 mg, quantitative). tert-Butyl 4-[4-(2-pyridyl)phenyl]piperazine-1-carboxylate (185 mg, 0.54 mmol) was then used in procedure 13 to afford the title intermediate (139 mg, quantitative)

LCMS (Method 2, ES⁺) 0.84 min, 240 *m/z* (M+H)⁺.

25

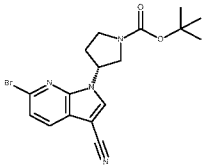
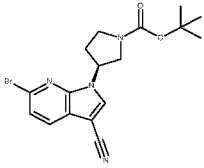
INTERMEDIATES 72-73

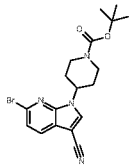
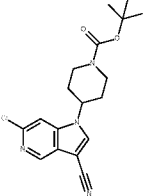
Intermediates 72-73 were synthesized according to General Procedure 9 from an appropriate heterocycle and alcohol tabulated below and analysed by LCMS Method 5.

Intermediate	Structure	SM Name	SM Intermediate number	Compound Name	LCMS RT (min)	Mass Ion
72		6-bromo-1H-pyrrolo[2,3-b]pyridine	tert-butyl 4-hydroxypiperidine-1-carboxylate	tert-butyl 4-(6-bromo-1H-pyrrolo[2,3-b]pyridin-1-yl)piperidine-1-carboxylate	2.13	324/326
73		6-Chloro-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile	tert-butyl 3-fluoro-4-hydroxy-piperidine-1-carboxylate	tert-butyl 4-(6-chloro-3-cyano-pyrrolo[2,3-b]pyridin-1-yl)-3-fluoro-piperidine-1-carboxylate	2.01/2.04 (2 diastereoisomers)	323/325

INTERMEDIATES 74-77

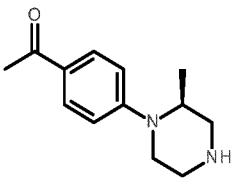
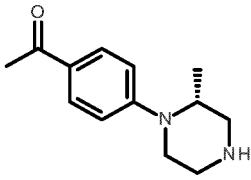
Intermediates 74-77 were prepared according to General Procedure 19 and LCMS method 5. Except for intermediate 76 which was analyzed using LCMS method 10.

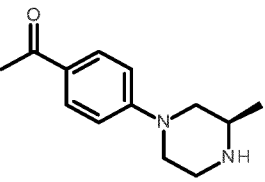
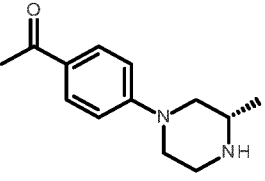
Intermediate	Structure	SM Name	SM Intermediate number	Compound Name	LCMS RT (min)	Mass Ion
74		tert-Butyl (3R)-3-(6-bromo-1H-pyrrolo[2,3-b]pyridin-1-yl)pyrrolidine-1-carboxylate	37	tert-Butyl (3R)-3-(6-bromo-3-cyano-1H-pyrrolo[2,3-b]pyridin-1-yl)pyrrolidine-1-carboxylate	2.03	335/337
75		tert-Butyl (3S)-3-(6-bromo-1H-pyrrolo[2,3-b]pyridin-1-yl)pyrrolidine-1-carboxylate	38	tert-Butyl (3S)-3-(6-bromo-3-cyano-1H-pyrrolo[2,3-b]pyridin-1-yl)pyrrolidine-1-carboxylate	2.03	335/337

76		tert-butyl 4-(6-bromo-1H-pyrrolo[2,3-b]pyridin-1-yl)piperidine-1-carboxylate	72	tert-Butyl (3R)-3-{6-bromo-3-cyano-1H-pyrrolo[2,3-b]pyridin-1-yl}piperidine-1-carboxylate	1.33	349/351
77		tert-butyl 4-(6-chloro-3-cyano-pyrrolo[3,2-c]pyridin-1-yl)piperidine-1-carboxylate	39	tert-butyl 4-(6-chloro-3-cyano-pyrrolo[3,2-c]pyridin-1-yl)piperidine-1-carboxylate	1.92	361/363

INTERMEDIATES 78-81

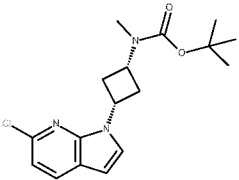
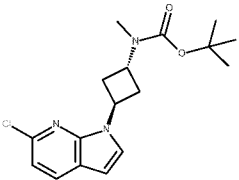
Intermediates 78-81 were prepared via general procedure 14 followed by general procedure 13, from 1-(4-fluorophenyl)ethanone and the appropriate N-Boc piperazine. The intermediates were analysed by LCMS method 6.

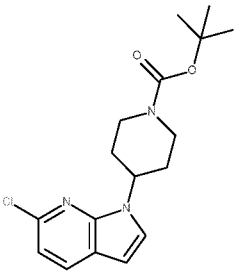
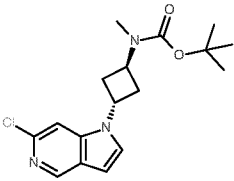
Intermediate	Structure	Piperazine	Compound Name	LCMS RT (min)	Mass ion
78		tert-butyl (3S)-3-methylpiperazine-1-carboxylate	1-[4-[(2S)-2-methylpiperazin-1-yl]phenyl]ethanone	1.50	219
79		tert-butyl (3R)-3-methylpiperazine-1-carboxylate	1-[4-[(2R)-2-methylpiperazin-1-yl]phenyl]ethanone	1.49	219

80		tert-butyl (2R)-2-methylpiperazine-1-carboxylate	1-[4-[(3R)-3-methylpiperazin-1-yl]phenyl]ethanone	1.47	219
81		tert-butyl (2S)-2-methylpiperazine-1-carboxylate	1-[4-[(3S)-3-methylpiperazin-1-yl]phenyl]ethanone	1.47	219

INTERMEDIATES 82-85

Intermediates 82-85 were synthesized from 6-Chloro-1H-pyrrolo[2,3-b]pyridine, according to General Procedure 9 from an appropriate heterocycle and alcohol tabulated below and analysed by LCMS Method 5 except for intermediate 85 which was analysed by LCMS Method 12

Intermediate	Structure	Secondary alcohol coupling partner	Compound Name	LCMS RT (min)	Mass Ion
82		tert-butyl N-methyl-N-[(1r,3r)-3-hydroxycyclobutyl]carbamate	tert-Butyl N-methyl-N-[(1s,3s)-3-{6-chloro-1H-pyrrolo[2,3-b]pyridin-1-yl}cyclobutyl]carbamate	2.13	336/338
83		tert-butyl N-methyl-N-[(1s,3s)-3-hydroxycyclobutyl]carbamate	tert-Butyl N-methyl-N-[(1r,3r)-3-{6-chloro-1H-pyrrolo[2,3-b]pyridin-1-yl}cyclobutyl]carbamate	2.11	280/282 [M-tBu+H] ⁺

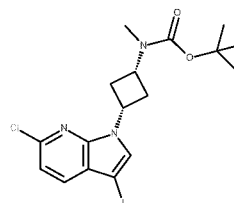
84		tert-butyl 4-hydroxypiperidine-1-carboxylate	tert-butyl 4-{6-chloro-1H-pyrrolo[2,3-b]pyridin-1-yl}piperidine-1-carboxylate	2.10	280/282 [M-tBu+H] ⁺
85		tert-butyl N-methyl-N-[(1s,3s)-3-hydroxycyclobutyl]carbamate	tert-butyl N-[(1r,3r)-3-(6-chloropyrrolo[3,2-c]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate	1.21	336/338

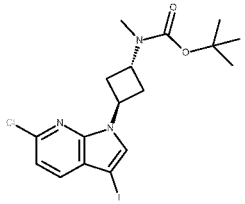
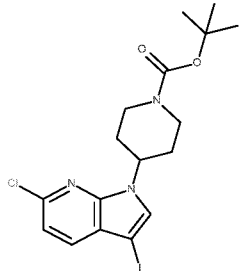
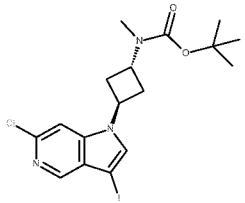
INTERMEDIATES 86-89

5 Intermediates 86-89 were prepared from the appropriate aza-indole according to general procedures 20.

Intermediates 86 & 87 were analysed using LCMS method 5

Intermediates 88 & 89 were analysed using LCMS method 10

Intermediate	Structure	Aza-indole	Compound Name	LCMS RT (min)	Mass Ion
86		82	tert-Butyl N-methyl-N-[(1s,3s)-3-{6-chloro-3-iodo-1H-pyrrolo[2,3-b]pyridin-1-yl}cyclobutyl]carbamate	2.28	462/464

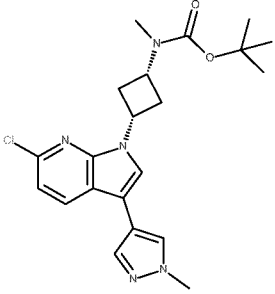
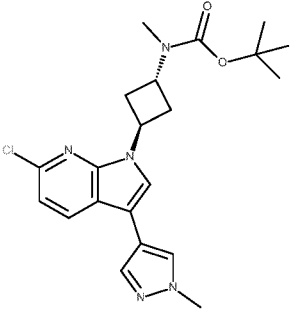
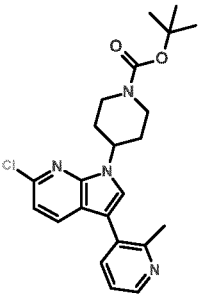
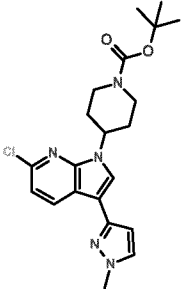
87		83	tert-Butyl N-methyl-N-[(1r,3r)-3-(6-chloro-3-iodo-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]carbamate	2.26	406/408
88		84	tert-butyl 4-(6-chloro-3-iodo-pyrrolo[2,3-b]pyridin-1-yl)piperidine-1-carboxylate	1.48	406/408
89		85	tert-butyl N-[(1r,3r)-3-(6-chloro-3-iodo-pyrrolo[3,2-c]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate	1.34	462/464

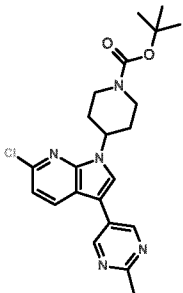
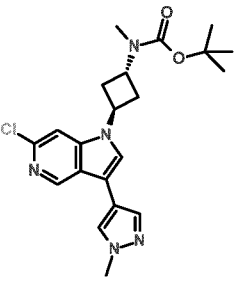
INTERMEDIATES 90-95

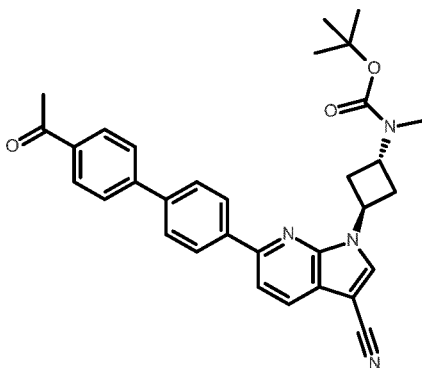
Intermediates 90-95 were prepared from the corresponding iodo aryl intermeidate and commercial boronic ester / acid according to general procedures 21.

Intermediates 90 & 93-95 were analysed by LCMS method 10.

Intermediates 91-92 were analysed by LCMS method 5.

Intermediate	Structure	Iodo aryl intermediate	Boronic acid / ester	Compound Name	LCMS RT (min)	Mass Ion
90		86	(1-methylpyrazol-4-yl)boronic acid	tert-Butyl N-methyl-N-[(1s,3s)-3-[6-chloro-3-(1-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]carbamate	1.34	416/418
91		87	1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole	tert-Butyl N-methyl-N-[(1r,3r)-3-[6-chloro-3-(1-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]carbamate	2.05	360/362 [M-tBu+H] ⁺
92		88	(2-methylpyridin-3-yl)boronic acid	tert-butyl 4-[6-chloro-3-(2-methyl-3-pyridyl)pyrrolo[2,3-b]pyridin-1-yl]piperidine-1-carboxylate	1.92	427/429
93		88	1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole	tert-butyl 4-[6-chloro-3-(1-methylpyrazol-3-yl)pyrrolo[2,3-b]pyridin-1-yl]piperidine-1-carboxylate	1.34	416/418

94		88	2-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidine	tert-butyl 4-[6-chloro-3-(2-methylpyrimidin-5-yl)pyrrolo[2,3-b]pyridin-1-yl]piperidine-1-carboxylate	1.30	428/430
95		89	1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole	tert-butyl N-[(1r,3r)-3-[6-chloro-3-(1-methylpyrazol-4-yl)pyrrolo[3,2-c]pyridin-1-yl]cyclobutyl]-N-methyl-carbamate	1.27	416/418

INTERMEDIATE 96

5

tert-butyl N-methyl-N-[(1r,3r)-3-(6-{4'-acetyl-[1,1'-biphenyl]-4-yl}-3-cyano-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]carbamate

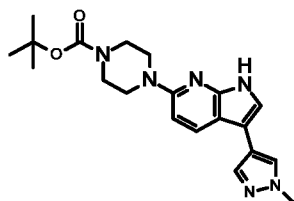
The mixture of tert-butyl N-[3-(6-chloro-3-cyano-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate (Intermediate 50) (84 mg, 0.23 mmol), [4-(4-acetylphenyl)phenyl]boronic acid (50.0 mg, 0.21 mmol) and disodium;carbonate (45 mg, 0.42 mmol) in 1,4-dioxane (3 mL) and was degassed by flushing with N₂ and then 1,1'-bis(diphenylphosphino)ferrocene palladium(II)chloride dichloromethane complex (17.4 mg, 0.02 mmol) was added.. The reaction mixture was stirred at 100 °C overnight and then allowed to cool to RT, diluted with DCM (5 mL) and filtered through

10

celite. The solids were washed with DCM (2 x 5 mL) and the combined filtrates were concentrated to dryness under vacuum. The residue obtained was purified by FCC (wet loaded in DCM to Biotage SNAP Ultra 10g cartridge, eluting 5% to 49% EtOAc in heptane) to yield 120 mg (84%) of the title compound as an off-white solid.

5 LCMS (Method 10, ES+) 1.49 min, 521 m/z $[M+H]^+$

INTERMEDIATE 97

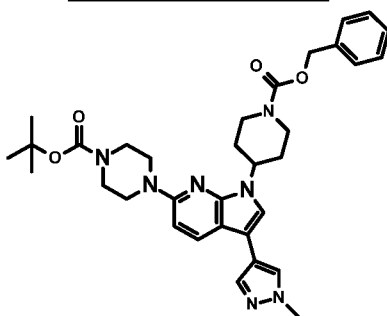


10 tert-butyl 4-[3-(1-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-6-yl]piperazine-1-carboxylate

A mixture of tert-butyl 4-[3-bromo-1-[tris(propan-2-yl)silyl]-1H-pyrrolo[2,3-b]pyridin-6-yl]piperazine-1-carboxylate (2.2 g, 4.09 mmol), intermediate 56 (936.59 mg, 4.5 mmol) (and 2M sodium carbonate (2M aq) (6.14 mL) in dioxane (12 mL) was degassed by N₂ bubbling for 10 min then Tetrakis(triphenylphosphine)palladium(0) (472. mg, 0.41 mmol) was added and reaction was heated at 100°C for 16h. The reaction mixture was diluted in EtOAc and washed successively with water and brine. The aqueous phase was extracted with EtOAc (3 x 30mL). The combined organic phase was dried over Na₂SO₄ and concentrated to dryness in vacuo. Purification by FCC (Biotage Isolera, 100g SNAP KP-Sil, gradient elution 10-100% EtOAc:Heptanes, then 0-20% MeOH:EtOAc) gave the title compound 440 mg (27.3%) as a yellow solid.

20 LCMS (Method 12, ES+) 1.32 min, 383 m/z $[M+H]^+$

INTERMEDIATE 98

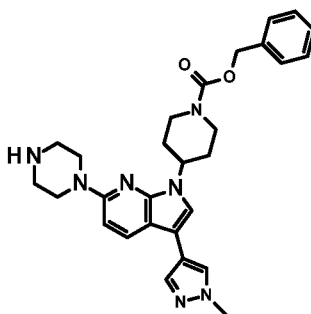


25 tert-butyl 4-(1-[1-[(benzyloxy)carbonyl]piperidin-4-yl]-3-(1-methyl-1H-pyrazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazine-1-carboxylate

The title compound was prepared from Intermediate_97 and benzyl 4-hydroxypiperidine-1-carboxylate via Mitsunobu, according to General Procedure 9.

LCMS (Method 10, ES+) 1.41min, 600 m/z $[M+H]^+$

5

INTERMEDIATE 99

benzyl 4-[3-(1-methyl-1H-pyrazol-4-yl)-6-(piperazin-1-yl)-1H-pyrrolo[2,3-b]pyridin-1-yl]piperidine-1-carboxylate

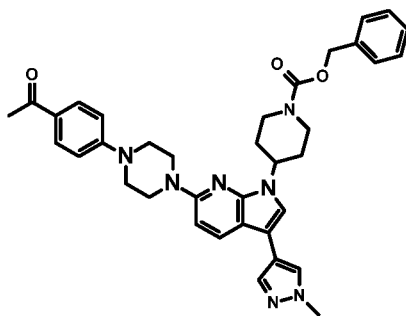
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The title compound was prepared from Intermediate_98 according to General Procedure 13.

LCMS (method 5, ES+) 1.69 min, 500 m/z $[M+H]^+$

INTERMEDIATE 100

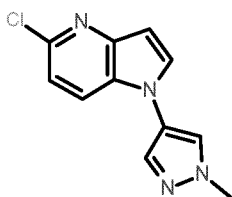
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benzyl 4-[6-[4-(4-acetylphenyl)piperazin-1-yl]-3-(1-methylpyrazol-4-yl)pyrrolo[2,3-b]pyridin-1-yl]piperidine-1-carboxylate

20 The title compound was prepared from Intermediate_99 and 1-(4-bromophenyl)ethenone according to General Procedure 14.

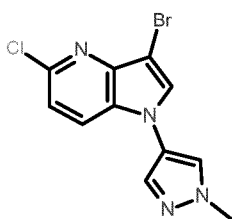
LCMS (method 10, ES+) 1.38 min, 618 m/z $[M+H]^+$

INTERMEDIATE 101**5-chloro-1-(1-methylpyrazol-4-yl)pyrrolo[3,2-b]pyridine**

5 The mixture of 5-chloro-1H-pyrrolo[3,2-b]pyridine (350 mg, 2.29 mmol), 4-bromo-1-methyl-1H-pyrazole (480 mg, 2.98 mmol), copper(1+) iodide (87 mg, 0.46 mmol), quinolin-8-ol (67 mg, 0.46 mmol) and dipotassium carbonate (476 mg, 3.44 mmol) was suspended in DMSO (6 mL) and was stirred at 130 °C for 16 hours under microwave irradiation. The reaction mixture was cooled to r.t and diluted with 10% aqueous ammonium hydroxide (20 mL), and then extracted with EtOAc
10 (3 × 25 mL). The combined organic was dried over Na₂SO₄, filtered and evaporated in vacuo to dryness. The residue was purified by flash silica column chromatography, gradient elution from 15% to 100% EtOAc in heptane to yield the title compound as off-white solid (320 mg, 56% yield).

LCMS (Method 10, ES⁺) 1.01 min, 233 & 235 *m/z* [M+H]⁺

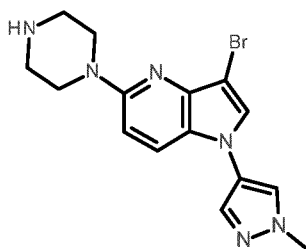
15

INTERMEDIATE 102**3-bromo-5-chloro-1-(1-methylpyrazol-4-yl)pyrrolo[3,2-b]pyridine**

To the solution of Intermediate 101 (320 mg, 1.38 mmol) in DCM (10 mL) was added NBS (269 mg, 1.51 mmol) portionwise over 5 min at r.t and then stirred for 90 mins. The reaction mixture diluted with DCM (10 mL), water (10 mL) and aqueous saturated Na₂CO₃ (10 mL). The organic phase was separated and the aqueous was extracted with DCM (2 × 10mL). The combined organic was dried over MgSO₄, filtered and evaporated to dryness. The residue was purified by flash silica column chromatography, gradient elution from 15% to 100% EtOAc in heptane to yield
20 of the title compound as off-white solid (400 mg, 89% yield).

25

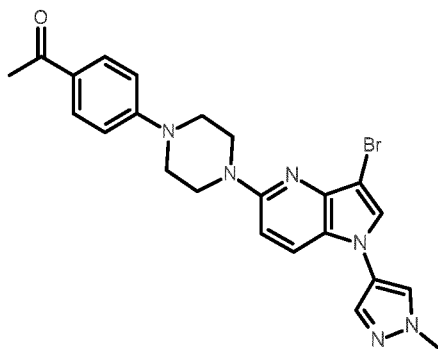
LCMS (Method 10, ES⁺) 1.08 min, 311 & 313 *m/z* [M+H]⁺

INTERMEDIATE 1035 **3-bromo-1-(1-methylpyrazol-4-yl)-5-piperazin-1-yl-pyrrolo[3,2-b]pyridine**

To the mixture of Intermediate 102 (260 mg, 0.83 mmol) and piperazine (1.08 g, 12.52 mmol) in DMSO (3 mL) was added 4N HCl in dioxane (0.21 mL) and then stirred at 136 °C for 16 hours under microwave irradiation. The reaction mixture was diluted with water (20 mL) and then extracted with EtOAc (4 × 25 mL). The combined organic was dried over MgSO₄, filtered and
10 evaporated in vacuo. The residue was purified by flash NH-silica column chromatography, gradient elution from EtOAc to 11% MeOH in EtOAc to yield the title compound as brown gum (235 mg, 70% yield).

LCMS (Method 10, ES⁺) 0.87 min, 361 & 363 *m/z* [M+H]⁺

15

INTERMEDIATE 104**1-[4-[4-[3-bromo-1-(1-methylpyrazol-4-yl)pyrrolo[3,2-b]pyridin-5-yl]piperazin-1-yl]phenyl]ethanone**

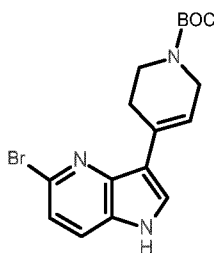
The mixture of Intermediate 103 (90% purity, 230 mg, 0.57 mmol), 1-(4-fluorophenyl)ethanone
20 (158 mg, 1.15 mmol) and dipotassium carbonate (207 mg, 1.5 mmol) in DMSO (3 mL) was stirred at 130°C for 19 hours under microwave irradiation. The reaction mixture was cooled to r.t and diluted with DCM (25 mL) and water (25 mL). The organic layer was separated and the aqueous was extracted with DCM (2 × 25 mL). The combined organic layers were dried over MgSO₄, filtered and evaporated in vacuo to yield a beige solid residue. This solid was triturated with 50%
25 EtOAc in heptane (5 mL) and the solid was collected by filtration, washed with 50% EtOAc in

heptane (2*3 mL) to give the title compound as beige solid (250 mg, 82% yield).

LCMS (Method 10, ES⁺) 1.21 min, 479, 481 *m/z* [M+H]⁺

INTERMEDIATE 105

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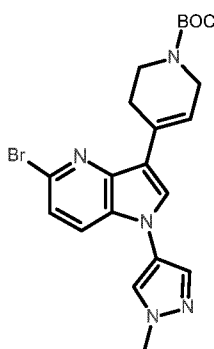


tert-butyl 4-(5-bromo-1H-pyrrolo[3,2-b]pyridin-3-yl)-3,6-dihydro-2H-pyridine-1-carboxylate

To the solution of 5-bromo-1H-pyrrolo[3,2-b]pyridine (400 mg, 2.03 mmol) and tert-butyl 4-oxopiperidine-1-carboxylate (607 mg, 3.05 mmol) in MeOH (10 mL) was added potassium hydroxide (167 μ L, 6.09 mmol) and then stirred at reflux for 20 hours. The reaction mixture was cooled to r.t, diluted with water (40 mL) and extracted with EtOAc (3 \times 30 mL). The combined organic was dried over MgSO₄, filtered and evaporated in vacuo to dryness. The residue was purified by flash silica column chromatography, gradient elution from 12% to 100% EtOAc in heptane to yield the title compound as off-white solid (560 mg, 65% yield).

15 LCMS (Method 10, ES⁺) 1.28 min, 378 & 380 *m/z* [M+H]⁺

INTERMEDIATE 106



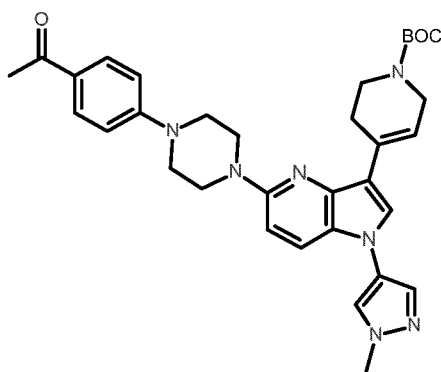
20 tert-butyl 4-[5-bromo-1-(1-methylpyrazol-4-yl)pyrrolo[3,2-b]pyridin-3-yl]-3,6-dihydro-2H-pyridine-1-carboxylate

The mixture of intermediate 105 (460 mg, 1.09 mmol), 4-iodo-1-methyl-1H-pyrazole (342 mg, 1.64 mmol), copper(1+) iodide (21 mg, 0.11 mmol), quinolin-8-ol (16 mg, 0.11 mmol) and K₂CO₃ (227 mg, 1.64 mmol) in DMSO (6 mL) was stirred at 110°C for 36 min under microwave irradiation.

The mixture was then cooled to r.t , diluted with 10% ammonium hydroxide (20 mL), extracted with EtOAc (4 × 20 mL), dried MgSO₄, filtered and evaporated in vacuo to dryness. The residue was purified by flash silica column chromatography, gradient elution from 17% to 59% EtOAc in heptane to yield the title compound as yellow solid (265 mg, 48% yield).

- 5 LCMS (Method 10, ES⁺) 1.35 min, 458 & 460 *m/z* [M+H]⁺

INTERMEDIATE 107

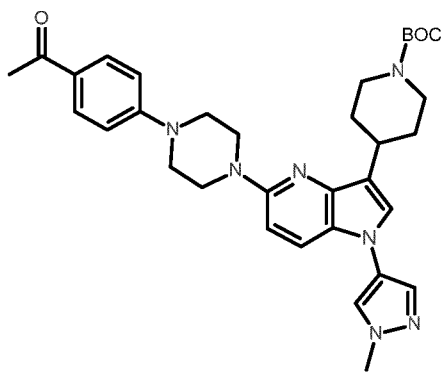


- 10 tert-butyl 4-[5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpyrazol-4-yl)pyrrolo[3,2-b]pyridin-3-yl]-3,6-dihydro-2H-pyridine-1-carboxylate

This intermediate was prepared following General Procedure 21 using intermediate 106 and 1-(4-piperazin-1-ylphenyl)ethanone.

- 15 LCMS (Method 10, ES⁺) 1.37 min, 582 *m/z* [M+H]⁺

INTERMEDIATE 108

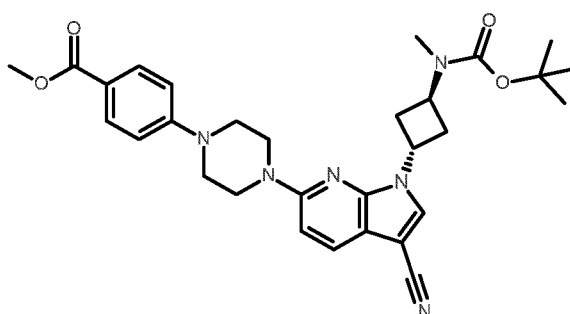


- 20 tert-butyl 4-[5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpyrazol-4-yl)pyrrolo[3,2-b]pyridin-3-yl]piperidine-1-carboxylate

The solution of intermediate 107 (105 mg, 0.16 mmol) in MeOH/EtOAc (1:1, 15 mL) was passed through a 10% Pd/C Cartridge in H-cube system (20 °C, H₂ pressure 5 bar) for 2 cycles. The solution was then evaporated in vacuo and the crude residue was purified by flash NH-silica column chromatography, gradient elution from 18% to 100% EtOAc in heptane] to yield the title compound as brown solid (40 mg, 31% yield).

LCMS (Method 10, ES⁺) 1.29 min, 584 *m/z* [M+H]⁺

INTERMEDIATE 109



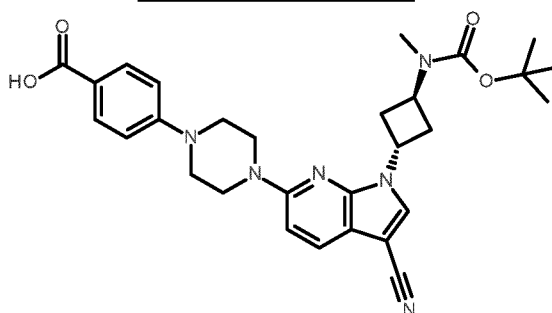
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methyl 4-[4-[1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]-3-cyano-pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]benzoate

15 This intermediate was prepared following General Procedure 3 using intermediate 40 and methyl 4-(piperazin-1-yl)benzoate.

LCMS (Method 2, ES⁺) 1.56 and 1.62 min, 545 *m/z* [M+H]⁺

INTERMEDIATE 110



20

4-[4-[1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]-3-cyano-pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]benzoic acid

25 Intermediate 109 (117 mg, 0.2 mmol) was dissolved in THF (5 mL) and a solution of lithium

- hydroxide monohydrate (45 mg, 1.1 mmol) in WATER (2 mL) added. The reaction mixture was stirred at RT for 2 hours, and a second portion of lithium hydroxide monohydrate (45 mg, 1.1 mmol) in water (0.5 mL) followed by 1,4-DIOXANE (1 mL). The reaction mixture was stirred at RT for 1 h then heated at 50 °C for ~ 2 hours. Then left to stand at RT for 2 days. The reaction mixture was diluted with pH 4 buffer and ethyl acetate. The aqueous layer was extracted with ethyl acetate three times. Organic layers combined, dried (Na₂SO₄) and concentrated under reduced pressure. The residue was then purified by flash column chromatography to give the title compound (110 mg, 96%).
- 10 LCMS (Method 2, ES⁺) 1.12 min, 531 *m/z* [M+H]⁺

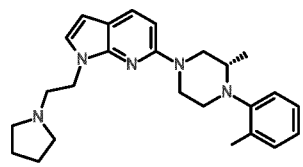
Examples 1-16

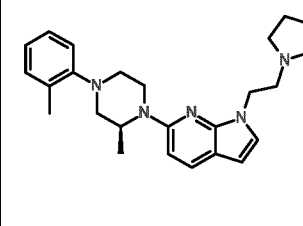
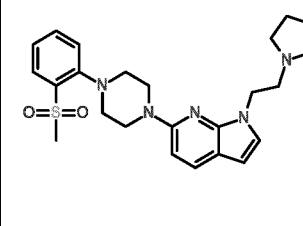
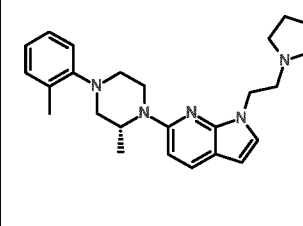
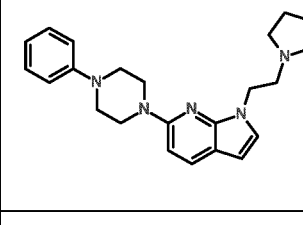
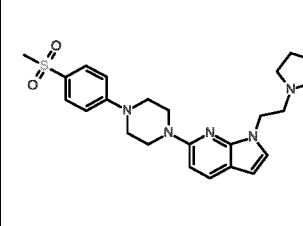
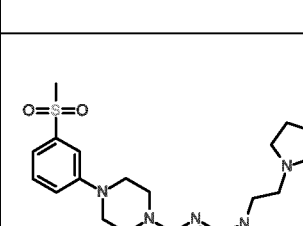
- The following compounds were synthesised using General Procedure 3 from heteroaryl halide and the appropriate amine as noted in the table below.

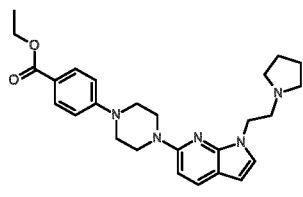
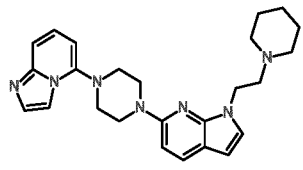
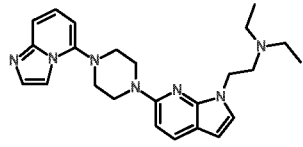
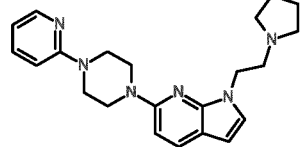
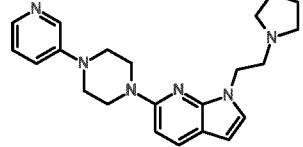
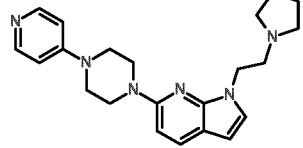
Examples 1-8, Example 10, and Examples 15-16: LCMS Method 1

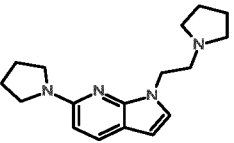
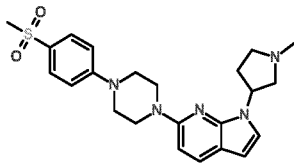
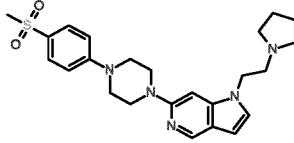
Example 9: LCMS Method 2

Examples 11-14: LCMS Method 4

Example	Structure	Amine or Intermediate	Heteroaryl halide	Compound Name	LCMS RT (min)	Mass Ion
1		Intermediate 4	Intermediate 6	6-[(3S)-3-methyl-4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	3.73	404

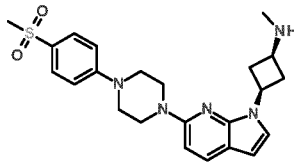
2		Intermediate 3	Intermediate 6	6-[(2S)-2-methyl-4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	3.70	404
3		1-[2-(methylsulphonyl)phenyl]piperazine	Intermediate 6	6-{4-[2-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	2.80	454
4		Intermediate 2	Intermediate 6	6-[(2R)-2-methyl-4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	3.67	404
5		1-phenylpiperazine	Intermediate 6	6-(4-phenylpiperazin-1-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	3.16	376
6		1-(4-methylsulfonylphenyl)piperazine	Intermediate 6	6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	2.66	454
7		1-(3-methylsulfonylphenyl)piperazine.HCl	Intermediate 6	6-{4-[3-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	2.68	454

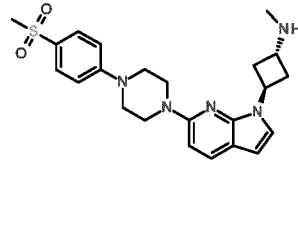
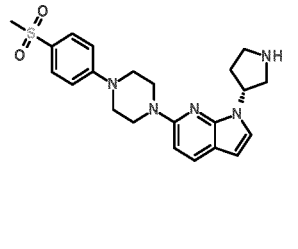
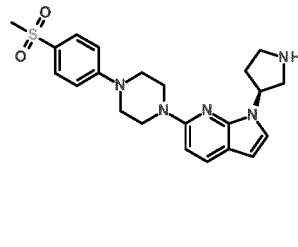
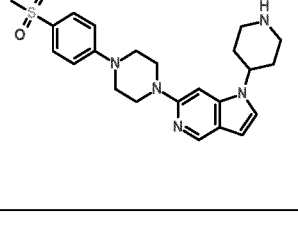
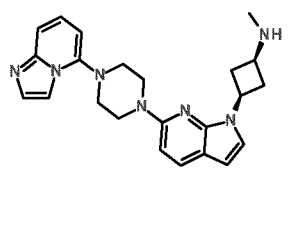
8		4-(piperazin-1-yl)-benzoic acid ethyl ester	Intermediate 6	ethyl 4-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)benzoate	3.28	448
9		Intermediate 5	Intermediate 10	5-(4-{1-[2-(piperidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine	2.51	430
10		Intermediate 5	Intermediate 11	N,N-diethyl-2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethanamine	2.30	418
11		1-(2-pyridyl)piperazine	Intermediate 6	6-[4-(pyridin-2-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	2.84	377
12		1-(3-pyridyl)piperazine	Intermediate 6	6-[4-(pyridin-3-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	2.52	377
13		1-(4-pyridyl)piperazine	Intermediate 6	6-[4-(pyridin-4-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	2.45	377

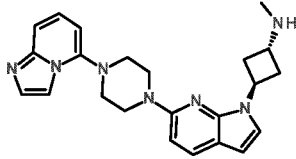
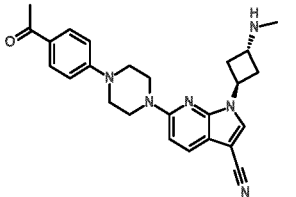
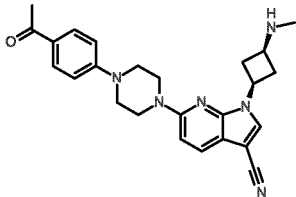
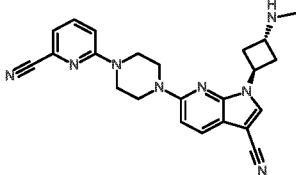
14		pyrrolidine	Intermediate 6	6-(pyrrolidin-1-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	2.85	285
15		1-[4-(Methylsulfonyl)phenyl]piperazine	Intermediate 36	1-(1-methylpyrrolidin-3-yl)-6-[4-(4-(methylsulfonyl)phenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine	2.10	440
16		1-[4-(Methylsulfonyl)phenyl]piperazine	Intermediate 27	6-[4-(4-(methylsulfonyl)phenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[3,2-c]pyridine	1.87	454

Examples 17-29

Examples 17-29 were prepared in two steps according to General Procedure 3 followed by General Procedure 13 and analysed by LCMS Method 1.

Example	Structure	Amine or Intermediate	Heteroaryl halide	Compound Name	LCMS RT (min)	Mass Ion
17		1-[4-(methylsulfonyl)phenyl]piperazine	Intermediate 34	cis-N-methyl-3-(6-[4-(4-(methylsulfonyl)phenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine	1.84	440

18		1-[4-(methylsulfonyl)phenyl]piperazine	Intermediate 35	trans-N-methyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine	1.53	440
19		1-[4-(methylsulfonyl)phenyl]piperazine	Intermediate 37	6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[(3R)-pyrrolidin-3-yl]-1H-pyrrolo[2,3-b]pyridine	1.45	426
20		1-[4-(methylsulfonyl)phenyl]piperazine	Intermediate 38	6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[(3S)-pyrrolidin-3-yl]-1H-pyrrolo[2,3-b]pyridine	1.69	426
21		1-[4-(methylsulfonyl)phenyl]piperazine	Intermediate 39	6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-(piperidin-4-yl)-1H-pyrrolo[3,2-c]pyridine	1.23	440
22		Intermediate 5	Intermediate 34	cis-3-{6-[4-(imidazo[1,2-a]pyridin-5-yl]piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}-N-methylcyclobutanamine	1.52	402

23		Intermediate 5	Intermediate 35	trans-3-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}-N-methylcyclobutanamine	1.55	402
24		1-(4-acetylphenyl) piperazine	Intermediate 40	6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[trans-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile	1.70	429
25		1-(4-acetylphenyl) piperazine	Intermediate 41	6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[cis-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile	1.74	429
26		Intermediate 43	Intermediate 40	6-[4-(6-cyanopyridin-2-yl)piperazin-1-yl]-1-[trans-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile	1.74	413

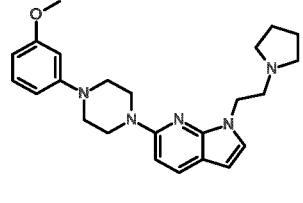
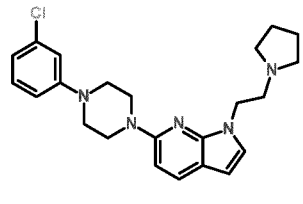
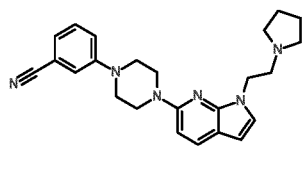
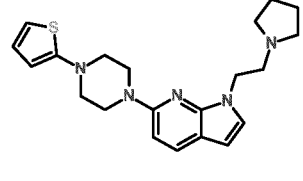
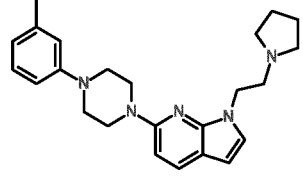
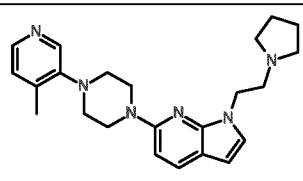
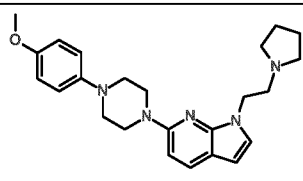
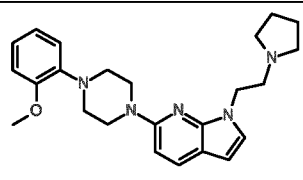
Example	Structure	Piperidine	Compound Name	LCMS RT (min)	Mass Ion
30		1-(4-phenyl-4-piperidyl)ethanone; hydrochloride	1-(4-phenyl-1-{1-[2-(pyrrolidin-1-yl)ethyl]}ethyl)-1H-pyrrolo[2,3-b]pyridin-6-yl)piperidin-4-yl)ethanone	3.15	417
31		4-hydroxy-4-phenylpiperidine	4-phenyl-1-{1-[2-(pyrrolidin-1-yl)ethyl]}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperidin-4-ol	2.75	390
32		4-phenylpiperidine	6-(4-phenylpiperidin-1-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	2.45	375
33		4-phenylpiperidine-4-carbonitrile	4-phenyl-1-{1-[2-(pyrrolidin-1-yl)ethyl]}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperidine-4-carbonitrile	3.13	400

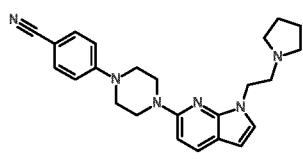
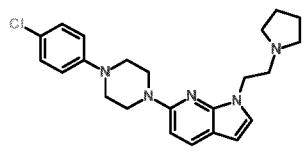
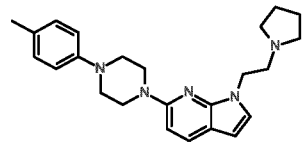
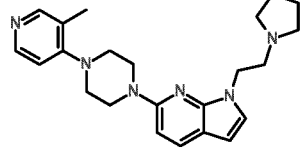
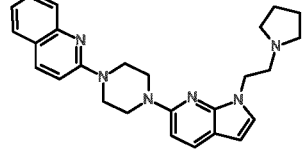
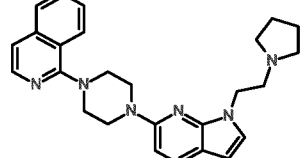
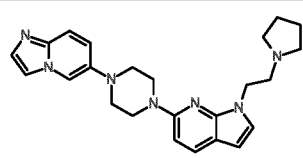
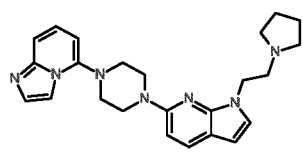
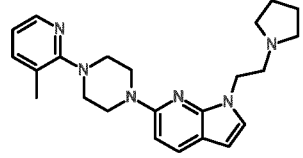
Examples 34-51

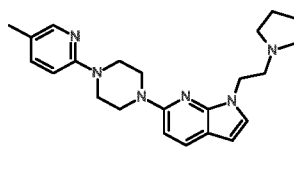
The following compounds were synthesized from Intermediate 7 and the appropriate aryl bromide in accordance with General Procedure 3.

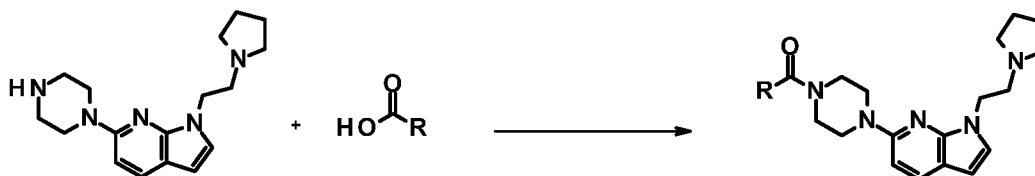
5 Examples 34-45 were analysed by LCMS Method 3.

Examples 46-51 were analysed by LCMS Method 1.

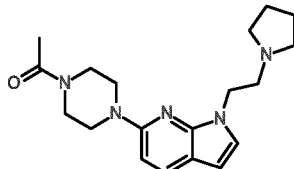
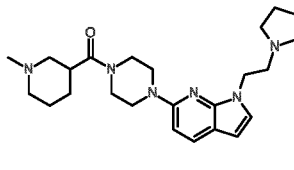
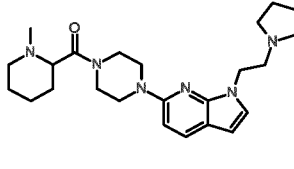
Example	Structure	Compound Name	LCMS RT (min)	Mass Ion
34		6-[4-(3-methoxyphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	1.83	406
35		6-[4-(3-chlorophenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	2.05	410
36		3-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)benzotrile	1.84	401
37		1-[2-(pyrrolidin-1-yl)ethyl]-6-[4-(thiophen-2-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine	1.86	382
38		6-[4-(3-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	1.86	390
39		6-[4-(4-methylpyridin-3-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	1.20	391
40		6-[4-(4-methoxyphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	1.56	406
41		6-[4-(2-methoxyphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	1.62	406

42		4-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)benzotrile	1.80	401
43		6-[4-(4-chlorophenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	2.02	410
44		6-[4-(4-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	1.80	390
45		6-[4-(3-methylpyridin-4-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	1.50	391
46		2-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)quinoline	3.14	427
47		1-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)isoquinoline	3.05	427
48		6-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine	2.31	416
49		5-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine	2.49	416
50		6-[4-(3-methylpyridin-2-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	2.83	391

51		6-[4-(5-methylpyridin-2-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	2.81	391
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Examples 52-54

- 5 Examples 52-54 were synthesized from Intermediate 7 and the appropriate carboxylic acid in accordance with General Procedure 6 and analysed by LCMS Method 3.

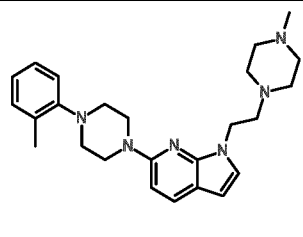
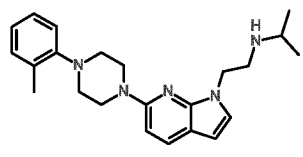
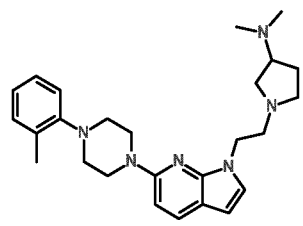
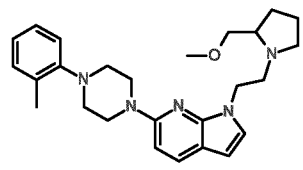
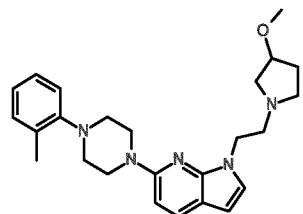
Example	Structure	Compound Name	LCMS RT (min)	Mass Ion
52		1-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)ethanone	1.24	342
53		(1-methylpiperidin-3-yl)(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)methanone	0.90	425
54		(1-methylpiperidin-2-yl)(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)methanone	0.94	425

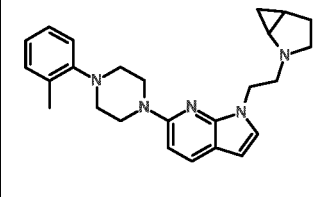
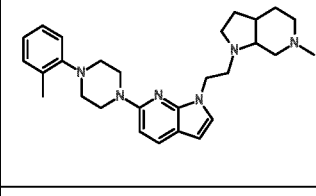
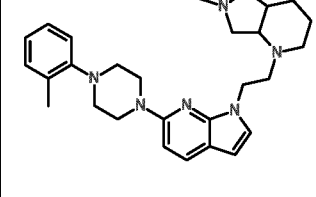
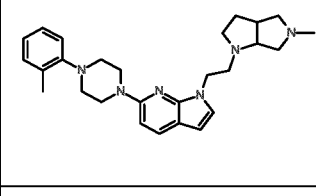
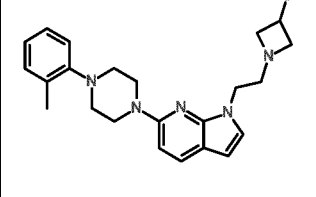
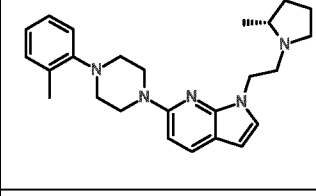
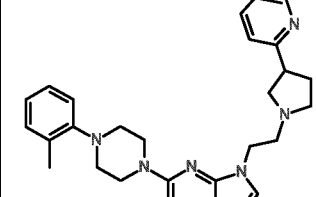
Examples 55-66

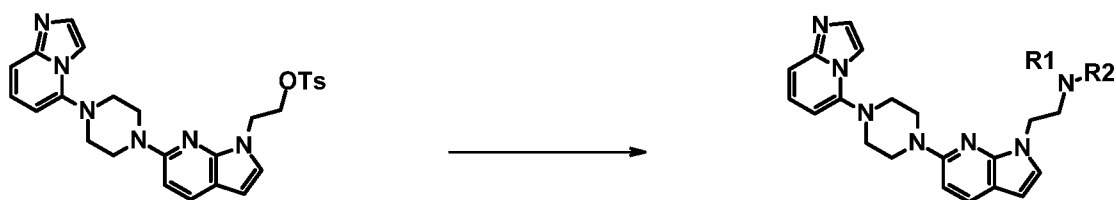
The following compounds were synthesised from Intermediate 17 and the appropriate amine in accordance with General Procedure 7.

Examples 55-65: LCMS Method 3

5 Example 66: LCMS Method 1

Example	Structure	Compound Name	LCMS RT (min)	Mass Ion
55		6-[4-(2-methylphenyl)piperazin-1-yl]-1-[2-(4-methylpiperazin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	1.98	419
56		N-(2-{6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)propan-2-amine	2.03	378
57		N,N-dimethyl-1-(2-{6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)pyrrolidin-3-amine	1.71	433
58		1-[2-[2-(methoxymethyl)pyrrolidin-1-yl]ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine	2.12	434
59		1-[2-(3-methoxypyrrolidin-1-yl)ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine	2.03	420

60		1-[2-(2-azabicyclo[3.1.0]hex-2-yl)ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine	2.04	402
61		6-methyl-1-(2-{6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)octahydro-1H-pyrrolo[2,3-c]pyridine	2.02	459
62		6-methyl-1-(2-{6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)octahydro-1H-pyrrolo[3,4-b]pyridine	2.18	459
63		1-[2-(5-methylhexahydropyrrolo[3,4-b]pyrrol-1(2H)-yl)ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine	2.04	445
64		1-[2-(3-methoxyazetid-1-yl)ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine	1.98	406
65		6-[4-(2-methylphenyl)piperazin-1-yl]-1-[2-[(2R)-2-methylpyrrolidin-1-yl]ethyl]-1H-pyrrolo[2,3-b]pyridine	2.08	404
66		6-[4-(2-methylphenyl)piperazin-1-yl]-1-[2-[3-(pyridin-2-yl)pyrrolidin-1-yl]ethyl]-1H-pyrrolo[2,3-b]pyridine	3.03	467

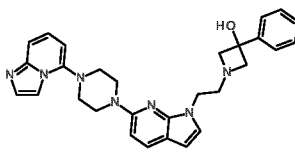
Examples 67-81

The following compounds were synthesised from Intermediate 15 and the appropriate amine in accordance with General Procedure 8.

5 Examples 67-81 were analysed by LCMS Method 3.

Example	Structure	Compound Name	LCMS RT (min)	Mass Ion
67		1-(2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)-N,N-dimethylpyrrolidin-3-amine	1.00	459
68		5-(4-{1-[2-(6-azabicyclo[3.2.0]hept-6-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine	1.27	442
69		5-[4-(1-[2-[3-(1-methyl-1H-imidazol-2-yl)pyrrolidin-1-yl]ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine	0.97	496
70		5-[4-(1-[2-[2-(1-methyl-1H-pyrazol-4-yl)pyrrolidin-1-yl]ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine	1.22	496
71		5-[4-(1-[2-[3-(4,4-difluoropiperidin-1-yl)azetidin-1-yl]ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine	1.34	521

72		5-[4-(1-{2-[3-(pyrrolidin-1-yl)azetid-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine	1.06	471
73		5-(4-{1-[2-(2-oxa-7-azaspiro[3.5]non-7-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl)imidazo[1,2-a]pyridine	1.19	472
74		5-(4-{1-[2-(5-azaspiro[3.4]oct-5-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl)imidazo[1,2-a]pyridine	1.31	456
75		5-(4-{1-[2-(6-azaspiro[3.5]non-6-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl)imidazo[1,2-a]pyridine	1.37	470
76		N-benzyl-2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}-N-methylethanamine	1.35	466
77		5-(4-{1-[2-(3-phenoxypropyl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl)imidazo[1,2-a]pyridine	1.43	508
78		5-(4-{1-[2-(2-phenylpropyl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl)imidazo[1,2-a]pyridine	1.38	478
79		5-[4-(1-{2-[3-(2-fluorophenyl)azetid-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine	1.41	496
80		5-(4-{1-[2-(3-phenoxypropyl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl)imidazo[1,2-a]pyridine	1.40	494

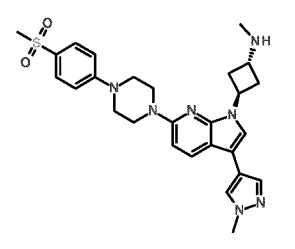
81		1-(2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)-3-phenylazetidin-3-ol	1.33	494
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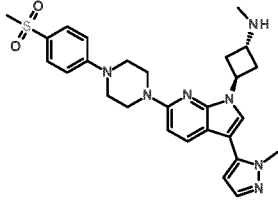
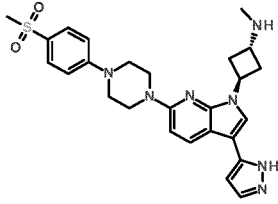
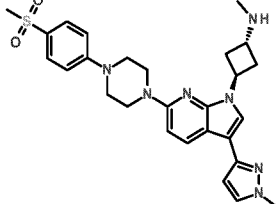
Examples 82-85

Intermediate 23 (70 mg, 0.11 mmol), boronic ester (2 eq., 0.23 mmol), K₂CO₃ (2 eq., 0.23 mmol) and PdCl₂(dppf)-DCM complex (0.1 equiv., 0.01 mmol) were dissolved in 1,4-dioxane (0.1 M, 1 mL). H₂O (1 M, 0.1 mL) was added and the mixture degassed for 1 min. The mixture was stirred overnight at 100 °C. The mixture was cooled to ambient temperature and DCM (3 mL) and H₂O (2 mL) were added and the layers separated. TFA (1 mL) was added to the DCM solution and the reaction mixture was stirred at r.t. for 2 hours. The residue was filtered through an SCX column, washing with MeOH and DCM, and then eluting the product with NH₃ (7 N) in MeOH. The volatiles were removed under vacuum and the residue purified by reverse phase column chromatography.

Examples 82-85 were synthesised from Intermediate 23 and the appropriate commercially available boronic ester in accordance with the foregoing procedure.

Examples were analysed by LCMS Method 1.

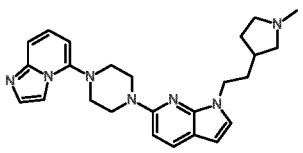
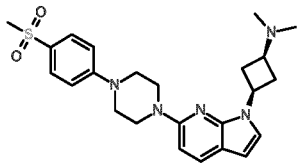
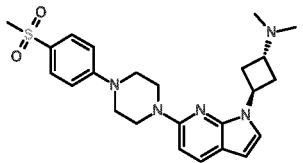
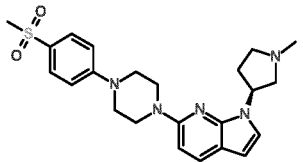
Example	Structure	Boronic ester	Compound Name	LCMS RT (min)	Mass Ion
82		1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole	<i>trans</i> -N-methyl-3-[3-(1-methyl-1H-pyrazol-4-yl)-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine	1.52	520

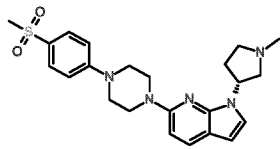
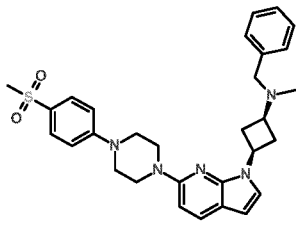
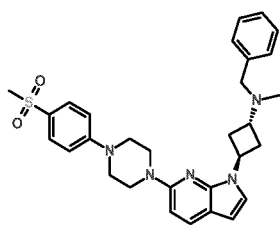
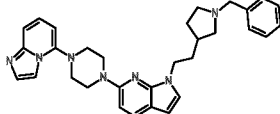
83		1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)pyrazole	<i>trans</i> -N-methyl-3-[3-(1-methyl-1H-pyrazol-5-yl)-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine	1.61	520
84		tert-butyl 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)pyrazole-1-carboxylate	<i>trans</i> -N-methyl-3-[6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-3-(1H-pyrazol-5-yl)-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine	1.51	506
85		1-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)pyrazole	<i>trans</i> -N-methyl-3-[3-(1-methyl-1H-pyrazol-3-yl)-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine	1.63	520

Examples 86-97

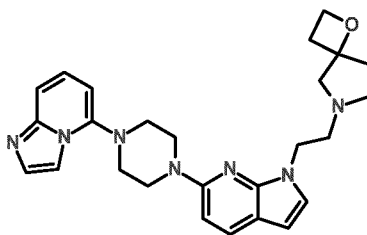
Examples 86-97 were synthesised from the appropriate amine and aldehyde in accordance with General Procedure 12.

5 Examples 86-97 were analysed by LCMS Method 1.

Example	Structure	Intermediate	Aldehyde	Compound Name	LCMS RT (min)	Mass Ion
86		Example 115	formaldehyde	5-(4-{1-[2-(1-methylpyrrolidin-3-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine	1.11	430
87		Example 17	formaldehyde	cis-N,N-dimethyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine	2.14	454
88		Example 18	formaldehyde	trans-N,N-dimethyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine	2.20	454
89		Example 20	formaldehyde	1-[(3S)-1-methylpyrrolidin-3-yl]-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine	2.11	440

90		Example 19	formaldehyde	1-[(3R)-1-methylpyrrolidin-3-yl]-6-[4-[4-(methylsulfonyl)phenyl]piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine	2.14	440
91		Example 17	benzaldehyde	cis-N-benzyl-N-methyl-3-(6-[4-[4-(methylsulfonyl)phenyl]piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine	2.92	530
92		Example 18	benzaldehyde	trans-N-benzyl-N-methyl-3-(6-[4-[4-(methylsulfonyl)phenyl]piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine	2.91	530
93		Example 115	benzaldehyde	5-(4-{1-[2-(1-benzylpyrrolidin-3-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine	2.74	506

94		Example 20	benzaldehyde	1-[(3S)-1-benzylpyrrolidin-3-yl]-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine	2.88	516
95		Example 19	benzaldehyde	1-[(3R)-1-benzylpyrrolidin-3-yl]-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine	2.87	516
96		Intermediate 7	formaldehyde	6-(4-methylpiperazin-1-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine	1.67	314
97		Example 116	formaldehyde	2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}-N,N-dimethylethanamine	1.03	390

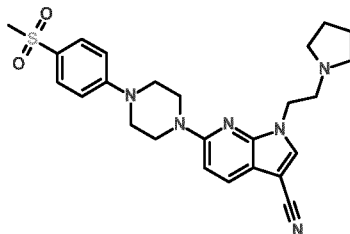
Example 98

5-(4-{1-[2-(1-oxa-6-azaspiro[3.4]oct-6-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine

Example 98 was prepared following General Procedure 8 using Intermediate 15 (50 mg, 0.09 mmol) and 1-oxa-7-azaspiro[3.4]octane (17 mg, 1.5 eq.). The reaction mixture was then heated at 80 °C overnight in a sealed vial. The reaction was cooled down to ambient temperature and H₂O and DCM added. The layers were separated and the aq. phase was extracted with DCM. The solvent was removed under vacuum and the residue was purified by chromatography gradient elution from DCM to 30% MeOH in DCM to yield Example 98 (5 mg, 12% yield).

LCMS (Method 1, ES⁺) 2.01 min, 458 m/z (M+H)⁺.

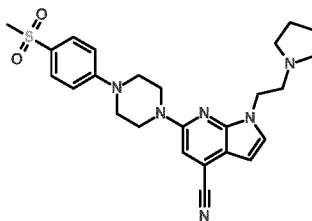
Example 99



6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile

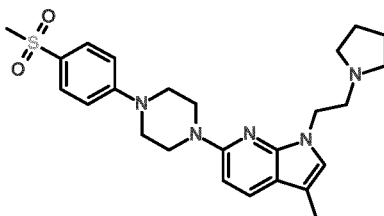
6-bromo-1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridine-3-carbonitrile (300 mg, 0.1 mmol) was dissolved in a mixture of DMF:THF (10 mL, 1:1) The pink solution was cooled to 0 °C and sodium hydride (79 mg, 0.11 mmol, 2.2 eq., 60 mass%) added slowly portion-wise over a period of 30 minutes. 1-(2-chloroethyl)pyrrolidine hydrochloride (1.5 eq., 1.4 mmol) was then added carefully portion-wise and the reaction mixture stirred at 80 °C overnight until the starting material was consumed. The crude was dissolved in DCM and H₂O added. The layers were separated and the aq. phase was extracted with DCM. The solvent was removed under vacuum and the resulting residue used in General Procedure 3 with 1-[4-(methylsulfonyl)phenyl]piperazine (1.5 eq., 0.94 mmol). The residue was purified by column chromatography gradient elution from DCM to 30% MeOH in DCM and then re-purified by reverse phase chromatography to yield Example 99 (4 mg, 1% yield).

LCMS (Method 1, ES⁺) 2.62 min, 479 m/z (M+H)⁺.

Example 1006-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile

5 4-Cyano-6-bromo-7-azaindole (200 mg, 0.9 mmol) reacted with 1-(2-chloroethyl)pyrrolidine hydrochloride (1.5 eq., 1.35 mmol) following General Procedure 2. H₂O and EtOAc were added and the layers separated and the aq. phase was extracted with EtOAc. The solvent was removed under vacuum and the residue used following General Procedure 3 without any further purification using 1-[4-(methylsulfonyl)phenyl]piperazine (1.5 equiv., 1.97 mmol). The residue
10 was purified by column chromatography gradient elution from DCM to 30% MeOH in DCM, and then re-purified by reverse phase column chromatography give Example 100 (5 mg, 7% yield).

LCMS (Method 1, ES⁺) 2.26 min, 479 m/z (M+H)⁺.

Example 101

15

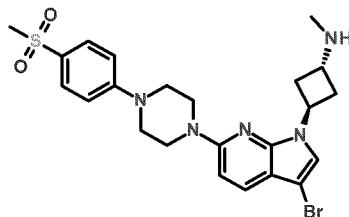
3-methyl-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine

Intermediate 18 (100 mg, 0.28 mmol), cobalt tetrafluoroborate hexahydrate (0.1 mmol), tris[2-(diphenylphosphino)ethyl]phosphine (0.1 mmol) and K₂CO₃ (1 mmol, 1 mmol) were dissolved in methanol (1 mL). The mixture was heated to 100°C in a sealed vial overnight. The crude reaction mixture was filtered over celite and the volatiles removed under vacuum. The residue was submitted to alkylation following General Procedure 2 using 1-(2-chloroethyl)pyrrolidine hydrochloride (1.5 equiv.). The crude reaction mixture was diluted with EtOAc and H₂O added. The layers were separated and the aq. phase was extracted with EtOAc. Combined organic
20 layers were dried over Na₂SO₄ and the solvent was removed under vacuum. The residue was
25

filtered over celite and rinsed with DCM. After removing the solvent, the residue was purified by reverse phase column chromatography to give Example 101 (2 mg, 2% yield).

LCMS (Method 1, ES⁺) 2.83 min, 468 m/z (M+H)⁺.

5 **Example 102**

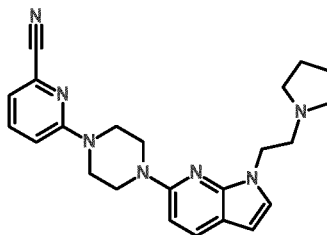


trans-3-(3-bromo-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-methylcyclobutanamine

Intermediate 26 (550 mg, 1.02 mmol) was dissolved in DCM (30 mL) and cooled to 0 °C. NBS (165 mg, 0.92 mmol) was added portion-wise. The reaction mixture was stirred in a cooling bath for 10 min then quenched with saturated NaHCO₃ aq. solution (20 mL) and diluted with DCM (20 mL). The aqueous layer was extracted with DCM (2 x 10 mL), the combined organics were dried over Na₂SO₄ and concentrated under reduced pressure. The crude was purified by flash chromatography gradient elution from 20% EtOAc to EtOAc and then to DCM in MeOH giving a mixture of brominated products. The white solid was dissolved in DCM (0.25 M) and TFA (5 mL) and stirred at r.t. until completion of the reaction. The volatiles were removed under vacuum and the residue was dissolved in MeOH and filtered through an SCX column, washing with MeOH and DCM and then eluting with NH₃ (4M) in MeOH. The solvent was removed under vacuum and the residue was purified by preparative HPLC affording Example 102 (7 mg, 1 % yield).

LCMS (Method 1, ES⁺) 1.89 min, 518 & 520 m/z (M+H)⁺.

Example 103



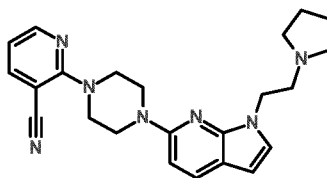
6-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)pyridine-2-carbonitrile

5 A mixture of Intermediate 7 (107 mg, 0.35 mmol), 2-cyano-6-fluoropyridine (44 mg, 0.36 mmol), and potassium carbonate (100 mg, 0.71 mmol) was dissolved in dimethylsulfoxide (2 mL) and heated at 100 °C overnight. The cooled reaction mixture was then treated with an aqueous work up, the organic solvent dried (Na₂SO₄) and concentrated under reduced pressure. A third of the crude residue was purified by reverse phase column chromatography to give the title compound (19.5 mg, 14% yield).

LCMS (Method 1, ES⁺) 2.53 min, 402 m/z (M+H)⁺.

10

Example 104



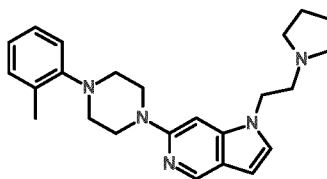
2-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)pyridine-3-carbonitrile

15 A mixture of intermediate 7 (90 mg, 0.30 mmol) and 3-cyano-2-fluoropyridine (45 mg, 0.36 mmol) was dissolved in tetrahydrofuran (2 mL) and triethylamine (0.1 mL, 0.7 mmol) added. The resulting yellow solution was heated at 100 °C overnight. The cooled reaction mixture was then treated with an aqueous work up and the organic layer concentrated under reduced pressure. Half of the crude residue was purified by reverse phase column chromatography to give the title compound (31.2 mg, 25% yield).

20

LCMS (Method 1, ES⁺) 2.39 min, 402 m/z (M+H)⁺.

Example 105



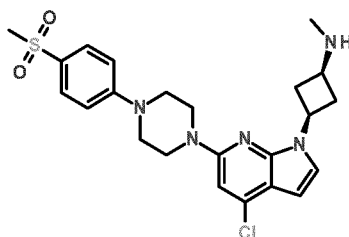
25 6-[4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[3,2-c]pyridine

Example 105 was prepared according to General Procedure 2 with Intermediate 22 (46 mg, 0.16 mmol) and 1-(2-chloroethyl)pyrrolidine hydrochloride (33 mg, 0.19 mmol). Reverse phase column chromatography for the final purification gave the title compound (16 mg, 26% yield).

LCMS (Method 1, ES⁺) 2.61 min, 390 m/z (M+H)⁺.

5

Example 106

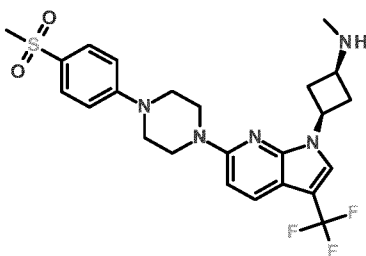


cis-3-(4-chloro-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-methylcyclobutanamine

10 Intermediate 24 (330 mg, 1 eq.) and 1-[4-(methylsulfonyl)phenyl]piperazine (1.1 eq., 0.88 mmol) were reacted following General Procedure 3. The residue was purified by flash column chromatography using gradient elution from hexane to EtOAc. The obtained product was dissolved in DCM (5 mL) and TFA (1 mL) added. The mixture was stirred for 1 hour at ambient temperature. Then the mixture was filtered through an SCX-column and rinsed with DCM and
15 MeOH. The product was eluted with NH₃ (4N) in MeOH. The volatiles were removed under vacuum and then the residue was purified by reverse phase column chromatography to yield the title compound as a white solid (19 mg, 5% yield).

LCMS (Method 1, ES⁺) 1.81 min, 474 m/z (M+H)⁺.

20 **Example 107**

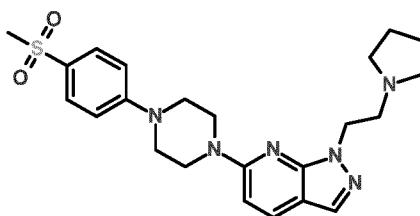


cis-N-methyl-3-[6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-3-(trifluoromethyl)-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine

Intermediate 25 (160 mg, 0.36 mmol) and 1-[4-(methylsulfonyl)phenyl]piperazine (1.1 eq., 0.4 mmol) were reacted following General Procedure 3. The residue was purified by flash column chromatography using gradient elution from hexane to EtOAc. The resulting residue was dissolved in DCM (5 mL) and TFA (2 mL) was added. The mixture was stirred at ambient temperature for 2 hours and the volatiles removed under vacuum. The residue was purified by flash column chromatography using gradient elution from hexane to EtOAc, and then 20% MeOH in EtOAc to give Example 107 (2 mg, 8% yield).

LCMS (Method 1, ES⁺) 1.92 min, 408 m/z (M+H)⁺.

10 Example 108



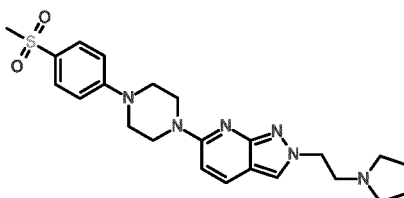
6-[4-[4-(methylsulfonyl)phenyl]piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrazolo[3,4-b]pyridine

6-bromo-1H-pyrrolo[3,4-b]pyridine (100 mg, 0.51 mmol) and 1-(2-chloroethyl)pyrrolidine hydrochloride (1.2 eq., 0.61 mmol) were reacted following General Procedure 2. After work-up, the mixture was reacted with 1-[4-(methylsulfonyl)phenyl]piperazine (1.5 eq., 0.76 mmol) following General Procedure 3. The residue was purified by reverse phase column chromatography to yield the title compound as a white solid (8 mg, 3% yield).

LCMS (Method 1, ES⁺) 1.59 min, 455 m/z (M+H)⁺.

20

Example 109

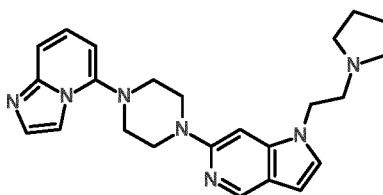


6-[4-[4-(methylsulfonyl)phenyl]piperazin-1-yl]-2-[2-(pyrrolidin-1-yl)ethyl]-2H-pyrazolo[3,4-b]pyridine

Example 109 was prepared according to the procedure described for Example 108 and isolated as an alternative regioisomer during purification.

LCMS (Method 1, ES⁺) 1.82 min, 455 *m/z* (M+H)⁺.

5 **Example 110**

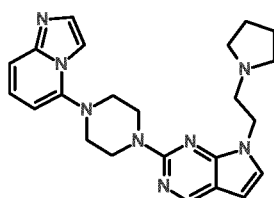


5-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[3,2-c]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine

10 Intermediate 27 (75 mg, 0.30 mmol) and Intermediate 5 (75 mg, 0.37 mmol) were reacted using General Procedure 3 to give the title compound (63 mg, 50% yield).

LCMS (Method 1, ES⁺) 1.79 min, 416 *m/z* (M+H)⁺.

Example 111

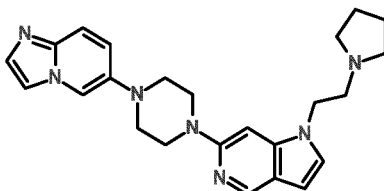


15 2-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-7-[2-(pyrrolidin-1-yl)ethyl]-7H-pyrrolo[2,3-d]pyrimidine

20 A mixture of 2-chloro-7H-pyrrolo[2,3-D]pyrimidine (120 mg, 0.76 mmol) and Intermediate 5 (117 mg, 0.58 mmol) were suspended in 1-butanol (3 mL) and trifluoroacetic acid (0.07 mL, 0.9 mmol) added. The reaction mixture was then heated at 120 °C overnight. The reaction mixture was cooled to room temperature and filtered through a SCX cartridge washing first with methanol then eluting with 2 M ammonia in methanol. The ammonia in methanol solution was concentrated under reduced pressure and the residue partially purified using silica column chromatography. The crude mixture was then reacted with 1-(2-chloroethyl)pyrrolidine hydrochloride (102 mg, 0.59 mmol) according to General Procedure 2 to give the title compound
25 (38 mg, 15% yield).

LCMS (Method 1, ES⁺) 1.92 min, 417 *m/z* (M+H)⁺.

Example 112

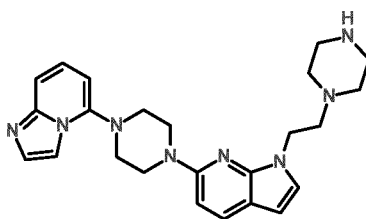


5 6-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[3,2-c]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine

The title compound was prepared according to General Procedure 3 using intermediate 28 (48 mg, 0.16 mmol) instead of intermediate 7. The crude reaction mixture was directly filtered through celite followed by SCX filtration. The SCX cartridge was washed with methanol and the product eluted with 2 M ammonia in methanol. Final purification of the residue by reverse phase column chromatography gave the title compound (3 mg, 4% yield).

LCMS (Method 1, ES⁺) 1.58 min, 416 *m/z* (M+H)⁺.

Example 113



15

5-(4-{1-[2-(piperazin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine

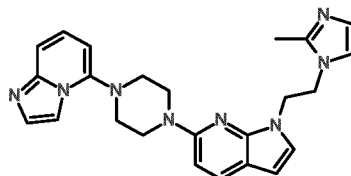
Using General Procedure 3, Intermediate 31 (175 mg, 0.43 mmol) and Intermediate 5 (90 mg, 0.44 mmol) gave tert-butyl 4-[2-[6-(4-imidazo[1,2-a]pyridin-6-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]piperazine-1-carboxylate. This was then dissolved in dichloromethane (3 mL) and treated with trifluoroacetic acid (1 mL). The reaction mixture was stirred at room temperature for 36 h then passed through an SCX cartridge, washing first with methanol then eluting with 2 M ammonia in methanol. The ammonia in methanol solution was concentrated under reduced

20

pressure and the residue purified by reverse phase chromatography to give the title compound (10 mg, 8% yield).

LCMS (Method 1, ES⁺) 1.69 min, 431 *m/z* (M+H)⁺.

5 **Example 114**

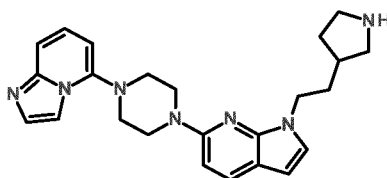


5-(4-{1-[2-(2-methyl-1H-imidazol-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine

10 Intermediate 29 (100 mg, 0.28 mmol) and intermediate 5 (60 mg, 0.29 mmol) were treated according to General Procedure 3 to give the title compound (17 mg, 13% yield).

LCMS (Method 1, ES⁺) 1.82 min, 427 *m/z* (M+H)⁺.

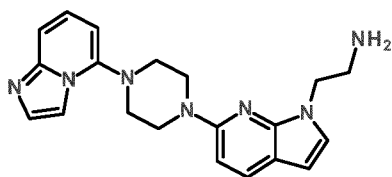
Example 115



15 5-(4-{1-[2-(pyrrolidin-3-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine

20 Intermediate 32 (130 mg, 0.28 mmol) and Intermediate 5 (60 mg, 0.29 mmol) were treated according to General Procedure 3 to give tert-butyl 3-[2-[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]pyrrolidine-1-carboxylate, which was dissolved in DCM (4 mL) and treated with TFA (1 mL). The reaction mixture was stirred at room temperature for 3 hours then passed through an SCX cartridge, washing first with methanol then eluting with 2 M ammonia in methanol. The ammonia in methanol solution was concentrated under reduced pressure and a fraction of the residue (50 mg) purified by reverse phase chromatography to give the title compound (11 mg).

25 LCMS (Method 1, ES⁺) 1.62 min, 416 *m/z* (M+H)⁺.

Example 116**2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethanamine**

Intermediate 33 (110 mg, 0.23 mmol) was dissolved in dichloromethane (3 mL) and trifluoroacetic acid (0.5 mL) added. The reaction mixture was stirred at room temperature for 3 h then passed through an SCX cartridge eluting with methanol then with 2 M ammonia in methanol. 20% of the resulting residue was purified by reverse phase column chromatography to afford the title compound (6 mg, 7% yield)

LCMS (Method 1, ES⁺) 1.60 min, 362 *m/z* (M+H)⁺.

10

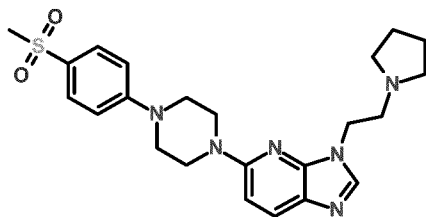
Examples 117-118

The following compounds were synthesized from Intermediate 7 and the appropriate aryl bromide in accordance with General Procedure 3.

Examples were analysed by LCMS Method 3.

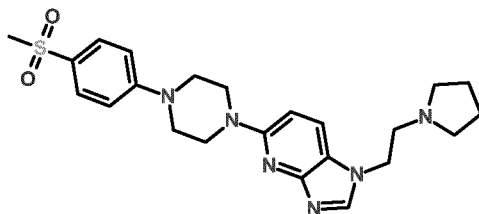
15

Example	Structure	Compound Name	LCMS RT (min)	Mass Ion
117		4-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenol	1.16	391
118		6-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyridine-3-carbonitrile	1.68	401

Example 119

5-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-3-[2-(pyrrolidin-1-yl)ethyl]-3H-imidazo[4,5-b]pyridine

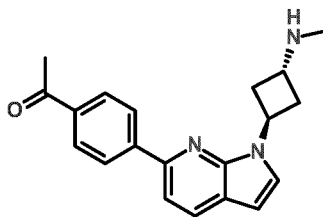
- 5 5-Bromo-1H-imidazo[4,5,b]pyridine (150 mg, 0.75 mmol) and 1-(2-chloroethyl)pyrrolidine hydrochloride (1.2 eq., 0.8 mmol) were reacted following General Procedure 2. After an aq. work-up, the crude residue was reacted with 1-[4-(methylsulfonyl)phenyl]piperazine (1.5 eq.) following General Procedure 3. The residue was purified by reverse phase column chromatography to yield Example 119 (2 mg, 1% yield).
- 10 LCMS (Method 1, ES⁺) 1.52 min, 455 m/z (M+H)⁺.

Example 120

- 15 5-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-imidazo[4,5-b]pyridine

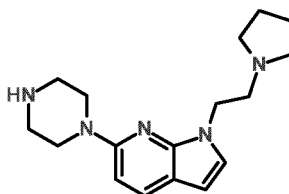
Example 120 was prepared according to the procedure described for Example 119 and isolated as an alternative regioisomer during purification.

LCMS (Method 1, ES⁺) 1.61 min, 455 m/z (M+H)⁺.

Example 1211-(4-{1-[trans-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}phenyl)ethanone

5 Intermediate 35 (100 mg, 0.3 mmol) and 4-acetylphenylboronic acid (1.5 eq., 0.4 mmol), were reacted following General Procedure 10. The residue was dissolved in DCM (0.05 M) and TFA (1 mL) was added at 0°C, then the reaction was stirred at ambient for an additional 2 hours. The residue was filtered over a SCX column and washed with DCM and MeOH, then eluted with methanolic NH₃ (4 M). The product was purified by reverse phase chromatography to yield
10 Example 121 (35 mg, 42% yield).

LCMS (Method 1, ES+) 1.71 min, 320 m/z (M+H)⁺.

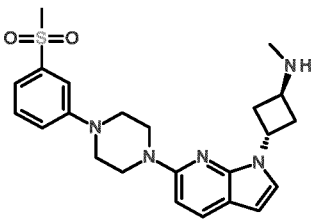
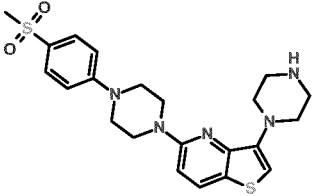
Example 122

15 6-piperazin-1-yl-1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridine

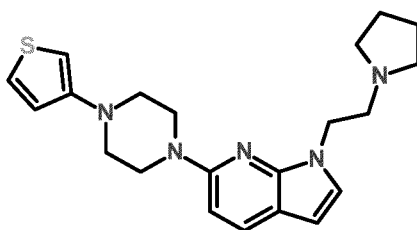
Example 122 is also Intermediate 7. Synthesis and characterisation are described above.

Examples 123-124

Examples 123-124 were prepared in two steps according to General Procedure 3 followed by general procedure 13 and analysed by LCMS Method 1.

Example	Structure	Amine or Intermediate	Heteroaryl halide	Compound Name	LCMS RT (min)	Mass Ion
123		1-(3-methylsulfonyl)piperazine. HCl	Intermediate 35	trans-N-methyl-3-[6-[4-(3-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutan-1-amine	1.75	440
124		1-[4-(methylsulphonyl)phenyl]piperazine	Intermediate 44	5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-3-piperazin-1-yl-thieno[3,2-b]pyridine	1.64	458

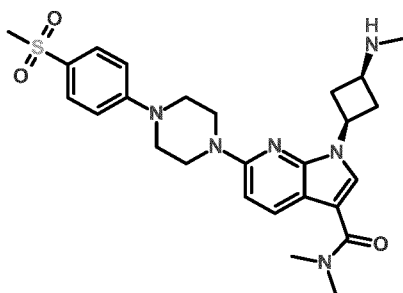
5

Example 1251-(2-pyrrolidin-1-ylethyl)-6-[4-(3-thienyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine

Example 125 was prepared from Intermediate 7 and 3-bromothiophene in accordance with General Procedure 3 and analysed by LCMS Method 3.

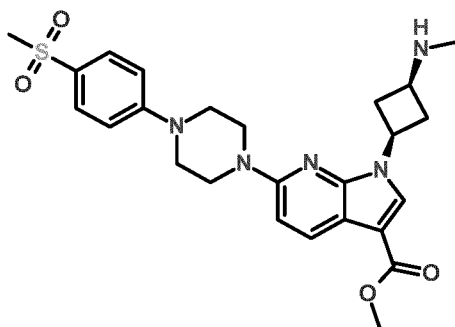
LCMS (Method 3, ES⁺) 1.73 min, 382 m/z (M+H)⁺

10

Example 126

cis-N,N-dimethyl-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carboxamide

- 5 Intermediate 48 (20 mg, 0.05 mmol), dimethylamine (1.2 equiv., 0.06 mmol, 2 mmol/mL) and HATU (25 mg, 0.07 mmol, 1.4 equiv.) were dissolved in DMF (0.25 mL, 0.25 M) and DIPEA (0.04 mL, 0.2 mmol, 4 equiv) was added. The mixture was then stirred at room temperature under N₂ until the reaction was complete (1h). Then, DCM and NH₄Cl aq. sat solution were added to the reaction mixture and the layers were separated. The aq. phase was extracted with
- 10 DCM, the layers were separated and the volatiles were removed under vacuum. The resulting residue was dissolved in 1,4-dioxane (0.05 M) and was reacted with 1-[4-(methylsulfonyl)phenyl]piperazine (1.5 equiv., 0.07 mmol) following General Procedure 3. The reaction mixture was cooled to r.t. and DCM and H₂O were added. The layers were separated and the aqueous phase was extracted with EtOAc. The combined organic layers were dried
- 15 over Na₂SO₄ and the solvents were removed under vacuum. The residue was dissolved in DCM (5 mL) and TFA (1mL) was added. The mixture was stirred at ambient temperature for 2 hours. The reaction crude was filtered through an SCX column and washed with MeOH and DCM. The product was eluted with NH₃ (4N) in MeOH. Volatiles were removed under vacuum and the residue purified by preparative chromatography to give
- 20 Example 126 (8 mg, 34% yield).
LCMS (Method 1, ES⁺) 1.44 min, 511 m/z (M+H)⁺

Example 127

cis-methyl 1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carboxylate

Intermediate 47 (100 mg, 0.17 mmol) was dissolved in DCM (8 mL, 0.02 M) and cooled to 0°C. TFA (2 mL) was added and the mixture stirred at r.t. for 2 h. The mixture was filtered through an SCX column and the column washed with MeOH and then eluted with 4 N NH₃ in MeOH. After removing the volatiles, the residue was purified by preparative column chromatography to afford Example 127 (11 mg, 13% yield).

LCMS (Method 1, ES⁺) 1.67 min, 498 m/z (M+H)⁺

10 **Examples 128-169**

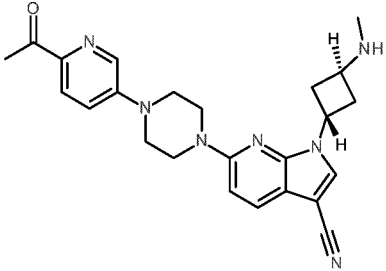
Examples 128-169 were prepared in two steps according to General Procedure 3 then 13.

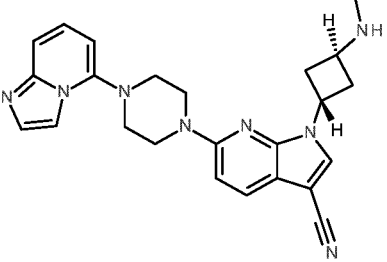
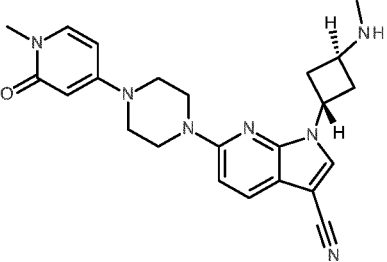
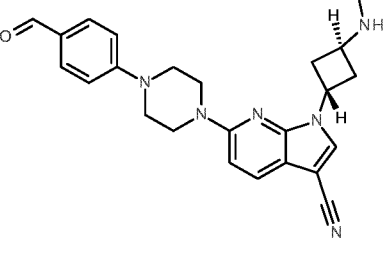
Examples 128-152 were analysed by LCMS Method 1.

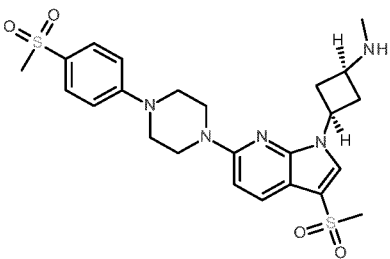
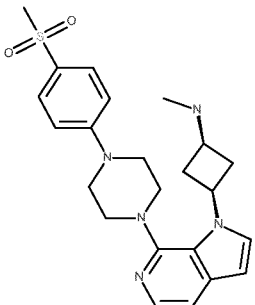
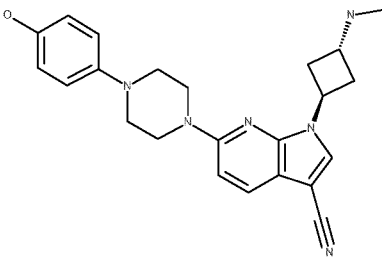
Examples 153-165 and example 168 were analysed by LCMS Method 11.

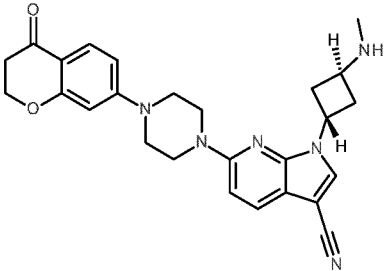
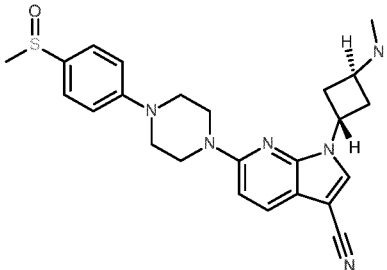
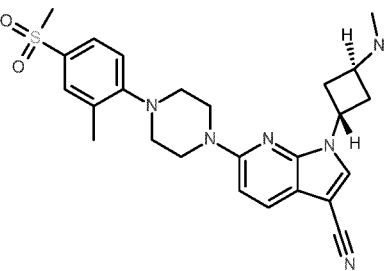
Examples 166-167 and example 169 were analysed by LCMS Method 13.

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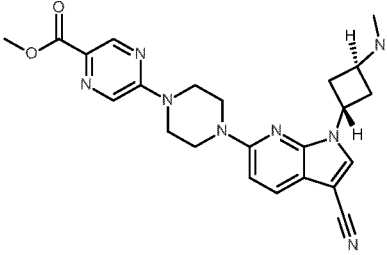
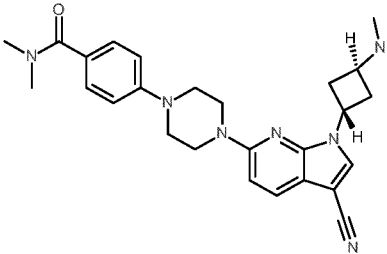
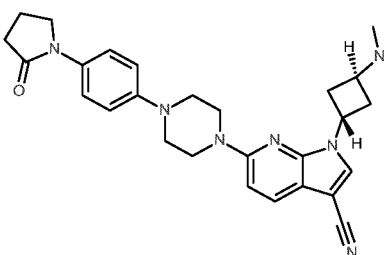
Example	Structure	Amine	Heteroaryl halide	Compound Name	LCM S RT (min)	Mass Ion
128		49	2-acetyl-5-bromopyridine	trans-6-[4-(6-acetyl-3-pyridyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.50	430

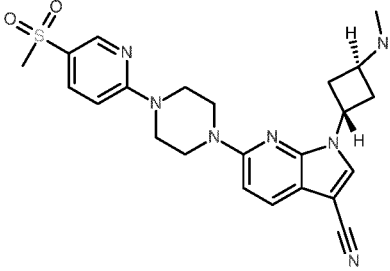
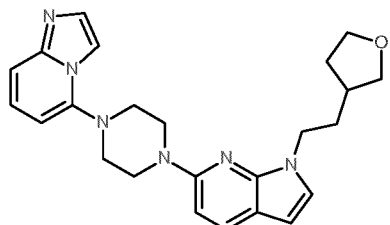
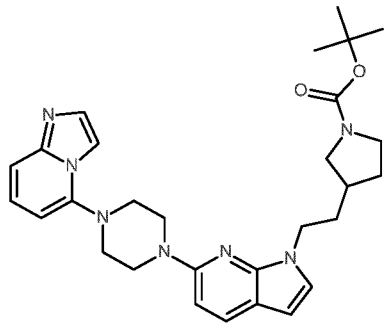
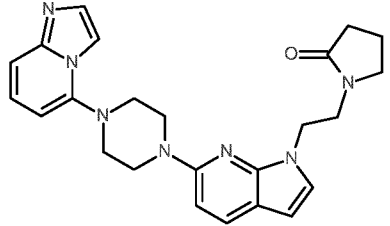
129		49	5-bromoimidazo[1,2-a]pyridine	trans-6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl)-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.81	427
130		49	4-bromo-1-methylpyridin-2(1H)-one	trans-1-[3-(methylamino)cyclobutyl]-6-[4-(1-methyl-2-oxo-4-pyridyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.47	418
131		49	(4-piperazin-1-ylphenyl)methanol	trans-6-[4-(4-formylphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.08	415

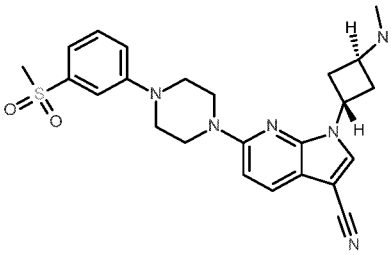
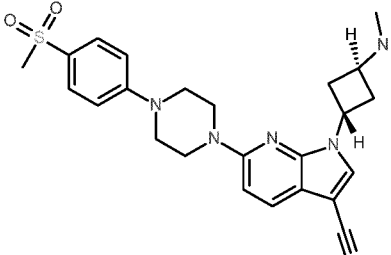
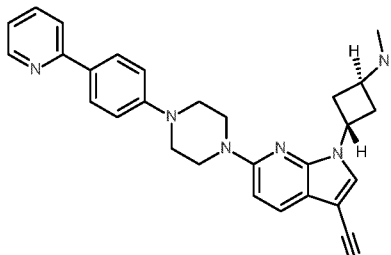
132		1-[4-(methylsulfonyl)phenyl]piperazine	53	cis-N-methyl-3-[3-methylsulfonyl-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutylamine	1.34	518
133		1-[4-(methylsulfonyl)phenyl]piperazine	54	trans-N-methyl-3-[7-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-c]pyridin-1-yl]cyclobutylamine	1.38	440
134		1-(4-hydroxyphenyl)piperazine	40	trans-6-[4-(4-hydroxyphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.65	403

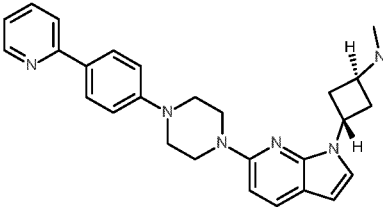
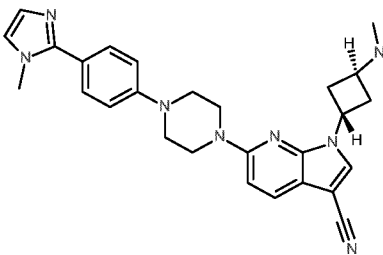
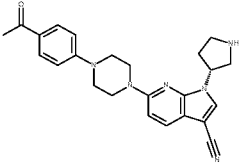
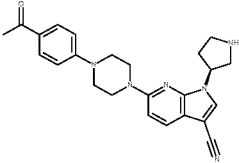
135		49	7-bromochroman-4-one	trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-oxochroman-7-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.03	457
136		49	1-bromo-4-[(R)-methylsulfinyl]benzene	trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-[(R)-methylsulfinyl]phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.87	449
137		49	1-bromo-4-methanesulfonyl-2-methylbenzene	trans-1-[3-(methylamino)cyclobutyl]-6-[4-(2-methyl-4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.26	479

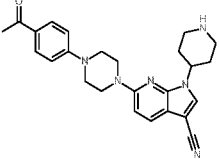
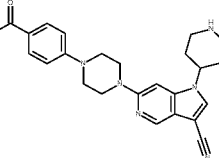
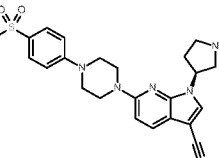
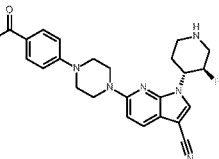
<p>138</p>		<p>49</p>	<p>5-bromo-2-methylisoindol-1-one</p>	<p>trans-1-[3-(methylamino)cyclobutyl]-6-[4-(2-methyl-1-oxo-3H-isoindol-5-yl)pyrazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile</p>	<p>1.92</p>	<p>456</p>
<p>139</p>		<p>49</p>	<p>methyl 5-bromonicotinate</p>	<p>trans-methyl 5-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyridine-3-carboxylate</p>	<p>1.98</p>	<p>446</p>
<p>140</p>		<p>49</p>	<p>methyl 2-bromopyridine-4-carboxylate</p>	<p>trans-methyl 2-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyridine-4-carboxylate</p>	<p>2.07</p>	<p>446</p>

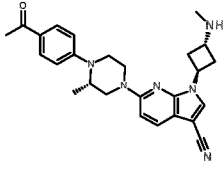
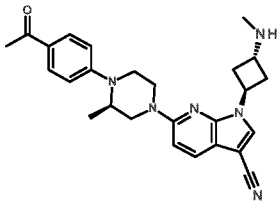
<p>141</p>	 <p>The structure shows a methyl 5-bromopyrazine-2-carboxylate group connected via a piperazine ring to a pyridine ring, which is further connected to a pyrrolo[2,3-b]pyridine-6-yl group. The pyrrolo[2,3-b]pyridine core has a cyano group at the 3-position and a methylamino group at the 4-position.</p>	<p>49</p>	<p>methyl 5-bromopyrazine-2-carboxylate</p>	<p>trans-methyl 5-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyrazine-2-carboxylate</p>	<p>1.74</p>	<p>447</p>
<p>142</p>	 <p>The structure shows a 4-bromo-N,N-dimethylbenzamide group connected via a piperazine ring to a pyridine ring, which is further connected to a pyrrolo[2,3-b]pyridine-6-yl group. The pyrrolo[2,3-b]pyridine core has a cyano group at the 3-position and a methylamino group at the 4-position.</p>	<p>49</p>	<p>4-bromo-N,N-dimethylbenzamide</p>	<p>trans-4-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]-N,N-dimethylbenzamide</p>	<p>1.81</p>	<p>458</p>
<p>143</p>	 <p>The structure shows a 1-(4-bromophenyl)pyrrolidin-2-one group connected via a piperazine ring to a pyridine ring, which is further connected to a pyrrolo[2,3-b]pyridine-6-yl group. The pyrrolo[2,3-b]pyridine core has a cyano group at the 3-position and a methylamino group at the 4-position.</p>	<p>49</p>	<p>1-(4-bromophenyl)pyrrolidin-2-one</p>	<p>trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-(2-oxopyrrolidin-1-yl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile</p>	<p>1.90</p>	<p>470</p>

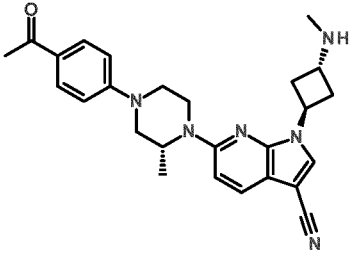
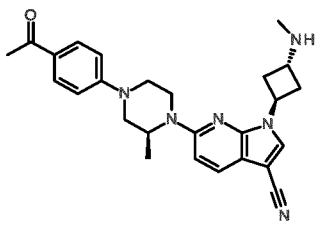
144		49	2-bromo-5-(methylsulfonyl)pyridine	trans-1-[3-(methylamino)cyclobutyl]-6-[4-(5-methylsulfonylpyridin-2-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.76	466
145		5	67	6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl)-1-[2-(oxolan-3-yl)ethyl]pyrrolo[2,3-b]pyridine	2.27	417
146		5	68	tert-butyl 3-[2-[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]pyrrolidine-1-carboxylate	2.80	516
147		5	69	1-[2-[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]pyrrolidin-2-one	1.36	430

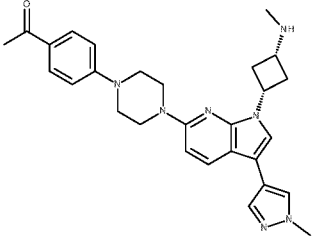
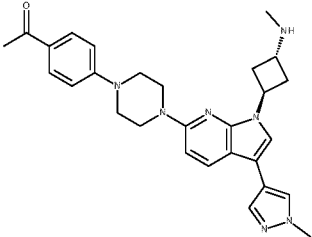
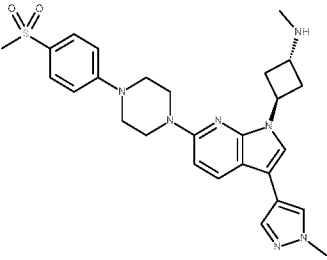
148		1-(3-(methylsulfonyl)phenyl)piperazine HCl	40	trans-1-[3-(methylamino)cyclobutyl]-6-[4-(3-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.07	465
149		1-[4-(methylsulfonyl)phenyl]piperazine	40	trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.04	465
150		71	40	trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-pyridin-2-ylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.38	464

<p>151</p>		<p>71</p>	<p>35</p>	<p>trans-N-methyl-3-[6-[4-(4-pyridin-2-ylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutan-1-amine</p>	<p>1.94</p>	<p>439</p>
<p>152</p>		<p>49</p>	<p>70</p>	<p>trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-(1-methylimidazol-2-yl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile</p>	<p>1.35</p>	<p>467</p>
<p>153</p>		<p>1-[4-(piperazin-1-yl)phenyl]ethan-1-one</p>	<p>74</p>	<p>6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3R)-pyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile</p>	<p>2.01</p>	<p>415</p>
<p>154</p>		<p>1-[4-(piperazin-1-yl)phenyl]ethan-1-one</p>	<p>75</p>	<p>6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3S)-pyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile</p>	<p>2.00</p>	<p>415</p>

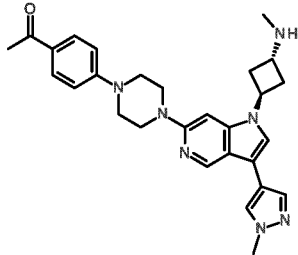
155		1-(4-(piperazin-1-yl)phenyl)ethanone	76	6-[4-(4-acetylphenyl)piperazin-1-yl]-1-piperidin-4-ylpyrrolo[2,3-b]pyridine-3-carbonitrile	2.08	429
156		1-(4-(piperazin-1-yl)phenyl)ethanone	77	6-[4-(4-acetylphenyl)piperazin-1-yl]-1-piperidin-4-ylpyrrolo[3,2-c]pyridine-3-carbonitrile	1.55	429
157		1-(4-(methylsulfonylphenyl)piperazin-1-yl)ethanone	75	6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-[(3S)-pyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.86	451
158	 OR Enantiomer	1-(4-(piperazin-1-yl)phenyl)ethanone	73	6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[rel-(3R,4R)-3-fluoropiperidin-4-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.15	448

159		78	50	Trans-6-[(3S)-4-(4-acetylphenyl)-3-methylpiperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.15	443
160		79	50	trans-6-[(3R)-4-(4-acetylphenyl)-3-methylpiperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.18	443

161		80	50	trans-6-[(2R)-4-(4-acetylphenyl)-2-methylpiperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.19	443
162		81	50	trans-6-[(2S)-4-(4-acetylphenyl)-2-methylpiperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.18	443

<p>163</p>		<p>1-(4-piperazin-1-ylphenyl)ethanone</p>	<p>90</p>	<p>cis-1-[4-[4-[1-[3-(methylamino)cyclobutyl]-3-(1-methylpyrazol-4-yl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone</p>	<p>2.06</p>	<p>484</p>
<p>164</p>		<p>1-(4-piperazin-1-ylphenyl)ethanone</p>	<p>91</p>	<p>trans-1-[4-[4-[1-[3-(methylamino)cyclobutyl]-3-(1-methylpyrazol-4-yl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone</p>	<p>2.06</p>	<p>484</p>
<p>165</p>		<p>1-(4-methanesulfonylphenyl)piperazine</p>	<p>91</p>	<p>trans-N-methyl-3-[3-(1-methylpyrazol-4-yl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutan-1-amine</p>	<p>1.83</p>	<p>520</p>

<p>166</p>		<p>1-(4-piperazin-1-ylphenyl)ethanone</p>	<p>92</p>	<p>1-[4-[4-[3-(2-methylpyridin-3-yl)-1-piperidin-4-yl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone</p>	<p>2.67</p>	<p>495</p>
<p>167</p>		<p>1-(4-piperazin-1-ylphenyl)ethanone</p>	<p>93</p>	<p>1-[4-[4-[3-(1-methylpyrazol-3-yl)-1-piperidin-4-yl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone</p>	<p>3.17</p>	<p>485</p>
<p>168</p>		<p>1-(4-piperazin-1-ylphenyl)ethanone</p>	<p>94</p>	<p>1-[4-[4-[3-(2-methylpyrimidin-5-yl)-1-piperidin-4-yl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone</p>	<p>2.00</p>	<p>429</p>

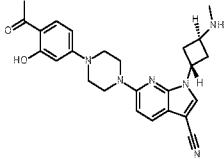
169		1-(4-piperazin-1-ylphenyl)ethanone	95	1-[4-[4-[1-[3-(methylamino)cyclobutyl]-3-(1-methylpyrazol-4-yl)pyrrolo[3,2-c]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone	2.45	484
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Examples 170-186

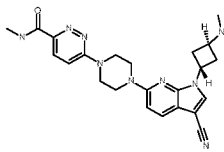
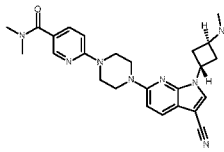
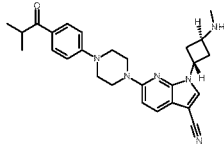
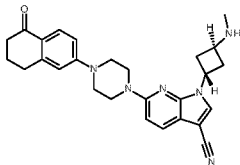
Examples 170-186 were prepared in two steps according to General Procedure 14 then 13.

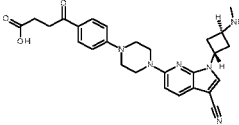
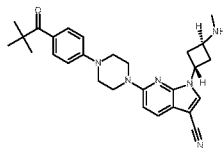
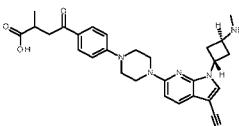
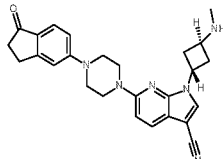
Examples 170-182 were analysed by LCMS Method 1. Examples 183-186 were analysed by LCMS Method 11.

5

Example	Structure	Intermediate	Heteroaryl halide	Compound Name	LCMS RT (min)	Mass Ion
170		49	4'-fluoro-2'-hydroxyacetophenone	trans-6-[4-(4-acetyl-3-hydroxyphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.27	445

171		49	2',4'-difluoroacetophenone	trans-6-[4-(4-acetyl-3-fluorophenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.09	447
172		49	2',4'-difluoroacetophenone	trans-6-[4-(2-acetyl-5-fluorophenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.18	447
173		49	2-chloropyrimidine-4-carboxamide	trans-2-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyrimidine-4-carboxamide	1.65	432
174		49	6-chloro-N,N-dimethylpyridine-2-carboxamide	trans-6-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]-N,N-dimethylpyridine-2-carboxamide	1.79	459

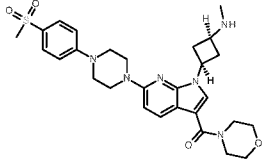
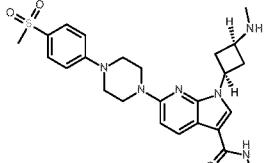
175		49	6-chloro-N-methylpyridazine-3-carboxamide	trans-6-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]-N-methylpyridazine-3-carboxamide	1.56	446
176		49	6-chloro-N,N-dimethylnicotinamide	trans-6-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]-N,N-dimethylpyridine-3-carboxamide	1.68	459
177		49	1-(4-fluorophenyl)-2-methylpropan-1-one	Trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-(2-methylpropanoyl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.46	457
178		49	6-fluoro-1-tetralone	Trans-1-[3-(methylamino)cyclobutyl]-6-[4-(1-oxotetralin-6-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.19	455

179		49	3-(4-fluorophenyl)propionic acid	Trans-4-[4-[4-[3-cyano-1-(3-(methylamino)cyclobutyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]-4-oxo-butanoic acid	1.49	487
180		49	1-(4-fluorophenyl)-2,2-dimethylpropan-1-one	Trans-6-[4-[4-(2,2-dimethylpropanoyl)phenyl]piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.65	471
181		49	2-methyl-4-oxo-4-(4'-fluorophenyl)butyric acid	Trans-4-[4-[4-[3-cyano-1-(3-(methylamino)cyclobutyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]-2-methyl-4-oxo-butanoic acid	1.52	499
182		49	5-fluoro-1-indanone	Trans-1-[3-(methylamino)cyclobutyl]-6-[4-(1-oxoindan-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.02	441

183		49	1-(6-chloropyridin-3-yl)ethanone	Trans-6-[4-(5-acetylpyridin-2-yl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.80	430
184		49	1-(2-chloropyrimidin-5-yl)ethan-1-one	Trans-6-[4-(5-acetylpyrimidin-2-yl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.86	431
185		49	1-(5-chloropyrazin-2-yl)ethan-1-one	Trans-6-[4-(5-acetylpyrazin-2-yl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.82	431
186		49	1-(6-chloropyridazin-3-yl)ethanone	Trans-6-[4-(6-acetylpyridazin-3-yl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.79	431

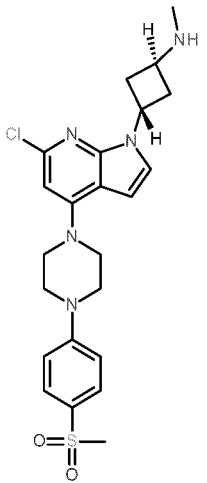
Examples 187-188

Examples 187-188 were prepared in two steps according to General Procedure 18 then 13 and analysed by LCMS Method 1.

Example	Structure	Carboxylic acid	Amine	Compound Name	LCMS RT (min)	Mass Ion
187		51	morpholine	cis-[1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-3-yl]-morpholinomethanone	1.40	553
188		51	methylamine	cis-N-methyl-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carboxamide	1.30	497

Example 189

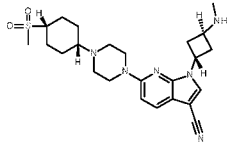
Example 189 was prepared in two steps according to General Procedure 9, 14 then 13 and analysed by LCMS Method 1.

Example	Structure	Intermediate	Secondary alcohol coupling partner	Amine	Compound Name	LCMS RT (min)	Mass Ion
189		4,6-dichloro-1H-pyrrolo[2,3-b]pyridine	cis-tert-butyl 3-hydroxycyclobutylcarbamate	1-[4-(methylsulfonyl)phenyl]piperazine	trans-3-[6-chloro-4-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]-N-methylcyclobutanamine	1.79	474 & 476

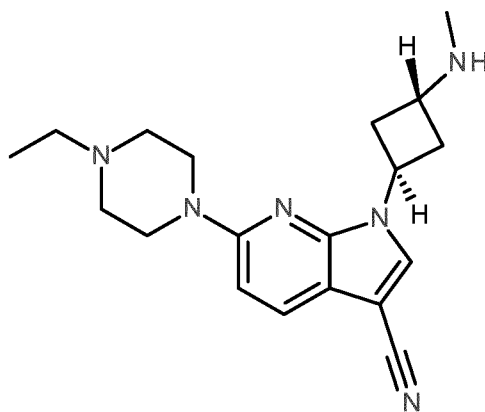
Examples 190-193

Examples 190-193 were prepared in two steps according to General Procedure 12 then 13 and analysed by LCMS Method 1.

5

Example	Structure	Intermediate	Ketone	Compound Name	LCMS RT (min)	Mass Ion
190		49	4-(methylsulfonyl)cyclohexanone	trans-1-[3-(methylamino)cyclohexyl]-6-[4-(4-methylsulfonylcyclohexyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.62	471

191		49	4-(methylsulfonyl)cyclohexanone	trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylcyclohexyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.75	471
192		49	1-N-(methylsulfonyl)-4-piperidinone	trans-1-[3-(methylamino)cyclobutyl]-6-[4-(1-methylsulfonyl-4-piperidinyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.75	472
193		49	1-acetyl-4-piperidone	trans-6-[4-(1-acetyl-4-piperidyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.60	436

Examples 194

trans-6-(4-ethylpiperazin-1-yl)-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile

Example 194, was isolated as a side-product in the synthesis of UCB1711019 Example 192

LCMS (Method 1, ES⁺) 1.71 min, 339 *m/z* (M+H)⁺

5 Examples 195-199

Examples 195-199 were prepared according to General Procedure 12 from the specified starting material example (SM example) and analysed by LCMS Method 11.

Example	Structure	SM name	SM example	Compound Name	LCMS RT (min)	Mass Ion
195		6-[4-(4-acetylphenyl)piperazin-1-yl]-1-piperidin-4-ylpyrrolo[2,3-b]pyridine-3-carbonitrile	155	6-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpiperidin-4-yl)pyrrolo[2,3-b]pyridine-3-carbonitrile	2.09	443
196		6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3S)-pyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	154	6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3S)-1-methylpyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.01	429
197		6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3R)-pyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	153	6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3R)-1-methylpyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.01	429

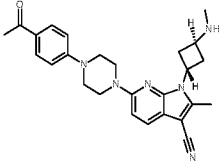
198		6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-[(3S)-pyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	157	1-[(3S)-1-methylpyrrolidin-3-yl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	1.83	465
199		6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(1r,3r)-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile	24	6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(1r,3r)-3-(dimethylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.07	443

Examples 200-201

Examples 200-201 were prepared in two steps according to General Procedure 5 (Example 200 used a modified procedure with toluene as solvent) then General Procedure 13.

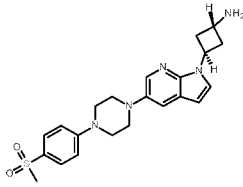
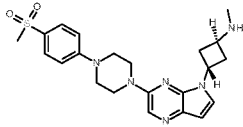
- 5 Example 200 was analysed by LCMS Method 1. Example 201 was analysed by LCMS Method 9.

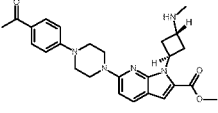
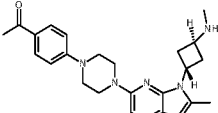
Example	Structure	Amine	Heteroaryl halide	Compound Name	LCMS RT (min)	Mass Ion
200		Intermediate 49	4'-bromo-2,2,2-trifluoroacetophenone	trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-(2,2,2-trifluoroacetyl)phenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.53	483

201		1-(4-piperazin-1-ylphenyl)ethanone	Intermediate 60	trans-6-[4-(4-acetylphenyl)piperazin-1-yl]-2-methyl-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile	2.56	443
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Examples 202-205

Examples 202-205 were prepared in three steps according to General Procedure 9, 5 then 13. Example 202 was analysed by LCMS Method 1. Examples 203-205 were analysed by LCMS Method 9.

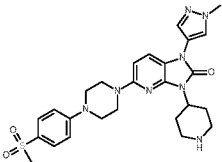
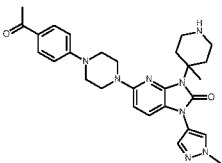
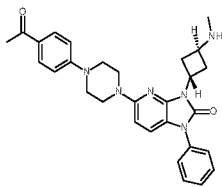
Example	Structure	Heterocycle	Secondary alcohol coupling partner	Amine	Compound Name	LCMS RT (min)	Mass Ion
202		5-bromo-1H-pyrrolo[2,3-b]pyridine	cis-tert-butyl 3-hydroxycyclobutyl carbamate	1-[4-(methylsulfonyl)phenyl]piperazine	trans-3-[5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutylamine	1.40	426
203		3-bromo-5H-pyrrolo[2,3-b]pyrazine	cis-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate	1-[4-(methylsulfonyl)phenyl]piperazine	trans-N-methyl-3-[3-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyrazin-5-yl]cyclobutylamine	1.34	441

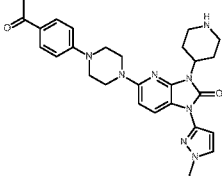
<p>204</p>		<p>methyl 6-chloro-1H-pyrrolo[2,3-b]pyridine-2-carboxylate</p>	<p>Cis-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate</p>	<p>1-(4-piperazin-1-ylphenyl)ethanone</p>	<p>trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate</p>	<p>2.98</p>	<p>462</p>
<p>205</p>		<p>6-chloro-2-methyl-1H-pyrrolo[2,3-b]pyridine</p>	<p>Cis-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate</p>	<p>1-(4-piperazin-1-ylphenyl)ethanone</p>	<p>trans-1-[4-[4-[2-methyl-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone</p>	<p>2.46</p>	<p>418</p>

Examples 206-211

Examples 206-211 were prepared in three steps according to General Procedure 17, 5 then 13 and analysed by LCMS Method 9.

Example	Structure	Intermediate	Aryl halide (1 st Buchwald)	Amine (2 nd Buchwald)	Compound Name	LCMS RT (min)	Mass Ion
206		62	4-iodo-1-methylpyrazole	1-(4-piperazin-1-ylphenyl)ethanone	trans-5-[4-(4-acetylphenyl)piperazin-1-yl]-3-[3-(methylamino)cyclobutyl]-1-(1-(4-phenyl)ethanone)imidazo[4,5-b]pyridin-2-one	2.10	501
207		63	4-iodo-1-methylpyrazole	1-(4-piperazin-1-ylphenyl)ethanone	5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-(4-phenyl)ethanone)-3-(4-piperidyl)imidazo[4,5-b]pyridin-2-one	2.27	501

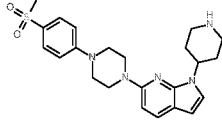
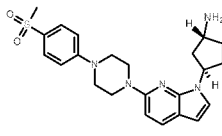
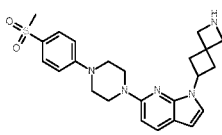
208		63	4-iodo-1-methylpyrazole	1-(4-methylsulfonylphenyl)piperazine	1-(1-methylpyrazol-4-yl)-5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-3-(4-piperidyl)imidazo[4,5-b]pyridin-2-one	2.20	537
209		64	4-iodo-1-methylpyrazole	1-(4-piperazin-1-ylphenyl)ethanone	5-[4-(4-acetylphenyl)piperazin-1-yl]-3-(4-methyl-4-piperidyl)-1-(1-methylpyrazol-4-yl)imidazo[4,5-b]pyridin-2-one	2.17	515
210		62	iodobenzene	1-(4-piperazin-1-ylphenyl)ethanone	trans-5-[4-(4-acetylphenyl)piperazin-1-yl]-3-[3-(methylamino)cyclobutyl]-1-phenylimidazo[4,5-b]pyridin-2-one	2.23	497

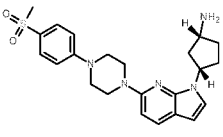
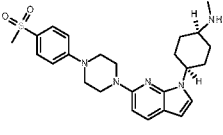
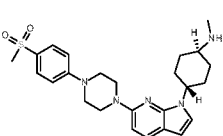
211		63	3-iodo-1-methylpyrazole	1-(4-piperazin-1-ylphenyl)ethanone	5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpyrazol-3-yl)-3-(4-piperidyl)imidazo[4,5-b]pyridin-2-one	2.19	501
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Examples 212-217

Examples 212-217 were prepared in two steps from intermediate 18 and a secondary alcohol according to General Procedure 9 then 13 and analysed by LCMS Method 3.

5

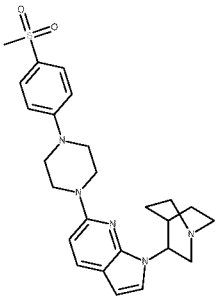
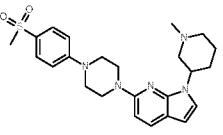
Example	Structure	Secondary alcohol	Compound Name	LCMS RT (min)	Mass Ion
212		1-boc-4-hydroxypiperidine	6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-(4-piperidyl)pyrrolo[2,3-b]pyridine	1.47	440
213		cis-3-N-boc-aminocyclopentanol	(1R,3R)-3-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclopentanamine	1.49	440
214		tert-butyl 6-hydroxy-2-azaspiro[3.3]heptane-2-carboxylate	1-(2-azaspiro[3.3]heptan-6-yl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine	1.62	452

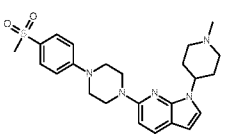
215		trans-3-N-boc-aminocyclopentanol	(1R,3S)-3-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclopentanamine	1.57	440
216		trans-(4-hydroxy-cyclohexyl)-methyl-carbamic acid tert-butyl ester	cis-N-methyl-4-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclohexanamine	1.60	468
217		cis-(4-hydroxy-cyclohexyl)-methyl-carbamic acid tert-butyl ester	trans-N-methyl-4-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclohexanamine	1.67	468

Examples 218-220

Examples 218-220 were prepared from intermediate 18 and a secondary alcohol according to General Procedure 9 and analysed by LCMS Method 3.

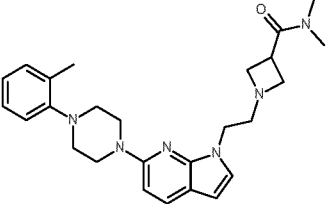
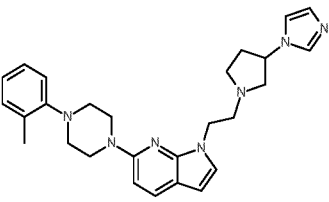
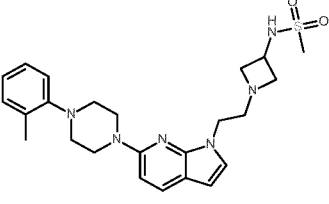
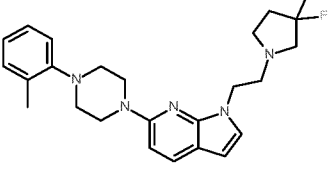
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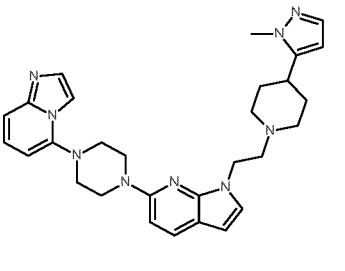
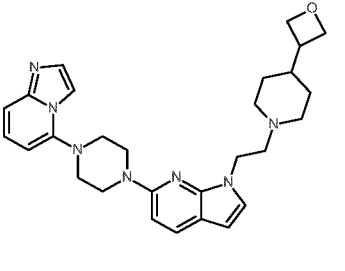
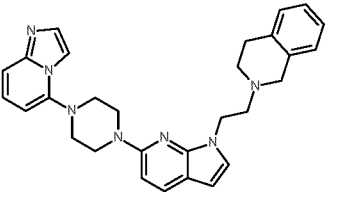
Example	Structure	Secondary alcohol	Compound Name	LCMS RT (min)	Mass Ion
218		quinuclidin-3-ol	6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-quinuclidin-3-yl-pyrrolo[2,3-b]pyridine	1.50	466
219		3-hydroxy-1-methylpiperidine	1-(1-methyl-3-piperidyl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine	1.45	454

220		1-methyl-4-piperidinol	1-(1-methyl-4-piperidyl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine	1.56	454
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Examples 221-227

The following compounds were synthesised from stated intermediate and the appropriate amine in accordance with General Procedure 7 or General Procedure 8, depending on the intermediate, and analysed by LCMS Method 3.

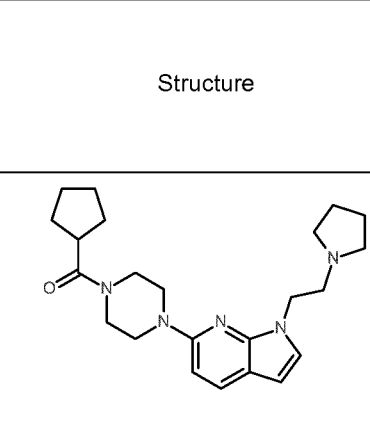
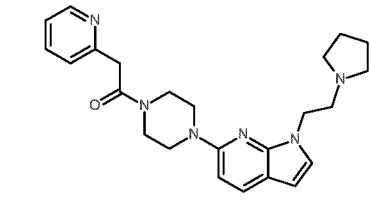
Example	Structure	Intermediate	Compound Name	LCMS RT (min)	Mass Ion
221		17	N,N-dimethyl-1-[2-[6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]azetidino-3-carboxamide	1.94	447
222		17	1-[2-(3-imidazol-1-ylpyrrolidin-1-yl)ethyl]-6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine	2.11	456
223		17	N-[1-[2-[6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]azetidino-3-yl]methanesulfonamide	1.93	469
224		17	1-[2-(3-fluoro-3-methyl-pyrrolidin-1-yl)ethyl]-6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine	2.07	422

225		15	6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl)-1-[2-[4-(2-methylpyrazol-3-yl)-1-piperidyl]ethyl]pyrrolo[2,3-b]pyridine	1.25	510
226		15	6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl)-1-[2-[4-(oxetan-3-yl)-1-piperidyl]ethyl]pyrrolo[2,3-b]pyridine	1.22	486
227		15	2-[2-[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]-3,4-dihydro-1H-isoquinoline	1.35	478

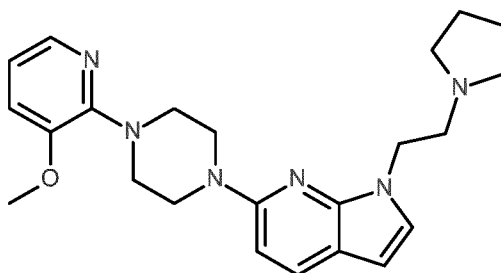
Examples 228-233

The following compounds were synthesised from Intermediate 7 and the appropriate carboxylic acid in accordance with General Procedure 7 and analysed by LCMS Method 3.

5

Example	Structure	Compound Name	LCMS RT (min)	Mass Ion
228		cyclopentyl-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]methanone	1.62	396
229		2-(2-pyridyl)-1-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]ethanone	1.11	419

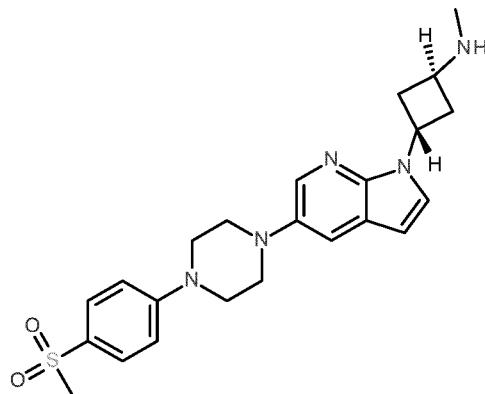
230		cyclobutyl-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]methanone	1.52	382
231		phenyl-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]methanone	1.58	404
232		4-pyridyl-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]methanone	1.20	405
233		4-piperidyl-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]methanone	0.85	411

Example 234

6-[4-(3-methoxy-2-pyridyl)piperazin-1-yl]-1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridine

5 Prepared using Intermediate 7 and 2-chloro-3-methoxypyridine using General Procedure 3.

LCMS (Method 3, ES⁺) 1.34 min, 407 *m/z* (M+H)⁺

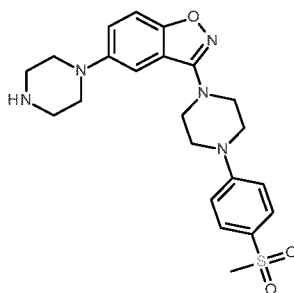
Example 235

5 trans-N-methyl-3-[5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine

General procedure 9 with 5-bromo-1H-pyrrolo[2,3-b]pyridine and cis-tert-butyl 3-hydroxycyclobutylcarbamate followed by general procedure 5 with 1-[4-(methylsulfonyl)phenyl]piperazine.

- 10 The intermediate trans-tert-butyl N-[3-[5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]carbamate (36 mg, 0.07 mmol) was dissolved in DMF (0.7 ml) then NaH (4 mg, 0.1 mmol) was added under nitrogen. After stirring for 5 minutes, MeI (0.006 ml, 0.1 mmol) was added and the mixture was stirred for a further 10 minutes. The mixture was quenched with brine (10 ml) and the product was extracted with DCM (3 x 10 ml). The combined organics were
- 15 washed with brine (2 x 10 ml), dried (Na₂SO₄) and concentrated in vacuo. The residue was then submitted to general procedure 13 to give the desired product (7 mg).

LCMS (Method 1, ES⁺) 1.45 min, 440 *m/z* (M+H)⁺

Example 236

20

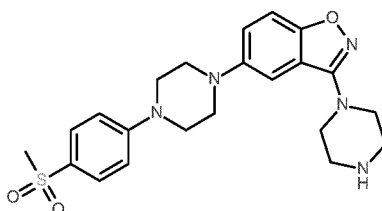
3-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-5-piperazin-1-yl-1,2-benzoxazole

A solution of 1-[4-(methylsulfonyl)phenyl]piperazine (216 mg, 0.90 mmol), 5-bromo-3-chlorobenzo[d]isoxazole (200 mg, 0.82 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.15 ml, 1.0 mmol) in pyridine (4.1 ml) was heated at 100 °C for 3 days. The mixture was cooled to rt, diluted with water (20 ml) and extracted with CHCl₃ (3 x 30 ml). The combined organics were washed with brine (20 ml), dried (Na₂SO₄) and concentrated in vacuo. The product was purified by column chromatography (hexane to EtOAc over 10 CVs) to give 5-bromo-3-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1,2-benzoxazole (140 mg, 40%). General procedure 5 with 1-boc-piperazine followed by general procedure 13 gave the desired product (10 mg).

LCMS (Method 1, ES⁺) 1.39 min, 442 *m/z* (M+H)⁺

10

Example 237



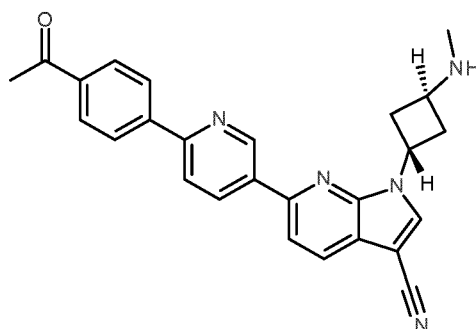
5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-3-piperazin-1-yl-1,2-benzoxazole

A solution of 1-boc-piperazine (171 mg, 0.90 mmol), 5-bromo-3-chlorobenzo[d]isoxazole (200 mg, 0.82 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.15 mL, 1.0 mmol) in pyridine (4.1 mL) was heated at 120 °C for 5 days. The mixture was cooled to rt, diluted with water (10 ml) and brine (10 ml) then extracted with CHCl₃ (3 x 20 ml). The combined organics were washed with brine (20 ml), dried (Na₂SO₄), concentrated in vacuo and purified by column chromatography (hexane/EtOAc) to give 152 mg tert-butyl 4-(5-bromo-1,2-benzoxazol-3-yl)piperazine-1-carboxylate.

20

The intermediate was reacted with 1-[4-(methylsulfonyl)phenyl]piperazine (115 mg) using General Procedure 5, followed by General Procedure 13 to give 23 mg product.

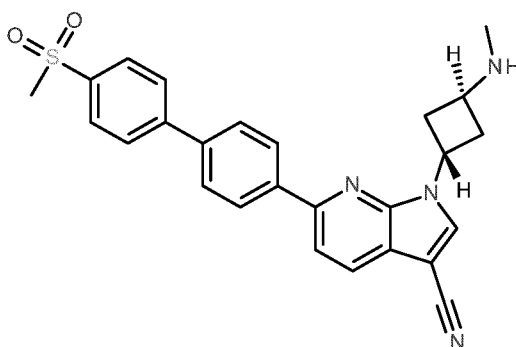
LCMS (Method 1, ES⁺) 1.43 min, 442 *m/z* (M+H)⁺

Example 238

5 trans-6-[6-(4-acetylphenyl)-3-pyridyl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-
carbonitrile

2-Chloropyridine-5-boronic acid (50 mg, 0.305 mmol), Intermediate 40 (124 mg, 0.306 mmol) and tetrakis(triphenylphosphine)palladium(0) (18 mg, 0.0154 mmol) in degassed N,N-dimethylformamide (1.0 mL) was stirred at rt for 40 mins. A degassed solution of sodium carbonate (48.5 mg, 0.458 mmol) in water (0.5 mL) was added, then the mixture was heated at
10 80 °C under N₂ for 2 hours. 4-Acetylphenylboronic acid (75 mg, 0.457 mmol) was added, then the reaction mixture was heated to 80 °C for a further 16 hours. The mixture was diluted with EtOAc (20 ml), water (10 ml) and brine (10 ml) and the layers were separated. The aqueous was further extracted with EtOAc (2 x 20 ml) then the combined organics were washed with brine (3 x 10 ml). The brine washings were back-extracted with DCM (2 x 10 ml) then the combined organics were
15 dried (Na₂SO₄) and concentrated in vacuo. The residue was purified by column chromatography (hexane/EtOAc) then subjected to General Procedure 13 to give 2 mg product.

LCMS (Method 1, ES⁺) 2.05 min, 422 *m/z* (M+H)⁺

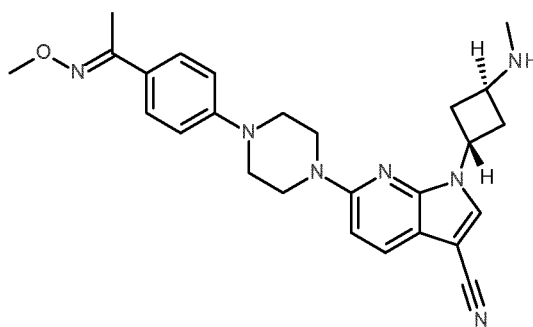
Example 239

trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)phenyl]pyrrolo[2,3-b]pyridine-3-carbonitrile

An oven-dried microwave vial was charged with 4'-bromo-4-methanesulfonyl-biphenyl (85 mg, 0.273 mmol), bis(pinacolato)diboron (69 mg, 0.272 mmol), 2nd generation XPhos precatalyst (19 mg, 0.024 mmol), and potassium acetate (67 mg, 0.683 mmol) before dry 1,4-dioxane (1.2 mL) was added. The resulting mixture was evacuated and backfilled with N₂ three times then stirred at 100 °C. After 1 hour, the mixture was cooled to rt and a freshly prepared solution of intermediate 40 (100 mg, 0.247 mmol) in dry and degassed 1,4-dioxane (0.5 mL) was added followed by a freshly prepared solution and degassed solution of potassium phosphate tribasic (79 mg, 0.372 mmol) in water (0.5 mL). The resulting mixture was stirred at 100 °C under N₂ for 3 hours. The mixture was cooled to rt, diluted with EtOAc (20 ml) and washed with a 1:1 mixture of water (10 ml) and brine (10 ml). The aqueous was further extracted with EtOAc (2 x 20 ml), then the combined organics were dried (Na₂SO₄) and concentrated in vacuo. The residue was purified by column chromatography then subjected to General Procedure 13 to give 44 mg product.

LCMS (Method 1, ES⁺) 2.27 min, 457 *m/z* (M+H)⁺

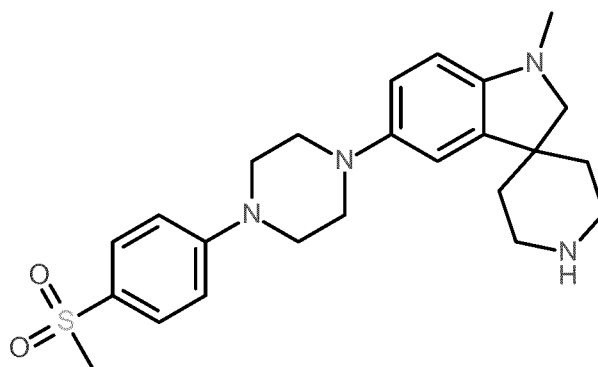
Example 240



trans-6-[4-[4-[(E)-N-methoxy-C-methyl-carbonimidoyl]phenyl]piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile

Intermediate 40 and 1-(4-acetylphenyl)piperazine were subjected to General Procedure 3. Following this, the resulting trans-tert-butyl N-[3-[6-[4-(4-acetylphenyl)piperazin-1-yl]-3-cyano-pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]-N-methyl-carbamate (10 mg, 0.0189 mmol) and O-methylhydroxylamine hydrochloride (2 mg, 0.0239 mmol) were dissolved in methanol (1.0 mL) and stirred at 50 °C. After 3 hours the mixture was concentrated in vacuo and subjected to General procedure 13 to give 1 mg product.

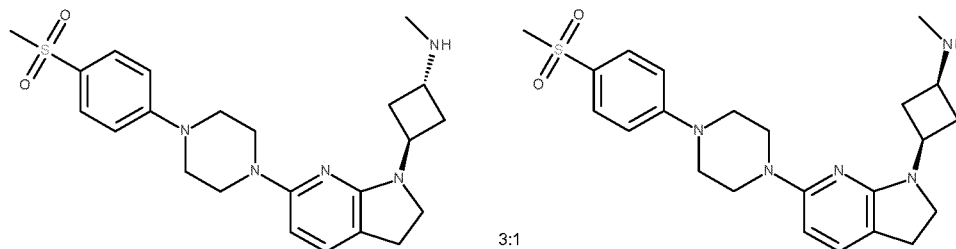
LCMS (Method 1, ES⁺) 2.47 min, 458 *m/z* (M+H)⁺

Example 241**1-methyl-5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]spiro[indoline-3,4'-piperidine]**

A solution of tert-butyl 5-bromospiro[indoline-3,4'-piperidine]-1'-carboxylate (200 mg, 0.52 mmol) in tetrahydrofuran (5 mL) was degassed then cooled with an ice/brine bath. Sodium hydride (31 mg, 0.78 mmol) was added and the mixture stirred for 30 minutes. Iodomethane (0.04 mL, 0.6 mmol, 1) was then added, the mixture stirred for 5 minutes then removed from the ice bath and heated at 40 °C for 16 hours. The reaction was quenched with water (20 ml) and the product was extracted with DCM (2 x 20 ml). The combined organics were washed with brine (20 ml), dried (Na₂SO₄) and concentrated in vacuo. The product tert-butyl 5-bromo-1-methyl-spiro[indoline-3,4'-piperidine]-1'-carboxylate was purified by column chromatography (hexane/EtOAc) then subjected to General Procedure 5 with 1-[4-(methylsulfonyl)phenyl]piperazine followed by General Procedure 13 to give 17 mg product.

LCMS (Method 1, ES⁺) 1.44 min, 441 *m/z* (M+H)⁺

15

Example 242**N-methyl-3-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-2,3-dihydropyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine**

Tert-butyl n-methyl-n-(3-oxocyclobutyl)carbamate (269 mg, 1.35 mmol), sodium triacetoxyborohydride (603 mg, 2.70 mmol) and acetic acid (0.007 mL) were added to a solution of 6-chloro-1H,2H,3H-pyrrolo[2,3-b]pyridine (200 mg, 1.2 mmol) in dichloromethane (1.2 mL) at 0

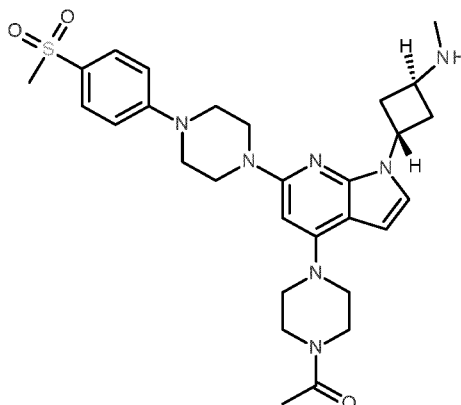
°C. After 5 hours, the mixture was diluted with EtOAc (30 ml) and water (10 ml), washed with sat. aq. NaHCO₃ (2 x 10 ml) and brine (10 ml), dried (Na₂SO₄) and concentrated in vacuo to give tert-butyl N-[3-(6-chloro-2,3-dihydropyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate (440 mg).

- 5 tert-butyl N-[3-(6-chloro-2,3-dihydropyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate (200 mg) and 1-[4-(methylsulfonyl)phenyl]piperazine (157 mg) were subjected to General Procedure 3, followed by General Procedure 13 to give 74 mg product as a 3:1 ratio of isomers.

LCMS (Method 1, ES⁺) 1.61 min, 442 *m/z* (M+H)⁺ [cis]; LCMS (Method 1, ES⁺) 1.66 min, 442 *m/z* (M+H)⁺ [trans]

10

Example 243



trans-1-[4-[1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-4-yl]piperazin-1-yl]ethenone

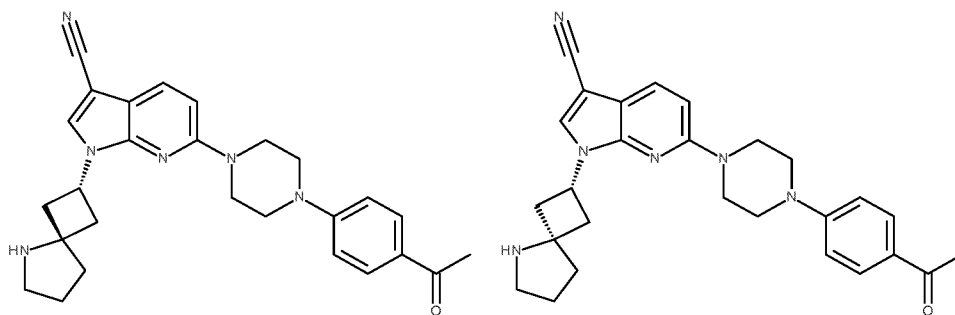
- 15 4,6-Dichloro-1H-pyrrolo[2,3-b]pyridine and cis-tert-butyl N-(cis-3-hydroxycyclobutyl)-N-methylcarbamate were subjected to General Procedure 9. The resulting product was then reacted with piperazine (5 equiv) using General Procedure 14, followed by General Procedure 3 with 1-[4-(methylsulfonyl)phenyl]piperazine to give trans-tert-butyl N-methyl-N-[3-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-4-piperazin-1-yl]-pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]carbamate.
- 20

Acetyl chloride (0.001 mL, 0.01 mmol) was added to a solution of trans-tert-butyl N-methyl-N-[3-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-4-piperazin-1-yl]-pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]carbamate (10 mg, 0.016 mmol) and triethylamine (0.01 mL, 0.07 mmol) in dichloromethane (0.50 mL) and stirred at rt for 5 minutes. Trifluoroacetic acid (0.1 mL) was then

added to the reaction mixture. After 30 minutes, the mixture was concentrated, neutralised with NH_3 in MeOH and purified by prep HPLC to give 3 mg product.

LCMS (Method 1, ES^+) 1.56 min, 566 m/z ($\text{M}+\text{H}$)⁺

5 Example 244



3:1 isomers

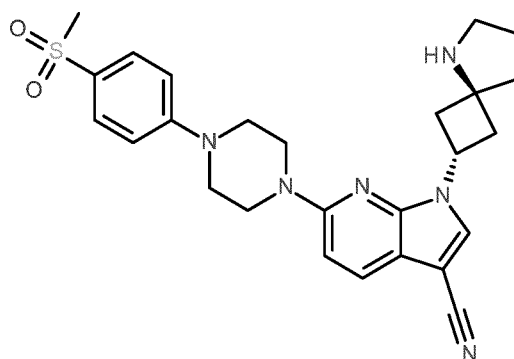
6-[4-(4-acetylphenyl)piperazin-1-yl]-1-(5-azaspiro[3.4]octan-2-yl)pyrrolo[2,3-b]pyridine-3-carbonitrile

10 Sodium borohydride (66 mg, 1.71 mmol) was added to a solution of 5-boc-5-aza-spiro[3.4]octane-2-one (200 mg, 0.86 mmol) in ethanol (10 mL) which was then stirred at rt under N_2 for 30 minutes. The reaction was quenched with sat. aq. NH_4Cl (20 ml) and the ethanol was removed in vacuo. The product was then extracted with EtOAc (3 x 20 ml), dried (Na_2SO_4) and concentrated in vacuo to give tert-butyl 2-hydroxy-5-azaspiro[3.4]octane-5-carboxylate (169 mg, 86%).

15 tert-butyl 2-hydroxy-5-azaspiro[3.4]octane-5-carboxylate (72 mg, 0.32 mmol) was reacted with 6-chloro-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile (55 mg, 0.29 mmol) using General Procedure 9 to give tert-butyl 2-(6-chloro-3-cyano-pyrrolo[2,3-b]pyridin-1-yl)-5-azaspiro[3.4]octane-5-carboxylate (66 mg, 58%).

20 tert-butyl 2-(6-chloro-3-cyano-pyrrolo[2,3-b]pyridin-1-yl)-5-azaspiro[3.4]octane-5-carboxylate (30 mg, 0.078 mmol) and 1-(4-acetylphenyl)piperazine (18 mg, 0.088 mmol) were subjected to General Procedure 14 followed by General Procedure 13 to give 3 mg product as a 3:1 mixture of isomers.

LCMS (Method 1, ES^+) 2.28 min, 455 m/z ($\text{M}+\text{H}$)⁺

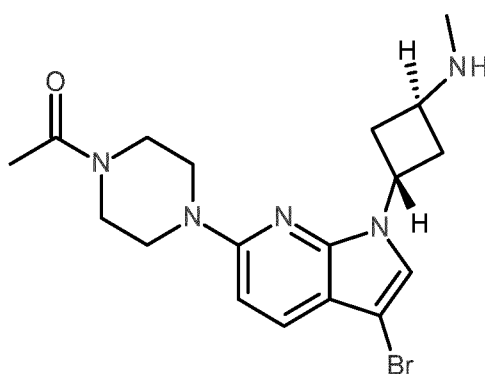
Example 245

trans-1-(5-azaspiro[3.4]octan-2-yl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile

- 5 trans-tert-butyl 2-(6-chloro-3-cyano-pyrrolo[2,3-b]pyridin-1-yl)-5-azaspiro[3.4]octane-5-carboxylate (30 mg, 0.078 mmol, see Example 244) and 1-[4-(methylsulfonyl)phenyl]piperazine (37 mg, 0.15 mmol) were subjected to General Procedure 14 followed by General Procedure 13 to give 7 mg product.

LCMS (Method 1, ES⁺) 2.15 min, 491 *m/z* (M+H)⁺

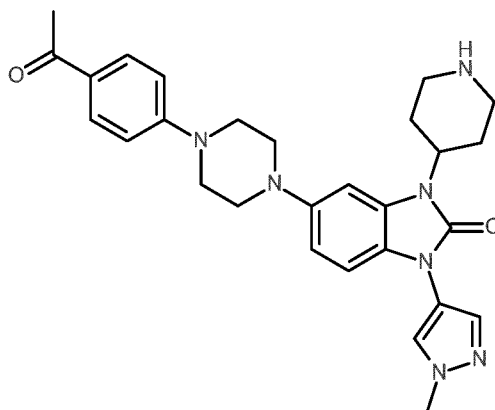
10

Example 246

trans-1-[4-[3-bromo-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]ethanone

- 15 Intermediate 59 (30 mg, 0.06 mmol) was reacted following General Procedure 13 to give the product as a white solid (22 mg, 91% yield).

LCMS (Method 1, ES⁺) 1.59 min, 406 & 408 *m/z* (M+H)⁺.

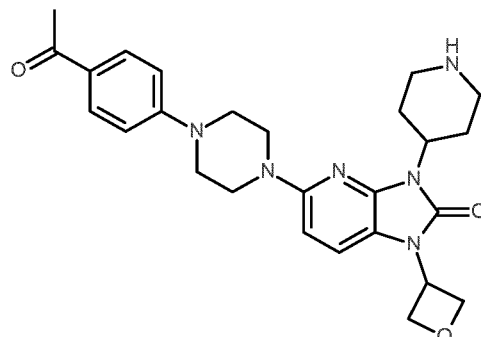
Example 2475-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpyrazol-4-yl)-3-(4-piperidyl)benzimidazol-2-one

Sodium carbonate (3.59 g, 34.2 mmol) and tert-butyl 4-aminopiperidine-1-carboxylate (2.74 g, 13.7 mmol) were added to a stirred solution of 4-chloro-2-fluoro-1-nitro-benzene (2.00 g, 11.4 mmol) in DMF (30 mL) at rt under argon. The resulting reaction mixture was heated at 80 °C for 2 h. After complete consumption of starting material, ice cold water (100 mL) was added and extracted with ethyl acetate (100 mL x 3). The organic layer was washed with ice cold water (200 mL x 2) and brine solution (200 mL), dried over sodium sulphate and concentrated in vacuo. The crude material was purified by column chromatography using 15% ethyl acetate in hexane to give tert-butyl 4-(5-chloro-2-nitro-anilino)piperidine-1-carboxylate (3.80 g, 10.7 mmol, 94%).

tert-butyl 4-(5-chloro-2-nitro-anilino)piperidine-1-carboxylate (3.8 g, 10.7 mmol) was submitted to General Procedure 15 then General Procedure 16 to give tert-butyl 4-(6-chloro-2-oxo-3H-benzimidazol-1-yl)piperidine-1-carboxylate (2.50 g, 7.1 mmol, 66% over 2 steps).

The product was prepared in three further steps according to General Procedure 17 with 4-iodo-1-methyl-pyrazole, General Procedure 5 with 1-(4-piperazin-1-yl)ethanone then General Procedure 13 to give 5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpyrazol-4-yl)-3-(4-piperidyl)benzimidazol-2-one (41 mg, 6% over 3 steps).

LCMS (Method 9, ES⁺) 2.03 min, 500 *m/z* (M+H)⁺

Example 2485-[4-(4-acetylphenyl)piperazin-1-yl]-1-(oxetan-3-yl)-3-(4-piperidyl)imidazo[4,5-b]pyridin-2-one

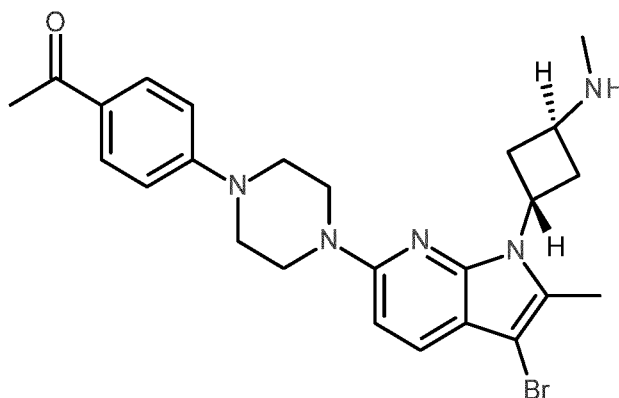
5 Caesium carbonate (1.35 g, 4.14 mmol) was added to a stirred solution of Intermediate 63 (500 mg, 1.38 mmol) and 3-iodooxetane (585 mg, 3.18 mmol) in DMF (10 mL) at rt. The mixture was heated at 100 °C for 4 h. After cooling to rt, the reaction mixture was diluted with water (100 mL) and extracted with ethyl acetate (100 mL x 2). The organic layer was separated, washed with brine (200 mL), dried over sodium sulphate and concentrated under reduced pressure. The
10 crude compound was purified by column chromatography using 2% methanol in DCM to give tert-butyl 4-[5-chloro-1-(oxetan-3-yl)-2-oxo-imidazo[4,5-b]pyridin-3-yl]piperidine-1-carboxylate (400 mg, 0.92 mmol, 66%).

To a stirred solution of tert-butyl 4-[5-chloro-1-(oxetan-3-yl)-2-oxo-imidazo[4,5-b]pyridin-3-yl]piperidine-1-carboxylate (200 mg, 0.46 mmol) in toluene (20 mL) was added 1-(4-piperazin-
15 1-ylphenyl)ethanone (143 mg, 0.687 mmol) and potassium phosphate tribasic (292 mg, 1.37 mmol) at rt. The reaction mixture was degassed using argon for 15 mins. Tris(dibenzylideneacetone)dipalladium(0) (83.8 mg, 0.0916 mmol) and X-Phos (39.7 mg, 0.0916 mmol) were then added, and the mixture was degassed again using argon for 15 mins. After heating at 100 °C for 4 h, the reaction mixture was diluted with ethyl acetate (100 mL) and
20 washed with water (100 mL x 2). The organic layer was separated, washed with brine (150 mL), dried over sodium sulphate and concentrated under reduced pressure to get crude product. Purification by prep HPLC gave tert-butyl 4-[5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(oxetan-3-yl)-2-oxo-imidazo[4,5-b]pyridin-3-yl]piperidine-1-carboxylate (150 mg, 0.26 mmol, 56%).

tert-butyl 4-[5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(oxetan-3-yl)-2-oxo-imidazo[4,5-b]pyridin-3-yl]piperidine-1-carboxylate (150 mg, 0.258 mmol) was submitted to General Procedure 13 to
25 give the product (60 mg, 0.13 mmol, 49%).

LCMS (Method 9, ES⁺) 1.99 min, 477 *m/z* (M+H)⁺

Example 249



5 trans-1-[4-[4-[3-bromo-2-methyl-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone

6-chloro-2-methyl-1H-pyrrolo[2,3-b]pyridine (200 mg, 1.20 mmol) and cis-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate (266 mg, 1.32 mmol) were reacted using General Procedure 9 to give trans-tert-butyl N-[3-(6-chloro-2-methyl-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate (400 mg, 1.06 mmol, 88%).

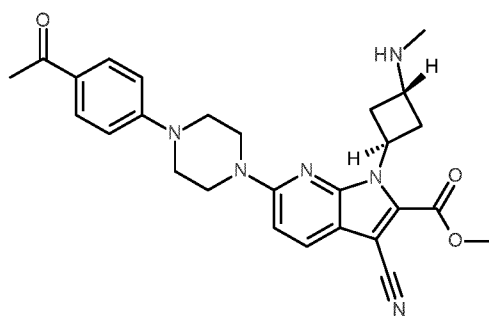
To a stirred solution of trans-tert-butyl N-[3-(6-chloro-2-methyl-pyrrolo[2,3-b]pyridin-1-yl)cyclobutyl]-N-methyl-carbamate (300 mg, 0.796 mmol) in toluene (10 mL) was added 1-(4-piperazin-1-ylphenyl)ethanone (249 mg, 1.19 mmol) and potassium phosphate tribasic (507 mg, 2.39 mmol) at rt. The reaction mixture was degassed using argon for 15 mins. Tris(dibenzylideneacetone)dipalladium(0) (146 mg, 0.159 mmol) and X-Phos (69 mg, 0.159 mmol) were then added, and the mixture was degassed again using argon for 15 mins. After heating at 100 °C for 2 h, the reaction mixture was diluted with water (50 mL) and extracted with ethyl acetate (50 mL x 2). The organic layer was separated, washed with brine (75 mL), dried over sodium sulphate and concentrated under reduced pressure to get the crude product. Purification by prep HPLC gave trans-tert-butyl N-[3-[6-[4-(4-acetylphenyl)piperazin-1-yl]-2-methyl-pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]-N-methyl-carbamate (130 mg, 0.248 mmol, 31%).

To a stirred solution of trans-tert-butyl N-[3-[6-[4-(4-acetylphenyl)piperazin-1-yl]-2-methyl-pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]-N-methyl-carbamate (130 mg, 0.248 mmol) in DCM (10 mL) was added NBS (37.5 mg, 0.211 mmol) at -50 °C. The resulting reaction mixture was stirred at -50 to -20 °C for 15 mins. After complete consumption of starting material, the mixture was

quenched with water (25 mL) and extracted with DCM (25 mL x 2). The collected organic layer was washed with brine (50 mL), dried over sodium sulphate and evaporated under reduced pressure to get crude material. The crude product was purified by column chromatography using 25% EtOAc in hexane, then submitted to General Procedure 13 to give the product (25 mg, 0.047 mmol, 19% over 2 steps).

LCMS (Method 9, ES⁺) 2.76 min, 496 & 498 *m/z* (M+H)⁺

Example 250



10 trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate

Methyl 6-chloro-1H-pyrrolo[2,3-b]pyridine-2-carboxylate (400 mg, 1.90 mmol) and cis-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate (459 mg, 2.28 mmol) were reacted using General Procedure 9 to give trans-methyl 1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]-6-chloro-pyrrolo[2,3-b]pyridine-2-carboxylate (650 mg, 1.61 mmol, 85%).

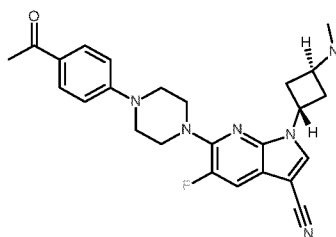
To a stirred solution of trans-methyl 1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]-6-chloro-pyrrolo[2,3-b]pyridine-2-carboxylate (300 mg, 0.741 mmol) in toluene (20 mL) was added 1-(4-piperazin-1-ylphenyl)ethanone (232 mg, 1.11 mmol) and potassium phosphate tribasic (472 mg, 2.22 mmol) at rt. The reaction mixture was degassed using argon for 15 mins. Tris(dibenzylideneacetone)dipalladium(0) (136 mg, 0.148 mmol) and X-Phos (64.3 mg, 0.148 mmol) were then added, and the mixture was degassed again using argon for 15 mins. After heating at 100 °C for 2 h, the reaction mixture was diluted with water (75 mL) and extracted with ethyl acetate (75 mL x 2). The organic layer was separated, washed with brine (100 mL), dried over sodium sulphate, concentrated under reduced pressure and purified by column chromatography using 30% ethyl acetate in hexane to give trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate (250 mg, 0.35 mmol, 48%).

To a stirred solution of trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate (250 mg, 0.35 mmol) in DCM (15 mL) was added NBS (53.3 mg, 0.300 mmol) at -50 °C. The resulting reaction mixture was stirred at -50 °C for 30 min. After complete consumption of starting material, water (50 mL) was added and the mixture was extracted with DCM (50 mL x 3). The collected organic layer was washed with brine (25 mL), dried over sodium sulphate and purified by column chromatography using 20% EtOAc in hexane to give trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-3-bromo-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate (100 mg, 0.14 mmol, 39%).

To a stirred solution of trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-3-bromo-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate (50 mg, 0.069 mmol) in NMP (2 mL) was added copper(I) cyanide (37 mg, 0.41 mmol) at rt. The contents were heated at 130 °C for 16 h. After cooling to rt, the reaction mixture was diluted with ethyl acetate (50 mL) and washed with water (50 mL x 2). The organic layer was separated, washed with brine (30 mL), dried over sodium sulphate, concentrated under reduced pressure and purified by column chromatography using 20% EtOAc in hexane to give trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]-3-cyano-pyrrolo[2,3-b]pyridine-2-carboxylate (50 mg, 0.061 mmol, 89%).

trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]-3-cyano-pyrrolo[2,3-b]pyridine-2-carboxylate (50.0 mg, 0.0611 mmol) was submitted to General Procedure 13 to give the title compound (30 mg, 0.034 mmol, 55%).

LCMS (Method 9, ES⁺) 2.41 min, 487 *m/z* (M+H)⁺

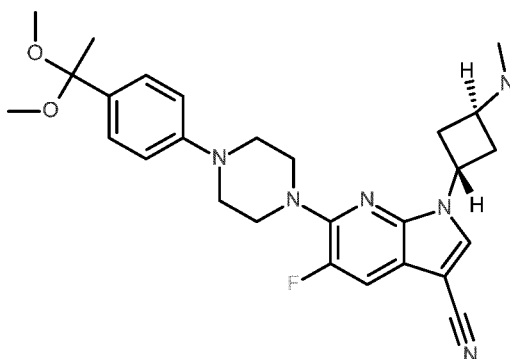
Example 251

Trans-6-[4-(4-acetylphenyl)piperazin-1-yl]-5-fluoro-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-
 5 b]pyridine-3-carbonitrile

Intermediate 42 (300 mg, 0.75 mmol) was dissolved in a mixture of DMF (2.5 mL) and acetonitrile (2.5 mL). The solution was cooled to 0 °C and chlorosulfonyl isocyanate (0.07 mL, 0.84 mmol) was added and the reaction stirred in the presence of the ice bath for 30 min then at rt for another 2 hours. The reaction mixture was cooled to 0 °C and a second portion of chlorosulfonyl isocyanate (0.07 mL, 0.84 mmol) added. The ice-bath was removed and the reaction mixture stirred for 15 min. The ice bath was returned and the reaction carefully quenched with water (10 mL). The biphasic solution was stirred for 10 mins then diluted with 50% saturated ammonium chloride (50 mL), diethyl ether (30 mL) and ethyl acetate (10 mL). The organic layer was extracted with water (50 mL), then dried (Na₂SO₄) and concentrated under reduced pressure. A mixture of the resulting residue, 1-(4-acetylphenyl)piperazine (184 mg, 0.90 mmol), RuPhos G3 (62 mg, 0.07 mmol) and sodium tert-butoxide (217 mg, 2.26 mmol) was suspended in degassed 1,4-dioxane (4 mL, 46.9 mmol). The reaction mixture was heated at 90 °C for ~ 3 hours then left to stand at rt overnight. The reaction mixture was passed through a celite plug eluting with ethyl acetate. The solvent was removed and the crude purified by flash column chromatography to give trans-tert-butyl N-[3-[6-[4-(4-acetylphenyl)piperazin-1-yl]-3-cyano-5-fluoro-pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]-N-methyl-carbamate (253 mg, 61%).

Trans-tert-butyl N-[3-[6-[4-(4-acetylphenyl)piperazin-1-yl]-3-cyano-5-fluoro-pyrrolo[2,3-b]pyridin-1-yl]cyclobutyl]-N-methyl-carbamate (167 mg, 0.3 mmol) was then treated according to general procedure 13 to give the title compound (110 mg, 80%)

25 LCMS (Method 1, ES⁺) 2.15 min, 447 m/z (M+H)⁺

Example 252

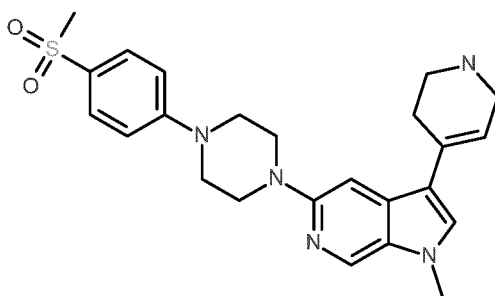
5 6-[4-[4-(1,1-dimethoxyethyl)phenyl]piperazin-1-yl]-5-fluoro-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile

Example 252 was isolated as a by-product during synthesis of example 251 (42 mg, 28%).

LCMS (Method 1, ES⁺) 2.56 min, 461 m/z (M+H)⁺

Example 253

10



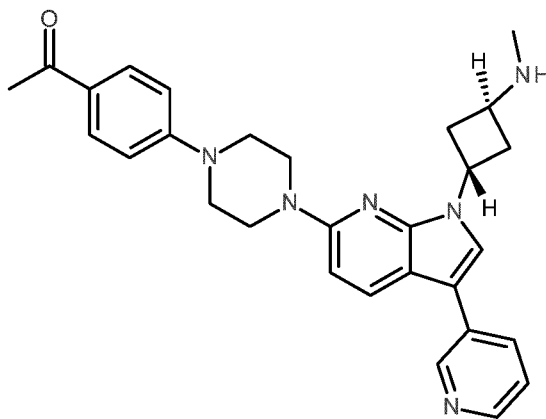
1-methyl-5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-3-(1,2,3,6-tetrahydropyridin-4-yl)pyrrolo[2,3-c]pyridine

15 N-Iodosuccinimide (491 mg, 2.07 mmol) was added to a suspension of Intermediate 66 (641 mg, 1.73 mmol) in acetone (15 mL) and the reaction mixture stirred at rt for 30 min. The reaction mixture was then concentrated under reduced pressure, diluted with DCM and washed with

saturated aqueous bicarbonate. The aqueous layer was extracted with DCM, organics combined, dried (Na_2SO_4) and concentrated under reduced pressure. The crude residue was then purified by flash column chromatography to give 3-iodo-1-methyl-5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-c]pyridine (350 mg, 40%). A fraction of the iodinated product (100 mg, 0.20 mmol) was mixed with N-boc-1,2,5,6-tetrahydropyridine-4-boronic acid pinacol ester (75 mg, 0.24 mmol), potassium carbonate (60 mg, 0.43 mmol) and 1,1'-bis(diphenylphosphino)ferrocene-palladium(ii)dichloride dichloromethane complex (17 mg, 0.02 mmol) and dissolved in pre-degassed DMF (1 mL). The mixture was then heated at 100 °C for 1 h and left to stand at rt for 72 h. The crude mixture was passed through an SCX cartridge eluting with MeOH and ethyl acetate and concentrated under reduced pressure. The residue was purified by flash column chromatography to give tert-butyl 4-[1-methyl-5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-c]pyridin-3-yl]-3,6-dihydro-2H-pyridine-1-carboxylate (20 mg, 0.04 mmol, 18%) which was then treated according to general procedure 13 to give the title compound (5 mg, 30%).

LCMS (Method 1, ES+) 1.36 min, 452 m/z (M+H)+.

15

Example 254

trans-1-[4-[4-[1-[3-(methylamino)cyclobutyl]-3-(3-pyridyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone trifluoroacetate

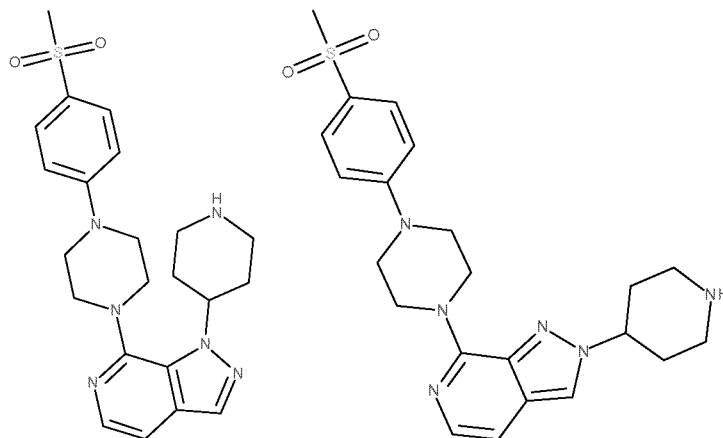
To a mixture of Intermediate 65 (21 mg, 0.04 mmol) and pyridine-3-boronic acid (11 mg, 0.09 mmol) in degassed 1,4-dioxane (0.4 mL), Na_2CO_3 (0.1 mL, 2 M in dioxane) and $\text{Pd}(\text{PPh}_3)_4$ (7.8 mg, 0.007 mmol) were added. The reaction mixture was heated at 140 °C for 2 h in a microwave apparatus. The mixture was filtered and rinsed with 0.6 mL of MeCN/ H_2O (7/3) before injection on prep HPLC and purified using a basic mode. The solvent was removed under vacuum and the yellow solid was dissolved in 1 mL of DCM/TFA (1/1). The mixture was stirred at r.t. for 1 hour

25

until the reaction was complete. The solvent was removed under vacuum to give a white solid (4.4 mg, 20% yield over two steps.)

LCMS (Method 3, ES⁺) 2.78 min, 481 m/z (M+H)⁺.

5 Examples 255 and 256



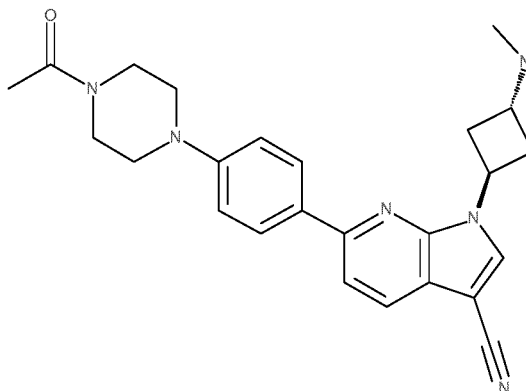
7-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-2-piperidin-4-ylpyrazolo[3,4-c]pyridine and 7-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-(4-piperidyl)pyrazolo[3,4-c]pyridine

A mixture of 7-bromo-1H-pyrazolo[3,4-c]pyridine (266 mg, 1.34 mmol) and tert-butyl 4-hydroxypiperidine-1-carboxylate (405.52 mg, 2.0149 mmol) was dissolved in THF (13 ml). Triphenylphosphine (422 mg, 1.61 mmol) and diisopropylazodicarboxylate (428 mg, 2.01 mmol) was added and the reaction mixture stirred overnight. Reaction mixture was then partitioned between EtOAc (50 ml) and aq. NaHCO₃ (50 ml). The organic layer was separated, washed with brine and then vac'd down. The crude material was columned with hexane/ethyl acetate 0-100% gradient elution and then the 96:4 mixture of regioisomers was mixed with 1-[4-(methylsulfonyl)phenyl]piperazine (311 mg, 1.3 mmol). This was treated with NaO^tBu (297 mg, 3.1 mmol), RuPhos G3 (102.1 mg, 0.12 mmol) in 1,4-dioxane (12.4 ml), degassed and stirred at 50 °C for 2 h then 90 °C for a further 2 h. The reaction mixture was partitioned between EtOAc (100 ml) and NaHCO₃ (100 ml). The organic layer was separated and the aq. washed with further EtOAc. The combined organics were dried with sodium sulfate and then vac'd down to a brown oil. This was columned with Hex/EtOAc 10-100% to afford a brown oil. Product was treated with DCM (1 ml) and TFA (1ml) then stirred for 30 mins. Solution was vac'd down and partitioned between NaHCO₃ and DCM. The organic layer was separated and vac'd down and the products isolated by reverse phase HPLC.

Example 255: LCMS (Method 1, ES⁺) 1.29 min, 441 *m/z* (M+H)⁺

Example 256: LCMS (Method 1, ES⁺) 1.37 min, 441 *m/z* (M+H)⁺

Example 257



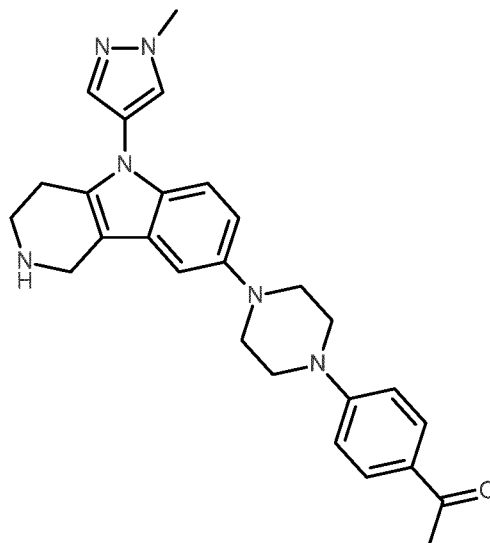
5

6-[4-(4-acetylpiperazin-1-yl)phenyl]-1-[trans-3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile

Intermediate 50 (68 mg, 0.18 mmol), 4-(4-acetyl-1-piperazinyl)phenylboronic acid (70.14 mg, 0.28 mmol) and (XPhos) palladium (II) phenethylamine chloride (28 mg, 0.038 mmol) were dissolved in 1,4-dioxane (3.8 ml) and aqueous Na₂CO₃ (0.40 mmol) then degassed. The reaction was heated at 100 °C for 3 h and allowed to cool to room temperature. The reaction mixture was partitioned between DCM and water then separated and the organic layer was vac'd down. The residue was dissolved in DCM (1.5 ml) and TFA (1.5 ml) was added. The reaction was stirred at r.t. for 1 h. The product was captured on an SCX column and eluted with NH₃/MeOH (7M). The solution was evaporated under reduced pressure and the oil was triturated with MeCN. The solid was filtered off and dried to afford the title compound (40 mg) as a white solid.

15

LCMS (Method 1, ES⁺) 1.91 min, 429 *m/z* (M+H)⁺

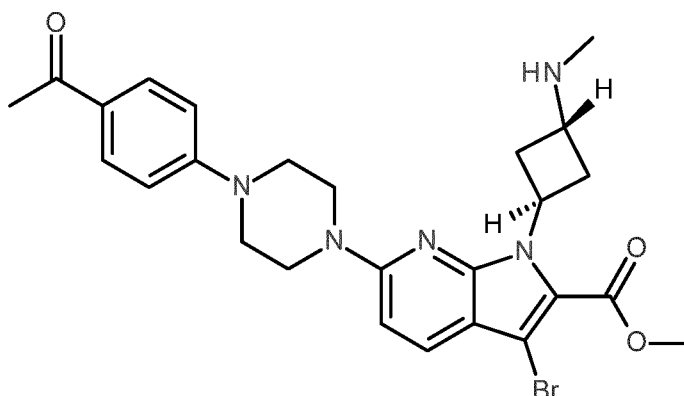
Example 258

1-[4-[4-[5-(1-methylpyrazol-4-yl)-1,2,3,4-tetrahydropyrido[4,3-b]indol-8-yl]piperazin-1-yl]phenyl]ethanone

- 5 To a solution of 8-chloro-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole (400 mg, 1.94 mmol) in THF (40 mL) was added BOC anhydride (0.534 mL, 2.32 mmol) at 0 °C. The reaction mixture was stirred at rt for 10 mins then diluted with water (50 mL) and extracted with EtOAc (2 x 50 mL). The organic layer was washed with water (50 mL), brine (50 mL), dried over sodium sulfate and evaporated under reduced pressure. The crude material was purified by column
- 10 chromatography on silica using 30% ethyl acetate in hexane to give tert-butyl 8-chloro-1,3,4,5-tetrahydropyrido[4,3-b]indole-2-carboxylate (420 mg, 1.34 mmol, 70%).

- tert-butyl 8-chloro-1,3,4,5-tetrahydropyrido[4,3-b]indole-2-carboxylate (1 equiv) was subjected to a modified General Procedure 17 (with the stated intermediate instead of arylimidazol-2-one) with 4-iodo-1-methyl-pyrazole (1.5 equiv). The resulting product was then subjected to General
- 15 Procedure 3 with 1-(4-piperazin-1-ylphenyl)ethenone then General Procedure 13 to give the title product (125 mg, 28% over 3 steps).

LCMS (Method 9, ES⁺) 1.83 min, 455 *m/z* (M+H)⁺

Example 259

trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-3-bromo-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate

- 5 Methyl 6-chloro-1H-pyrrolo[2,3-b]pyridine-2-carboxylate (400 mg, 1.90 mmol) and cis-tert-butyl N-(3-hydroxycyclobutyl)-N-methyl-carbamate (459 mg, 2.28 mmol) were reacted using General Procedure 9 to give trans-methyl 1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]-6-chloro-pyrrolo[2,3-b]pyridine-2-carboxylate (650 mg, 1.61 mmol, 85%).

To a stirred solution of trans-methyl 1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]-6-chloro-pyrrolo[2,3-b]pyridine-2-carboxylate (300 mg, 0.741 mmol) in toluene (20 mL) was added
 10 1-(4-piperazin-1-yl)phenyl)ethanone (232 mg, 1.11 mmol) and potassium phosphate tribasic (472 mg, 2.22 mmol) at rt. The reaction mixture was degassed using argon for 15 mins. Tris(dibenzylideneacetone)dipalladium(0) (136 mg, 0.148 mmol) and X-Phos (64.3 mg, 0.148 mmol) were then added, and the mixture was degassed again using argon for 15 mins. After
 15 heating at 100°C for 2 h, the reaction mixture was diluted with water (75 mL) and extracted with ethyl acetate (75 mL x 2). The organic layer was separated, washed with brine (100 mL), dried over sodium sulphate, concentrated under reduced pressure and purified by column chromatography using 30% ethyl acetate in hexane to give trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]pyrrolo[2,3-
 20 b]pyridine-2-carboxylate (250 mg, 0.35 mmol, 48%).

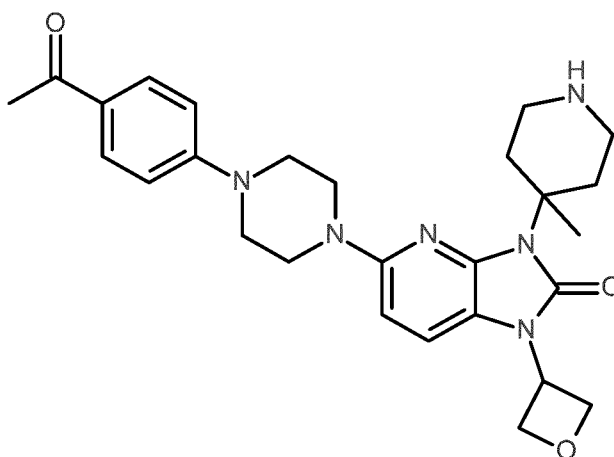
To a stirred solution of trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate (250 mg, 0.35 mmol) in DCM (15 mL) was added NBS (53.3 mg, 0.300 mmol) at -50°C. The resulting reaction mixture was stirred at -50°C for 30 min. After complete consumption of starting material, water
 25 (50 mL) was added and the mixture was extracted with DCM (50 mL x 3). The collected organic layer was washed with brine (25 mL), dried over sodium sulphate and purified by column chromatography using 20% EtOAc in hexane to give trans-methyl 6-[4-(4-

acetylphenyl)piperazin-1-yl]-3-bromo-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate (100 mg, 0.14 mmol, 39%).

trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-3-bromo-1-[3-[tert-butoxycarbonyl(methyl)amino]cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate (45 mg, 0.07 mmol) was subjected to General Procedure 13 to give the title product (28 mg, 0.05 mmol, 74%).

LCMS (Method 9, ES⁺) 2.52 min, 540 & 542 *m/z* (M+H)⁺

Example 260



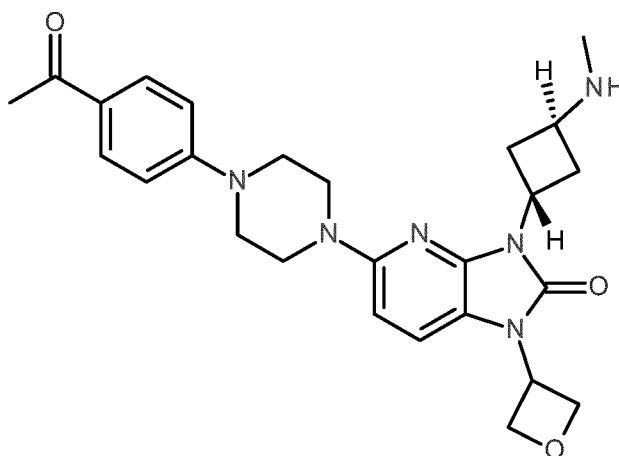
10

5-[4-(4-acetylphenyl)piperazin-1-yl]-3-(4-methyl-4-piperidyl)-1-(oxetan-3-yl)imidazo[4,5-b]pyridin-2-one

To a stirred solution of Intermediate 64 (300 mg, 0.789 mmol) and 3-iodooxetane (218 mg, 1.18 mmol) in DMF (30 mL) was added caesium carbonate (771 mg, 2.37 mmol) at rt. The mixture was heated at 100°C for 5 h then diluted with water (50 mL) and extracted with ethyl acetate (50 mL x 2). The organic layer was separated, washed with brine (50 mL), dried over sodium sulfate and concentrated under reduced pressure. The crude compound was purified by column chromatography using 2% methanol in DCM to give tert-butyl 4-[5-chloro-1-(oxetan-3-yl)-2-oxo-imidazo[4,5-b]pyridin-3-yl]-4-methyl-piperidine-1-carboxylate (280 mg, 0.58 mmol, 73%).

tert-butyl 4-[5-chloro-1-(oxetan-3-yl)-2-oxo-imidazo[4,5-b]pyridin-3-yl]piperidine-1-carboxylate was subjected to General Procedure 3 with 1-(4-piperazin-1-yl)phenylethanone then General Procedure 13 to give the title product (27% over two steps).

LCMS (Method 9, ES⁺) 2.19 min, 491 *m/z* (M+H)⁺

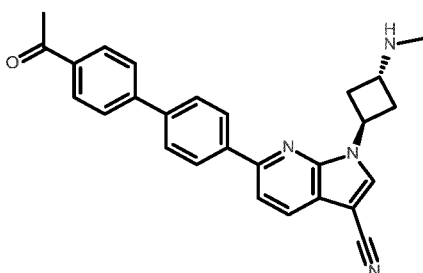
Example 261

trans-5-[4-(4-acetylphenyl)piperazin-1-yl]-3-[3-(methylamino)cyclobutyl]-1-(oxetan-3-yl)imidazo[4,5-b]pyridin-2-one

- 5 To a stirred solution of Intermediate 62 (250 mg, 0.69 mmol) and 3-iodooxetane (191 mg, 1.04 mmol) in DMF (15 mL) was added caesium carbonate (677 mg, 2.08 mmol) at rt. The mixture was heated at 100°C for 5 h then diluted with water (50 mL) and extracted with ethyl acetate (50 mL x 2). The organic layer was separated, washed with brine (50 mL), dried over sodium sulfate and concentrated under reduced pressure. The crude compound was purified by column chromatography using 2% methanol in DCM to give trans-tert-butyl N-[3-[5-chloro-1-(oxetan-3-yl)-2-oxo-imidazo[4,5-b]pyridin-3-yl]cyclobutyl]-N-methyl-carbamate (240 mg, 0.56 mmol, 80%).

trans-tert-butyl N-[3-[5-chloro-1-(oxetan-3-yl)-2-oxo-imidazo[4,5-b]pyridin-3-yl]cyclobutyl]-N-methyl-carbamate was subjected to General Procedure 3 with 1-(4-piperazin-1-ylphenyl)ethanone then General Procedure 13 to give the title product (58% over two steps).

- 15 LCMS (Method 9, ES⁺) 2.03 min, 477 *m/z* (M+H)⁺

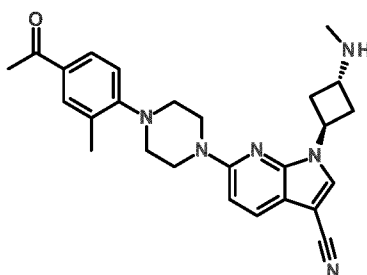
Example 262

6-[4-(4-Acetylphenyl)phenyl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile

The title compound was prepared via boc de-protection of Intermediate 96, according to General Procedure 13.

LCMS (Method 11, ES⁺) 2.42 min, 421 *m/z* [M+H]⁺.

5

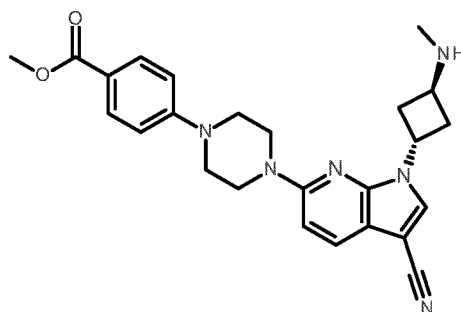
Example 263

10 6-[4-(4-acetyl-2-methylphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile

The title compound was prepared by Buchwald amination and de-Boc, according to General procedure 3 and General Procedure 13 from intermediate 50 with 1-(4-bromo-3-methylphenyl)ethanone.

15

LCMS (Method 11, ES⁺) 2.30 min, 443 *m/z* [M+H]⁺

Example 264

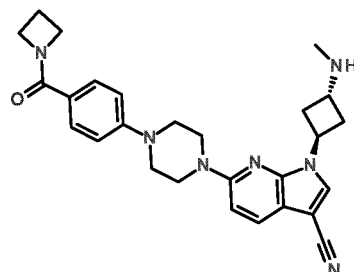
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trans-methyl 4-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]benzoate

The title compound was prepared using intermediate 109 according to General procedure 13.

LCMS (Method 1) 2.16 min, 445 m/z [M+H]⁺

Example 265



5

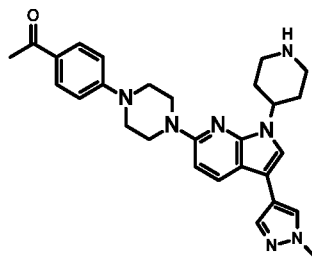
6-[4-[4-(azetidine-1-carbonyl)phenyl]piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile

To a mixture of intermediate 110 (70 mg, 0.132 mmol) and N-ethyl-N-isopropyl-propan-2-amine (46 μ L, 0.264 mmol) in DMF (3 mL) was added HATU (75 mg, 0.198 mmol) at r.t and stirred for 5 min. Then azetidine (18 μ L, 0.264 mmol) was added and stirred at r.t for 30 min. The reaction was then quenched with water (0.2 ml). The mixture was then evaporated in vacuo and the residue was purified by Biotage [wet loaded to SNAP KP NH 11 g cartridge, eluent from 0% to 58% (10% MeOH in DCM) in DCM]. The product fractions were evaporated in vacuo to yield the title compound as off-white solid.

15

LCMS (Method 11, ES⁺) 3.08 min, 470 m/z [M+H]⁺

Example 266



20

1-[4-[4-[3-(1-methylpyrazol-4-yl)-1-piperidin-4-yl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenylethanone

A suspension of 10% Pd/C (50% wet) (41.3 mg, 0.04 mmol) and Intermediate 100 (80 mg, 0.13 mmol) in THF (4 mL) and EtOH (1 mL) was evacuated and back-filled with nitrogen three times and then evacuated and back-filled with hydrogen three times. The suspension was stirred

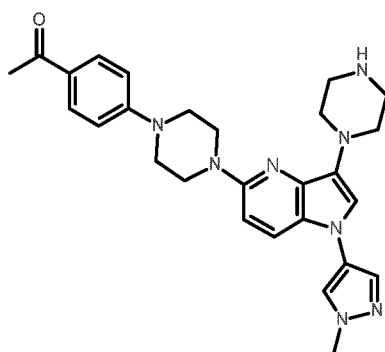
25

under an atmosphere of hydrogen for 16 h at rt.

The reaction mixture was filtered through a pad of celite and glass fibre filter paper, the filtrate was concentrated in vacuo to afford the crude title compound (65 mg) as a brown gum. The residue was purified by high pH prep HPLC. The product containing fractions were combined and the solvent was removed in vacuo to afford 7 mg (12%) of the title compound as an off white solid.

LCMS (Method 11, ES+) 2.03 min, 484 m/z $[M+H]^+$

10 Example 267

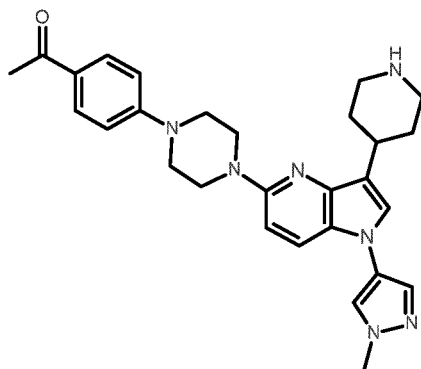


1-[4-[4-[1-(1-methylpyrazol-4-yl)-3-piperazin-1-yl]pyrrolo[3,2-b]pyridin-5-yl]piperazin-1-yl]phenylethanone

15 The title compound was prepared from Intermediate 104 and tert-butyl piperazine-1-carboxylate, in accordance with General Procedure 1.

LCMS (Method 11, ES⁺) 1.70 min, 485 m/z $[M+H]^+$

Example 268



20

1-[4-[4-[1-(1-methylpyrazol-4-yl)-3-piperidin-4-yl]pyrrolo[3,2-b]pyridin-5-yl]piperazin-1-

ylphenylethanone

To the solution of Intermediate 108 (40 mg, 0.05 mmol) in DCM (5 mL) / MeOH (2 mL) was added 4 N HCl in dioxane (0.5 mL) and then stirred at r.t overnight. The reaction was then evaporated in vacuo and the residue was purified by low pH preparative HPLC. The desired fraction was basified with 2 N NH₃ in MeOH and evaporated in vacuo to dryness. The residue was then loaded to SCX 2 cartridge (1 g) in DCM / MeOH (1:1), and washed with MeOH (10 mL). The cartridge was then flushed with 2 N NH₃ in DCM/MeOH (1:1) to release the product. The desired fraction was evaporated in vacuo to yield the title compound as white solid (13 mg, 52%).

LCMS (Method 11, ES⁺) 1.58 min, 484 *m/z* [M+H]⁺.

10 - Biological assay

The ability of these compounds encompassed by the present invention to modulate 2'3'-cGAMP stimulated STING signaling as investigated in cell assays. HEK Blue ISG permeabilised cells were pre-incubated with compound for 60 mins at 37 °C, 5% CO₂. The cells were then stimulated with 2'3'-cGAMP. The effect of compound on the 2'3'-cGAMP induced production of Type I interferons is indirectly determined by an ISG54 reporter assay. Type 1 interferons produced by the cells were measured using HEK Blue detection reagent. The ability of compound to inhibit 2'3'-cGAMP stimulated production of Type I interferons from HEK Blue ISG cells was measured as pIC₅₀ WT (wild-type).

Compound activity was assayed for STING dependence using HEK Blue ISG KO STING cells (counter-screen). 2'3'-cGAMP does not induce production of Type I interferons from cells that lack the receptor STING.

In the counter-screen, compounds were tested for their ability to modulate the production of Type I interferons by pre-treating permeabilised HEK Blue ISG KO STING cells with compound for 60 mins at 37 °C, 5% CO₂ and then stimulating with interferon. The effect of compound on the interferon induced production of Type I interferons is indirectly determined by an ISG54 reporter assay. Type 1 interferons produced by the cells were measured using HEK Blue detection reagent. The ability of compound to inhibit interferon stimulated production of Type I interferons from HEK Blue ISG KO STING cells was measured as pIC₅₀ KO.

All the pharmaceutically active compounds described herein have pIC₅₀ superior to 4.5 in HEK Blue ISG cells and poorer pIC₅₀ in the HEK Blue ISG KO STING assay.

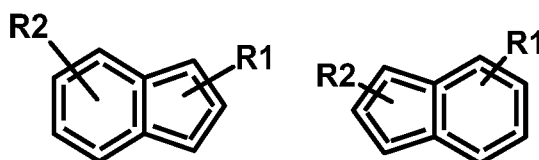
The compounds of the invention notably show a pIC₅₀ in HEK Blue ISG cells ranging from about 4.5 to greater than 8.5, preferably from 5 to greater than 8.5

IC₅₀ ranges from about 30 μ M to about less than 10 nM; notably from about 30 μ M to less than 10 nM.

CLAIMS

1. A compound of general formula I, or a pharmaceutically acceptable acid addition salt, a racemic mixture or its corresponding enantiomer and/or optical isomers thereof,

5



(I)

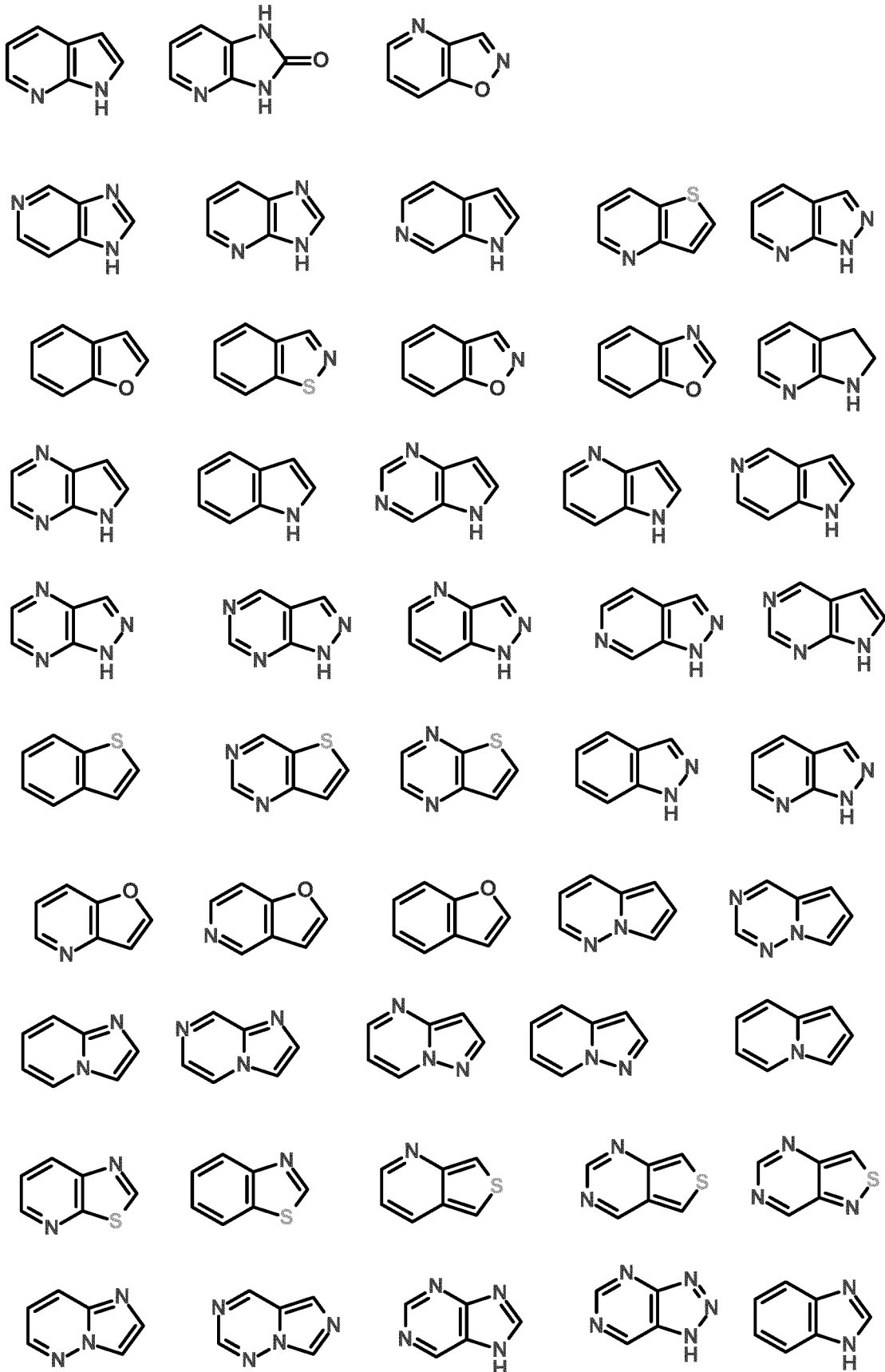
10 wherein

- the central core A which is the 6,5 heterobicyclic rings contains at least one heteroatom from O,N,S and C atoms can be optionally substituted by halogen, cyano, C1-6 alkyl, trifluoromethyl, difluoromethyl, (C2-6) alkenyl, hydroxy, (C1-6) alkoxy, difluoromethoxy, trifluoromethoxy, trifluoroethoxy, (C1-6) alkylthio, (C1-6) alkylsulphonyl, amino, (C1-6) alkylamino, di(C1-6)alkylamino, (C1-6)alkoxy(C1-6)alkyl-amino, N-[(C1-6)alkyl]-N-[hydroxy(C1-6)alkyl]amino, (C2-6) alkylcarbonylamino, (C2-6) alkoxy carbonylamino, (C1-6) alkylsulphonylamino, formyl, (C2-6) alkylcarbonyl, carboxy, (C2-6) alkoxy carbonyl, aminocarbonyl, (C1-6) alkylaminocarbonyl, di(C1-6)alkylaminocarbonyl, aminosulphonyl, (C1-6) alkylaminosulphonyl or di(C1-6)alkylaminosulphonyl; (C3-7)heterocycloalkyl or (C3-7)spiroheterocycloalkyl, either of which groups may be optionally substituted by one or more substituents;
- R1 represents alkyl or cycloalkyl amines including fused and spirocycloalkyl amines optionally substituted including (C1-3) aminoalkyl, (C3-7) aminocycloalkyl, (C1-3)alkylimidazole, (C1-3)alkyl isoindoline, (C1-3)alkylpiperazine, (C1-3)alkylpiperidine, (C1-3)alkyl imidazopiperazine, (C1-3)alkyl(C4-7)aminocycloalkyl, (C1-3)alkyl(C4-7)aminodicycloalkyl; and
- R2 represents aryl, heteroaryl, heterobicyclic, (C4-7) aminocycloalkyl, cycloalkyl, heterocycloalkyl, (C6-8) diaminocycloalkyl, morpholino, (C4-7)cycloalkylmethyl, piperziny, piperdiny. R2 is optionally substituted with groups including hydroxyl, (C1-6)alkyl, acetyl, halogen, cyano, C1-6 alkyl, trifluoromethyl, difluoromethyl, (C2-6) alkenyl, hydroxy, (C1-6) alkoxy, difluoromethoxy, trifluoromethoxy, trifluoroethoxy, (C1-6) alkylthio, (C1-6) alkylsulphonyl, amino, (C1-6) alkylamino, di(C1-6)alkylamino, (C1-

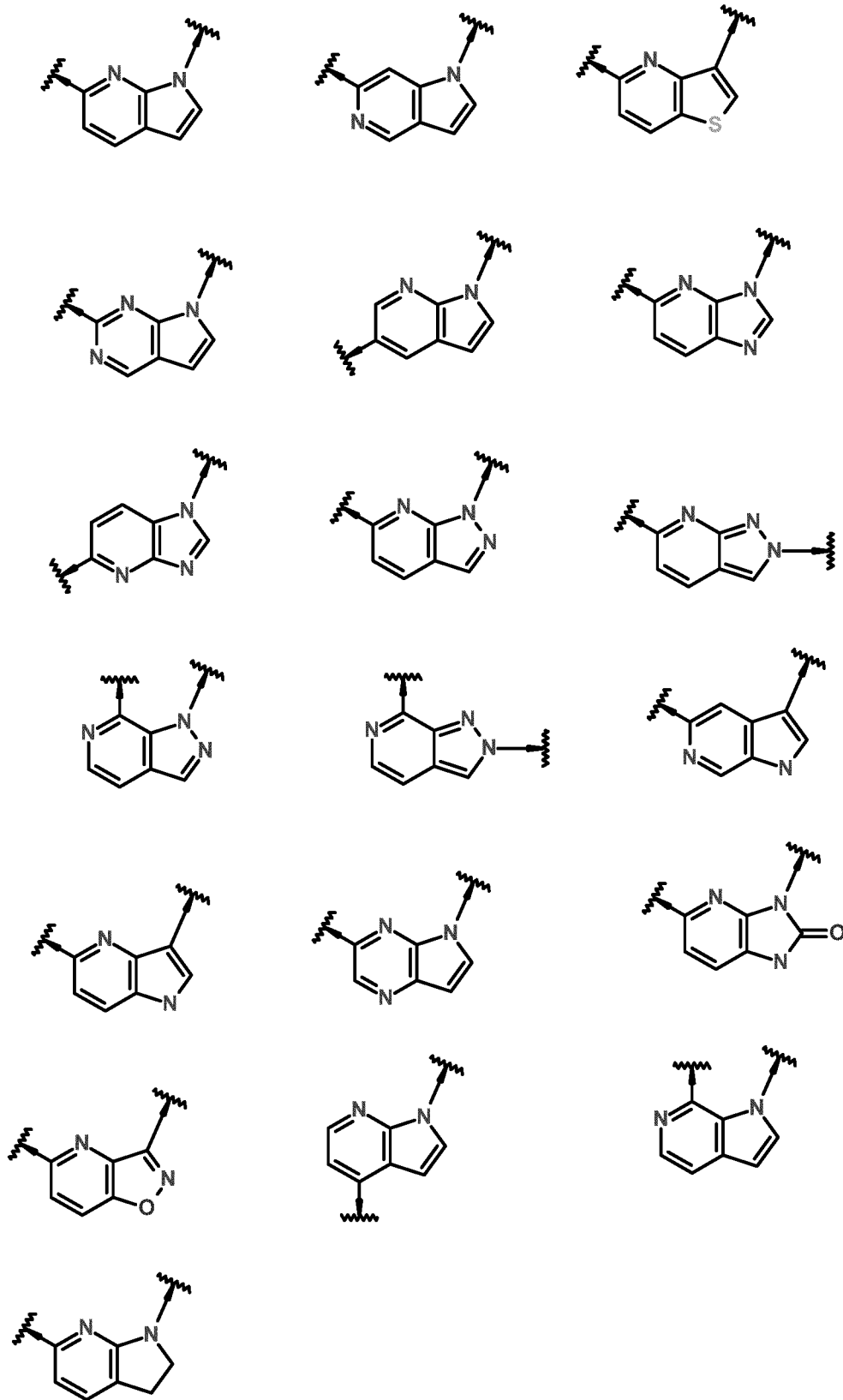
30

5 6)alkoxy(C1-6)alkyl-amino, N-[(C1-6)alkyl]-N-[hydroxy(C1-6)alkyl]amino, (C2-6) alkylcarbonylamino, (C2-6) alkoxy carbonylamino, (C1-6) alkylsulphonylamino, formyl, (C2-6) alkylcarbonyl, carboxy, (C2-6) alkoxy carbonyl, aminocarbonyl, (C1-6) alkylaminocarbonyl, di(C1-6)alkylaminocarbonyl, aminosulphonyl, (C1-6) alkylaminosulphonyl or di(C1-6)alkylaminosulphonyl; (C3-7)heterocycloalkyl or (C3-7)spiroheterocycloalkyl, either of which groups may be optionally substituted by one or more substituents.

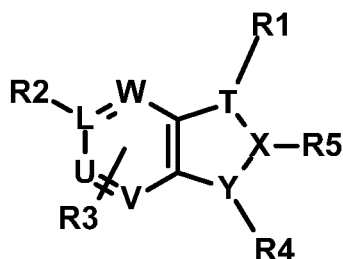
2. A compound according to claim 1, wherein the central core A is selected from the group consisting of



3. A compound according to claim 2, wherein the central core A is selected from the group consisting of



4. A compound according to claim 1, wherein the central core A is selected from the group consisting of:



- 5 Wherein
 L, U, V, W, is C or N;
 X, T is C, N or O;
 Y is C, N or S;
- 10 - R1 represents (C4-7)cycloalkyl; (4-9-membered)-heterocycloalkyl; fused cycloalkylamine; fused heterocycloalkylamine; spirocycloalkylamine; spiro-heterocycloalkylamine; (C1-3) aminoalkyl; (C3-7) aminocycloalkyl; (C1-3)alkylimidazole; (C1-3)alkyl isoindoline; (C1-3)alkylpiperazine; (C1-3)alkylpiperidine; (C1-3)alkyl imidazopiperazine; (C1-3)alkyl(C4-7)aminocycloalkyl; (C1-3)alkyl(C4-7)aminodicycloalkyl; a (C1-3)alkyl group substituted with one or more groups chosen
 15 amongst (C4-7)cycloalkyl, (4-9-membered)-heterocycloalkyl, fused cycloalkylamine, fused heterocycloalkylamine, spirocycloalkylamine, spiro-heterocycloalkylamine, (C1-C3) aminoalkyl, (C3-C7) aminocycloalkyl, (C1-C3)alkylimidazole, (C1-C3)alkyl isoindoline, (C1-C3)alkylpiperazine, (C1-C3)alkylpiperidine, (C1-C3)alkyl imidazopiperazine, (C1-C3)alkyl(C4-7)aminocycloalkyl, (C1-C3)alkyl(C4-7)aminodicycloalkyl ;
- 20 R1 is optionally substituted with Halogen, hydroxyl, (C1-C3)alkyl, (C1-C3)alkylcarboxy, (C1-C3)alkylamino, (C5-C6)heteroaryl optionally substituted with (C1-C3)alkyl, Halogen, (C3-C7) aminocycloalkyl substituted with halogen, aryl, aryl(C1-C3)alkyl, aryl(C1-C3)alkyl(C1-C3)dialkylamine, aryloxy ;
- 25 - R2 represents H; Halogen; aryl; heteroaryl; heterobicyclic; (C4-C7)aminocycloalkyl; cycloalkyl; heterocycloalkyl; (C6-C8) diaminocycloalkyl; morpholino; (C4-C7)cycloalkylmethyl; piperziny; piperdiny;
- 30 R2 is optionally substituted with groups including aryl; heteroaryl; hydroxyl; (C1-C6)alkyl; acetyl; halogen; cyano; (C1-C6) alkyl; trifluoromethyl; difluoromethyl; (C2-C6) alkenyl; hydroxy; (C1-C6)alkoxy; difluoromethoxy; trifluoromethoxy; trifluoroethoxy; (C1-C6)alkylthio; (C1-

6)alkylsulphonyl; amino; (C1-C6)alkylamino; di(C1-6)alkylamino; (C1-C6)alkoxy(C1-6)alkyl-
 amino; N-[(C1-6)alkyl]-N-[hydroxy(C1-6)alkyl]amino; (C2-C6)alkylcarbonylamino; (C2-
 C6)alkoxycarbonylamino; (C1-C6)alkylsulphonylamino; formyl; (C2-C6)alkylcarbonyl; carboxy;
 (C2-C6)alkoxycarbonyl; aminocarbonyl; (C1-C6)alkylaminocarbonyl; di(C1-
 5 C6)alkylaminocarbonyl; aminosulphonyl, (C1-6) alkylaminosulphonyl or di(C1-
 6)alkylaminosulphonyl; (C3-7)heterocycloalkyl or (C3-7)spiroheterocycloalkyl; either of which
 groups may be optionally substituted by one or more substituents chosen amongst hydroxyl,
 halogen, amino, methylamino, dimethylamino, (C1-3)alkyl, (C1-3)alkoxy, sulphonyl, (C1-
 3)carbonyl, (C1-4)alkylcarboxy, cyano, oxo, (C1-6)alkyl(C5-10)heteroaryl(C1-3)carbonyl,
 10 sulphonyl, methylsulphonyl, pyridinyl;

- R3 is selected independently from each other amongst H; halogen; cyano; (C4-
 7)heterocycloalkyl optionally substituted with (methylsulphonyl)aryl, acetyl, (C1-
 C3)alkylcarbonyl;

15 - R4 is selected amongst H; Halogen; difluoromethyl; trifluoromethyl; phenyl; cyano; (C1-3)alkyl;
 amino(C1-3)alkyl; (C4-C7)heterocycloalkyl; (C4-C7)heteroaryl wherein the heteroaryl group is
 optionally substituted with a (C1-C3)alkyl group; (C4-C7)heteroaryl-(C1-C3)alkyl wherein the
 heteroaryl group is optionally substituted with a (C1-C3)alkyl group; (C4-C7)heteroaryl group
 20 optionally substituted with (C1-C3)alkyl, amino-carbonyl, (C1-C3)-alkylamino-carbonyl; (C1-
 C3)-alkoxycarbonyl; (C1-C3)alkyl-sulfonyl; (C4-C7)heteroalkyl-carbonyl; (C1-C3)alkylamino-
 carbonyl; di(C1-C3)alkylamino-carbonyl;

R5 is selected amongst H; oxo; (C1-C3)alkyl; (C4-C7)heterocycloalkyl-(C1-C3)alkyl;
 25 methoxycarbonyl ;

Wherein

When T is O, X is N then L, U, V, W are C;

When W and T are N, then X, Y, V, U, L are C;

30 When W and Y are N, then L, T, X, V, U are C;

When W, T, X are N then Y, V, U, L is C;

When W, T, Y are N, L, X, V, U is C;

When V, W, T are N, L, X, Y, U is C;

When U, T are N, then L, X, Y, V, W are C;

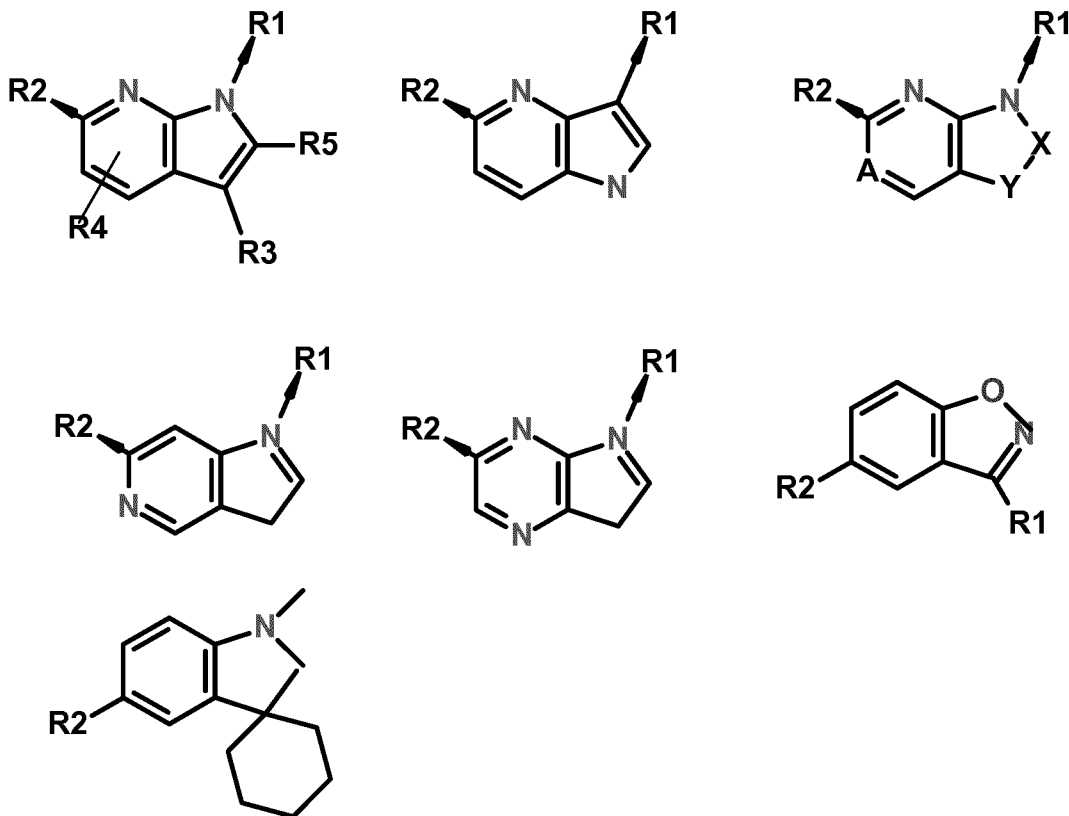
35 When L, T, X are N, then Y, V, U are C;

When W is N, Y is N or S, then T, X, V, U, L are C;

When T is N and W, X, Y, V, U are C then R4 forms a 6-membered carbocyclic ring; and R1, R3
 is methyl, R2, R5 is H;

When Y is N and L, U, V, W, T is C, then R1 and R5 form together a 6-membered heterocyclic ring, R3, R4, is hydrogen.

5. A compound according to claim 1 or 4, wherein the core A is selected amongst the following:



5

Wherein

X is O, C, or N, wherein C is optionally substituted with an oxo moiety,

10 Y is C, S or N,

A is C or N, optionally substituted with 1-C₍₁₋₄₎-4-aryl-piperazine or 1-C₍₁₋₄₎-4-heteroaryl-piperazine or 1-(4-C₍₁₋₄₎-aryl)piperazine or 1-(4-C₍₁₋₄₎-heteroaryl)piperazine or 1-C₍₁₋₄₎-4-aryl-piperidine or 1-C₍₁₋₄₎-4-heteroaryl-piperidine or 1-(4-C₍₁₋₄₎-aryl)piperidine or 1-(4-C₍₁₋₄₎-heteroaryl)piperidine with optional substitution on aryl, heteroaryl, piperazine or piperidine groups;

15

R1 is selected amongst H, ethyl-azabicyclo[3.2.0]heptane; or 2-substituted-5-azaspiro[3.4]octane; or ethyl-2-pyrrolidine optionally substituted with one or more (C1-3)alkyl, or (C4-7) cycloalkylamines including 3-substituted-N-methyl-cyclobutanamine and piperidine;

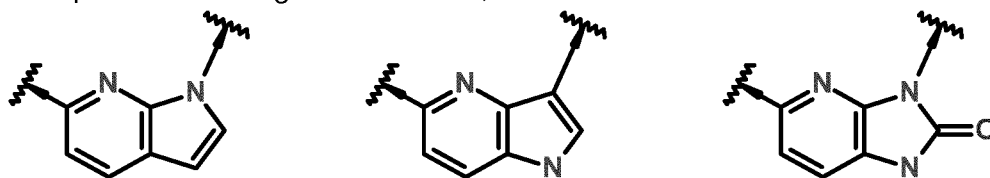
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R2 is selected amongst 1-C₍₁₋₄₎-4-aryl-piperazine or 1-C₍₁₋₄₎-4-heteroaryl-piperazine or 1-(4-C₍₁₋₄₎-aryl)piperazine or 1-(4-C₍₁₋₄₎-heteroaryl)piperazine or 1-C₍₁₋₄₎-4-aryl-piperidine or 1-C₍₁₋₄₎-4-heteroaryl-piperidine or 1-(4-C₍₁₋₄₎-aryl)piperidine or 1-(4-C₍₁₋₄₎-heteroaryl)piperidine with optional substitution on aryl, heteroaryl, piperazine or piperidine groups;

R3, R4 is selected independently from each other amongst H, halogen, cyano, C1-6 alkyl, trifluoromethyl, difluoromethyl, (C2-6) alkenyl, hydroxy, (C1-6) alkoxy, difluoromethoxy, trifluoromethoxy, trifluoroethoxy, (C1-6) alkylthio, (C1-6) alkylsulphonyl, amino, (C1-6) alkylamino, di(C1-6)alkylamino, (C1-6)alkoxy(C1-6)alkyl-amino, N-[(C1-6)alkyl]-N-[hydroxy(C1-6)alkyl]amino, (C2-6) alkylcarbonylamino, (C2-6) alkoxy carbonylamino, (C1-6) alkylsulphonylamino, formyl, (C2-6) alkylcarbonyl, carboxy, (C2-6) alkoxy carbonyl, aminocarbonyl, (C1-6) alkylaminocarbonyl, di(C1-6)alkylaminocarbonyl, aminosulphonyl, (C1-6) alkylaminosulphonyl or di(C1-6)alkylaminosulphonyl; (C3-7)heterocycloalkyl or (C3-7)spiroheterocycloalkyl

R5 is selected amongst H, 2-(Pyrrolidin-1-yl)ethyl.

6. A compound according to claim 1 to 3, wherein the central core A is



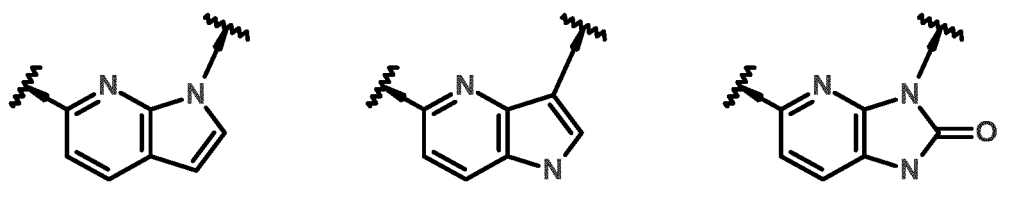
7. A compound according to any of the preceding claims, wherein R1 is ethylazabicyclo[3.2.0]heptane; or 2-substituted-5-azaspiro[3.4.]octane; or ethyl-2-methylpyrrolidine or (C4-7) cycloalkylamines including 3-substituted-N-methyl-cyclobutanamine and piperidine.
8. A compound according to claim 7, wherein R1 is 3-substituted-N-methyl-cyclobutanamine.
9. A compound according to claim 7, wherein R1 is 2-substituted-5-azaspiro[3.4.]octane.
10. A compound according to claim 7, wherein R1 is (C4-7) cycloalkylamines including 3-substituted-N-methyl-cyclobutanamine and piperidine.

11. A compound according to to any of the preceding claims, wherein R2 is 1-substituted-4-aryl-piperazine or 1-substituted-4-heteroaryl-piperazine or 1-(4-substituted-aryl)piperazine or 1-(4-substituted-heteroaryl)piperazine or 1-substituted-4-aryl-piperidine or 1-substituted-4-heteroaryl-piperidine or 1-(4-substituted-aryl)piperidine or 1-(4-substituted-heteroaryl)piperidine with optional substitution on aryl, heteroaryl, piperazine or piperidine groups.

12. A compound according to claim 11, wherein R2 is 1-substituted-4-aryl-piperazine or 1-substituted-4-heteroaryl-piperazine, 1-substituted-4-aryl-piperidine or 1-substituted-4-heteroaryl-piperidine.

13. A compound according to claim 1, wherein

- the central core A is

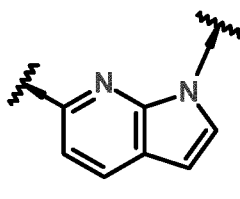


- R1 is ethyl-azabicyclo[3.2.0]heptane ; or 2 -substituted-5-azaspiro[3.4.]octane; or ethyl-2-methyl-pyrrolidine or (C4-7) cycloalkylamines including 3-substituted-N-methyl-cyclobutanamine and piperidine ;

- R2 is 1-substituted-4-aryl-piperazine or 1-substituted-4-heteroaryl-piperazine or 1-(4-substituted-aryl)piperazine or 1-(4-substituted-heteroaryl)piperazine or 1-substituted-4-aryl-piperidine or 1-substituted-4-heteroaryl-piperidine or 1-(4-substituted-aryl)piperidine or 1-(4-substituted-heteroaryl)piperidine with optional substitution on aryl, heteroaryl, piperazine or piperidine groups.

14. A compound according to claim 13, wherein

- the central core A is



- R1 is 2-substituted-5-azaspiro[3.4.]octane or 3-substituted-N-methyl-cyclobutanamine or 4-substituted piperidine;
- R2 is 1-substituted-4-aryl-piperazine or 1-substituted-4-heteroaryl-piperazine, 1-substituted-4-aryl-piperidine or 1-substituted-4-heteroaryl-piperidine.

15. A compound according to claim 1, selected from the group comprising:

- 5 6-[(3S)-3-methyl-4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[(2S)-2-methyl-4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-{4-[2-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 10 6-[(2R)-2-methyl-4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-(4-phenylpiperazin-1-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 15 6-{4-[3-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- ethyl 4-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)benzoate ;
- 5-(4-{1-[2-(piperidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 20 N,N-diethyl-2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethanamine ;
- 6-[4-(pyridin-2-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(pyridin-3-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(pyridin-4-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 25 6-(pyrrolidin-1-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 1-(1-methylpyrrolidin-3-yl)-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine ;
- 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[3,2-c]pyridine ;
- 30 cis-N-methyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine ;
- trans-N-methyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine ;
- 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[(3R)-pyrrolidin-3-yl]-1H-pyrrolo[2,3-b]pyridine ;

- 6-[4-[4-(methylsulfonyl)phenyl]piperazin-1-yl]-1-[(3S)-pyrrolidin-3-yl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-[4-(methylsulfonyl)phenyl]piperazin-1-yl]-1-(piperidin-4-yl)-1H-pyrrolo[3,2-c]pyridine ;
- cis-3-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}-N-methylcyclobutanamine ;
- 5 trans-3-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}-N-methylcyclobutanamine ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[trans-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 10 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[cis-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(6-cyanopyridin-2-yl)piperazin-1-yl]-1-[trans-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(6-cyanopyridin-2-yl)piperazin-1-yl]-1-[cis-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 15 1-[4-(4-{5-fluoro-1-[trans-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)phenyl]ethenone ;
- trans-3-(5-fluoro-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-methylcyclobutanamine ;
- 1-(4-phenyl-1-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperidin-4-yl)ethenone ;
- 20 4-phenyl-1-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperidin-4-ol ;
- 6-(4-phenylpiperidin-1-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 4-phenyl-1-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperidine-4-carbonitrile ;
- 6-[4-(3-methoxyphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(3-chlorophenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 25 3-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)benzonitrile ;
- 1-[2-(pyrrolidin-1-yl)ethyl]-6-[4-(thiophen-2-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(3-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(4-methylpyridin-3-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(4-methoxyphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 30 6-[4-(2-methoxyphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 4-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)benzonitrile ;
- 6-[4-(4-chlorophenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;

- 6-[4-(4-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(3-methylpyridin-4-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 2-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)quinoline ;
- 1-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)isoquinoline ;
- 5 6-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 6-[4-(3-methylpyridin-2-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 10 6-[4-(5-methylpyridin-2-yl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 1-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)ethenone ;
- (1-methylpiperidin-3-yl)(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)methanone ;
- (1-methylpiperidin-2-yl)(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)methanone ;
- 15 6-[4-(2-methylphenyl)piperazin-1-yl]-1-[2-(4-methylpiperazin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- N-(2-{6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)propan-2-amine ;
- N,N-dimethyl-1-(2-{6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)pyrrolidin-3-amine ;
- 20 1-{2-[2-(methoxymethyl)pyrrolidin-1-yl]ethyl}-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine ;
- 1-[2-(3-methoxypyrrolidin-1-yl)ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine ;
- 25 1-[2-(2-azabicyclo[3.1.0]hex-2-yl)ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine
- 6-methyl-1-(2-{6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)octahydro-1H-pyrrolo[2,3-c]pyridine ;
- 6-methyl-1-(2-{6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)octahydro-1H-pyrrolo[3,4-b]pyridine ;
- 30 1-[2-(5-methylhexahydropyrrolo[3,4-b]pyrrol-1(2H)-yl)ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine ;
- 1-[2-(3-methoxyazetid-1-yl)ethyl]-6-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridine ;

- 6-[4-(2-methylphenyl)piperazin-1-yl]-1-{2-[(2R)-2-methylpyrrolidin-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridine ;
- 6-[4-(2-methylphenyl)piperazin-1-yl]-1-{2-[3-(pyridin-2-yl)pyrrolidin-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridine ;
- 5 1-(2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)-N,N-dimethylpyrrolidin-3-amine ;
- 5-(4-{1-[2-(6-azabicyclo[3.2.0]hept-6-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 10 5-[4-(1-{2-[3-(1-methyl-1H-imidazol-2-yl)pyrrolidin-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine ;
- 5-[4-(1-{2-[2-(1-methyl-1H-pyrazol-4-yl)pyrrolidin-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine ;
- 5-[4-(1-{2-[3-(4,4-difluoropiperidin-1-yl)azetididin-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine ;
- 15 5-[4-(1-{2-[3-(pyrrolidin-1-yl)azetididin-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(2-oxa-7-azaspiro[3.5]non-7-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 20 5-(4-{1-[2-(5-azaspiro[3.4]oct-5-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(6-azaspiro[3.5]non-6-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- N-benzyl-2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}-N-methylethanamine ;
- 25 5-(4-{1-[2-(3-phenoxy pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(2-phenylazetididin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 30 5-[4-(1-{2-[3-(2-fluorophenyl)azetididin-1-yl]ethyl}-1H-pyrrolo[2,3-b]pyridin-6-yl)piperazin-1-yl]imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(3-phenoxyazetididin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 1-(2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethyl)-3-phenylazetididin-3-ol ;
- 35 *trans*-N-methyl-3-[3-(1-methyl-1H-pyrazol-4-yl)-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;

- trans*-N-methyl-3-[3-(1-methyl-1H-pyrazol-5-yl)-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- trans*-N-methyl-3-[6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-3-(1H-pyrazol-5-yl)-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- 5 *trans*-N-methyl-3-[3-(1-methyl-1H-pyrazol-3-yl)-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- 5-(4-{1-[2-(1-methylpyrrolidin-3-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 10 *cis*-N,N-dimethyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine ;
- trans*-N,N-dimethyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine ;
- 1-[(3*S*)-1-methylpyrrolidin-3-yl]-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine ;
- 15 1-[(3*R*)-1-methylpyrrolidin-3-yl]-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine ;
- cis*-N-benzyl-N-methyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine ;
- 20 *trans*-N-benzyl-N-methyl-3-(6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclobutanamine ;
- 5-(4-{1-[2-(1-benzylpyrrolidin-3-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 1-[(3*S*)-1-benzylpyrrolidin-3-yl]-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine ;
- 25 1-[(3*R*)-1-benzylpyrrolidin-3-yl]-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridine ;
- 6-(4-methylpiperazin-1-yl)-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}-N,N-dimethylethanamine ;
- 30 5-(4-{1-[2-(1-oxa-6-azaspiro[3.4]oct-6-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile ;

- 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile ;
- 3-methyl-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine ;
- 5 trans-3-(3-bromo-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-methylcyclobutanamine ;
- 6-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)pyridine-2-carbonitrile ;
- 2-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)pyridine-3-carbonitrile ;
- 10 6-[4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[3,2-c]pyridine ;
- cis-3-(4-chloro-6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-methylcyclobutanamine ;
- cis-N-methyl-3-[6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-3-(trifluoromethyl)-1H-pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- 15 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrazolo[3,4-b]pyridine;
- 6-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-2-[2-(pyrrolidin-1-yl)ethyl]-2H-pyrazolo[3,4-b]pyridine;
- 20 5-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[3,2-c]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 2-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-7-[2-(pyrrolidin-1-yl)ethyl]-7H-pyrrolo[2,3-d]pyrimidine ;
- 6-(4-{1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[3,2-c]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 25 5-(4-{1-[2-(piperazin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 5-(4-{1-[2-(2-methyl-1H-imidazol-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;

- 5-(4-{1-[2-(pyrrolidin-3-yl)ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}piperazin-1-yl)imidazo[1,2-a]pyridine ;
- 2-{6-[4-(imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]-1H-pyrrolo[2,3-b]pyridin-1-yl}ethanamine ;
- 4-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenol ;
- 5 6-[4-[1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyridine-3-carbonitrile ;
- 5-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-3-[2-(pyrrolidin-1-yl)ethyl]-3H-imidazo[4,5-b]pyridine ;
- 5-{4-[4-(methylsulfonyl)phenyl]piperazin-1-yl}-1-[2-(pyrrolidin-1-yl)ethyl]-1H-imidazo[4,5-b]pyridine ;
- 10 1-(4-{1-[trans-3-(methylamino)cyclobutyl]-1H-pyrrolo[2,3-b]pyridin-6-yl}phenyl)ethenone ;
- 6-piperazin-1-yl-1-(2-pyrrolidin-1-ylethyl)pyrrolo[2,3-b]pyridine ;
- trans-N-methyl-3-[6-[4-(3-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutan-1-amine ;
- 5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-3-piperazin-1-yl-thieno[3,2-b]pyridine ;
- 15 1-(2-pyrrolidin-1-ylethyl)-6-[4-(3-thienyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine ;
- cis-N,N-dimethyl-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carboxamide ;
- cis-methyl 1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carboxylate ;
- 20 trans-6-[4-(6-acetyl-3-pyridyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl)-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-(1-methyl-2-oxo-4-pyridyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 25 trans-6-[4-(4-formylphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- cis-N-methyl-3-[3-methylsulfonyl-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;

- trans-N-methyl-3-[7-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-c]pyridin-1-yl]cyclobutanamine ;
- trans-6-[4-(4-hydroxyphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 5 trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-oxochroman-7-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-[(R)-methylsulfinyl]phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-(2-methyl-4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 10 trans-1-[3-(methylamino)cyclobutyl]-6-[4-(2-methyl-1-oxo-3H-isoindol-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-methyl 5-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyridine-3-carboxylate ;
- 15 trans-methyl 2-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyridine-4-carboxylate ;
- trans-methyl 5-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyrazine-2-carboxylate ;
- trans-4-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]-N,N-dimethylbenzamide ;
- 20 trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-(2-oxopyrrolidin-1-yl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-(5-methylsulfonylpyridin-2-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile;
- 25 6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl)-1-[2-(oxolan-3-yl)ethyl]pyrrolo[2,3-b]pyridine ;
- tert-butyl 3-[2-[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]pyrrolidine-1-carboxylate ;
- 1-[2-[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]pyrrolidin-2-one ;

- trans-1-[3-(methylamino)cyclobutyl]-6-[4-(3-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 5 trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-pyridin-2-ylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-N-methyl-3-[6-[4-(4-pyridin-2-ylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutan-1-amine ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-(1-methylimidazol-2-yl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 10 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3R)-pyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3S)-pyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-piperidin-4-ylpyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-piperidin-4-ylpyrrolo[3,2-c]pyridine-3-carbonitrile ;
- 15 6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-[(3S)-pyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[rel-(3R,4R)-3-fluoropiperidin-4-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-[(3S)-4-(4-acetylphenyl)-3-methylpiperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 20 Trans-6-[(3R)-4-(4-acetylphenyl)-3-methylpiperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-[(2R)-4-(4-acetylphenyl)-2-methylpiperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 25 trans-6-[(2S)-4-(4-acetylphenyl)-2-methylpiperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- cis-1-[4-[4-[1-[3-(methylamino)cyclobutyl]-3-(1-methylpyrazol-4-yl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;

- trans-1-[4-[4-[1-[3-(methylamino)cyclobutyl]-3-(1-methylpyrazol-4-yl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- trans-N-methyl-3-[3-(1-methylpyrazol-4-yl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutan-1-amine ;
- 5 1-[4-[4-[3-(2-methylpyridin-3-yl)-1-piperidin-4-yl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- 1-[4-[4-[3-(1-methylpyrazol-3-yl)-1-piperidin-4-yl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- 1-[4-[4-[3-(2-methylpyrimidin-5-yl)-1-piperidin-4-yl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- 10 1-[4-[4-[1-[3-(methylamino)cyclobutyl]-3-(1-methylpyrazol-4-yl)pyrrolo[3,2-c]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- trans-6-[4-(4-acetyl-3-hydroxy-phenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 15 trans-6-[4-(4-acetyl-3-fluoro-phenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-[4-(2-acetyl-5-fluoro-phenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-2-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]pyrimidine-4-carboxamide ;
- 20 trans-6-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]-N,N-dimethylpyridine-2-carboxamide ;
- trans-6-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]-N-methylpyridazine-3-carboxamide ;
- 25 trans-6-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]-N,N-dimethylpyridine-3-carboxamide ;
- Trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-(2-methylpropanoyl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- Trans-1-[3-(methylamino)cyclobutyl]-6-[4-(1-oxotetralin-6-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 30

Trans-4-[4-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]-4-oxo-butanoic acid;

Trans-6-[4-[4-(2,2-dimethylpropanoyl)phenyl]piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

- 5 Trans-4-[4-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]-2-methyl-4-oxo-butanoic acid ;

Trans-1-[3-(methylamino)cyclobutyl]-6-[4-(1-oxoindan-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

- 10 Trans-6-[4-(5-acetylpyridin-2-yl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

Trans-6-[4-(5-acetylpyrimidin-2-yl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

Trans-6-[4-(5-acetylpyrazin-2-yl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

- 15 Trans-6-[4-(6-acetylpyridazin-3-yl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

cis-[1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-3-yl]-morpholino-methanone ;

- 20 cis-N-methyl-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carboxamide ;

trans-3-[6-chloro-4-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]-N-methyl-cyclobutanamine ;

trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylcyclohexyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

- 25 trans-1-[3-(methylamino)cyclobutyl]-6-[4-(4-methylsulfonylcyclohexyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

trans-1-[3-(methylamino)cyclobutyl]-6-[4-(1-methylsulfonyl-4-piperidyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile;

- 30 trans-6-[4-(1-acetyl-4-piperidyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

- trans-6-(4-ethylpiperazin-1-yl)-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpiperidin-4-yl)pyrrolo[2,3-b]pyridine-3-carbonitrile;
- 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3S)-1-methylpyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 5 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[(3R)-1-methylpyrrolidin-3-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 1-[(3S)-1-methylpyrrolidin-3-yl]-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 10 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-(dimethylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-1-[3-(methylamino)cyclobutyl]-6-[4-[4-(2,2,2-trifluoroacetyl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-6-[4-(4-acetylphenyl)piperazin-1-yl]-2-methyl-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 15 trans-3-[5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclobutanamine ;
- trans-N-methyl-3-[3-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyrazin-5-yl]cyclobutanamine ;
- trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate ;
- 20 trans-1-[4-[4-[2-methyl-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- trans-5-[4-(4-acetylphenyl)piperazin-1-yl]-3-[3-(methylamino)cyclobutyl]-1-(1-methylpyrazol-4-yl)imidazo[4,5-b]pyridin-2-one ;
- 25 5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpyrazol-4-yl)-3-(4-piperidyl)imidazo[4,5-b]pyridin-2-one ;
- 1-(1-methylpyrazol-4-yl)-5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-3-(4-piperidyl)imidazo[4,5-b]pyridin-2-one ;
- 5-[4-(4-acetylphenyl)piperazin-1-yl]-3-(4-methyl-4-piperidyl)-1-(1-methylpyrazol-4-yl)imidazo[4,5-b]pyridin-2-one ;
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- trans-5-[4-(4-acetylphenyl)piperazin-1-yl]-3-[3-(methylamino)cyclobutyl]-1-phenyl-imidazo[4,5-b]pyridin-2-one ;
- 5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(1-methylpyrazol-3-yl)-3-(4-piperidyl)imidazo[4,5-b]pyridin-2-one ;
- 5 6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-(4-piperidyl)pyrrolo[2,3-b]pyridine ;
- (1R,3R)-3-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclopentanamine ;
- 1-(2-azaspiro[3.3]heptan-6-yl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine;
- (1R,3S)-3-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclopentanamine ;
- 10 cis-N-methyl-4-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclohexanamine ;
- trans-N-methyl-4-[6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]cyclohexanamine ;
- 15 6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-quinuclidin-3-yl-pyrrolo[2,3-b]pyridine ;
- 1-(1-methyl-3-piperidyl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine ;
- 1-(1-methyl-4-piperidyl)-6-[4-(4-methylsulfonylphenyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine ;
- N,N-dimethyl-1-[2-[6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]azetidine-3-carboxamide ;
- 20 1-[2-(3-imidazol-1-ylpyrrolidin-1-yl)ethyl]-6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine ;
- N-[1-[2-[6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]azetidine-3-yl]methanesulfonamide ;
- 1-[2-(3-fluoro-3-methyl-pyrrolidin-1-yl)ethyl]-6-[4-(o-tolyl)piperazin-1-yl]pyrrolo[2,3-b]pyridine ;
- 6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl)-1-[2-[4-(2-methylpyrazol-3-yl)-1-piperidyl]ethyl]pyrrolo[2,3-b]pyridine ;
- 25 6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl)-1-[2-[4-(oxetan-3-yl)-1-piperidyl]ethyl]pyrrolo[2,3-b]pyridine ;
- 2-[2-[6-(4-imidazo[1,2-a]pyridin-5-yl)piperazin-1-yl]pyrrolo[2,3-b]pyridin-1-yl]ethyl]-3,4-dihydro-1H-isoquinoline ;

- 5-[4-(4-acetylphenyl)piperazin-1-yl]-1-(oxetan-3-yl)-3-(4-piperidyl)imidazo[4,5-b]pyridin-2-one ;
- trans-1-[4-[4-[3-bromo-2-methyl-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone ;
- trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate ;
- 5 Trans-6-[4-(4-acetylphenyl)piperazin-1-yl]-5-fluoro-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-[4-(1,1-dimethoxyethyl)phenyl]piperazin-1-yl]-5-fluoro-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 10 1-methyl-5-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-3-(1,2,3,6-tetrahydropyridin-4-yl)pyrrolo[2,3-c]pyridine ;
- trans-1-[4-[4-[1-[3-(methylamino)cyclobutyl]-3-(3-pyridyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethenone trifluoroacetate ;
- 7-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-2-piperidin-4-ylpyrazolo[3,4-c]pyridine ;
- 15 7-[4-(4-methylsulfonylphenyl)piperazin-1-yl]-1-(4-piperidyl)pyrazolo[3,4-c]pyridine
- 6-[4-(4-acetylpiperazin-1-yl)phenyl]-1-[trans-3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 1-[4-[4-[5-(1-methylpyrazol-4-yl)-1,2,3,4-tetrahydropyrido[4,3-b]indol-8-yl]piperazin-1-yl]phenyl]ethanone ;
- 20 trans-methyl 6-[4-(4-acetylphenyl)piperazin-1-yl]-3-bromo-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-2-carboxylate ;
- 5-[4-(4-acetylphenyl)piperazin-1-yl]-3-(4-methyl-4-piperidyl)-1-(oxetan-3-yl)imidazo[4,5-b]pyridin-2-one ;
- trans-5-[4-(4-acetylphenyl)piperazin-1-yl]-3-[3-(methylamino)cyclobutyl]-1-(oxetan-3-yl)imidazo[4,5-b]pyridin-2-one ;
- 25 6-[4-(4-Acetylphenyl)phenyl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- 6-[4-(4-acetyl-2-methylphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;
- trans-methyl 4-[4-[3-cyano-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-

yl]benzoate ;

6-[4-[4-(azetidine-1-carbonyl)phenyl]piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile ;

5 1-[4-[4-[3-(1-methylpyrazol-4-yl)-1-piperidin-4-yl]pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone ;

1-[4-[4-[1-(1-methylpyrazol-4-yl)-3-piperazin-1-yl-pyrrolo[3,2-b]pyridin-5-yl]piperazin-1-yl]phenyl]ethanone ;

1-[4-[4-[1-(1-methylpyrazol-4-yl)-3-piperidin-4-yl]pyrrolo[3,2-b]pyridin-5-yl]piperazin-1-yl]phenyl]ethanone.

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16. A compound according to any of the preceding claims selected from the group comprising:

1-[4-[4-[3-(1-methylpyrazol-4-yl)-1-(4-piperidyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone,

15 1-[4-[4-[3-(2-methyl-3-pyridyl)-1-(4-piperidyl)pyrrolo[2,3-b]pyridin-6-yl]piperazin-1-yl]phenyl]ethanone,

6-[(2S)-2-methyl-4-(2-methylphenyl)piperazin-1-yl]-1-[2-(pyrrolidin-1-yl)ethyl]-1H-pyrrolo[2,3-b]pyridine,

1-[4-[4-[1-(1-methylpyrazol-4-yl)-3-(4-piperidyl)pyrrolo[3,2-b]pyridin-5-yl]piperazin-1-yl]phenyl]ethanone,

20 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-(5-azaspiro[3.4]octan-2-yl)pyrrolo[2,3-b]pyridine-3-carbonitrile,

1-[3-(methylamino)cyclobutyl]-6-[4-[4-(2,2,2-trifluoroacetyl)phenyl]piperazin-1-yl]pyrrolo[2,3-b]pyridine-3-carbonitrile,

25 6-[4-(4-acetylphenyl)piperazin-1-yl]-1-(4-piperidyl)pyrrolo[2,3-b]pyridine-3-carbonitrile, 6-[4-(4-acetyl-3-hydroxy-phenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile,

6-[4-(4-acetyl-3-fluoro-phenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile,

30 6-[(-4-(4-acetylphenyl)-2-methyl-piperazin-1-yl)-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile,

6-[4-(4-acetylphenyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile,

5-[4-(4-acetylphenyl)piperazin-1-yl]-3-[3-(methylamino)cyclobutyl]-1-(1-methylpyrazol-4-yl)imidazo[4,5-b]pyridin-2-one,

35 6-[4-(4-acetylphenyl)-3-methyl-piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile,

6-[4-(4-acetylphenyl)piperazin-1-yl]-2-methyl-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile,

6-[4-(5-acetyl-2-pyridyl)piperazin-1-yl]-1-[3-(methylamino)cyclobutyl]pyrrolo[2,3-b]pyridine-3-carbonitrile.

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17. A compound according to any of claims 1 to 16 for use as a medicament.

18. A pharmaceutical composition comprising an effective amount of a compound according to claims 1 to 16 in combination with a pharmaceutically acceptable diluent or carrier.

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19. A compound according to any of claims 1 to 16 for use in the treatment of inflammatory conditions driven by STING activation.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2019/053893

A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61K31/437 A61K31/4375 A61K31/519 A61K31/4365 C07D471/04
 C07D498/04 C07D513/04 A61P29/00 A61P19/00
 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 A61P A61K

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, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2017/175156 A1 (GLAXOSMITHKLINE IP DEV LTD [GB]) 12 October 2017 (2017-10-12) the whole document -----	1-19

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

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- "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
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- "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 25 April 2019	Date of mailing of the international search report 06/05/2019
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Österle, Carmen
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2019/053893

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WO 2017175156	A1	12-10-2017	
		AU 2017247806 A1	08-11-2018
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		CA 3019628 A1	12-10-2017
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