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(54) Title: METTL3 INHIBITORY COMPOUNDS

(57) Abstract: The present invention relates to compounds of formula (I) that function as inhibitors of METTL3 (N6-adenosine-methyltransferase 70 kDa subunit) enzyme activity: X-Y-Z5 (I) wherein X, Y and Z are each as defined herein. The present invention also relates to processes for the preparation of these compounds, to pharmaceutical compositions comprising them, and to their use in the treatment of proliferative disorders, such as cancer, and autoimmune diseases, as well as other diseases or conditions in which METTL3 activity 10 is implicated.



METTL3 INHIBITORY COMPOUNDS

FIELD OF THE INVENTION

[0001] The present invention relates to certain compounds that function as inhibitors of METTL3 (N6-adenosine-methyltransferase 70 kDa subunit) activity. The present invention also relates to processes for the preparation of these compounds, to pharmaceutical compositions comprising them, and to their use in the treatment of proliferative disorders, such as cancer, autoimmune, neurological, infectious and inflammatory diseases, as well as other diseases or conditions in which METTL3 activity is implicated.

BACKGROUND OF THE INVENTION

[0002] N6-methyladenosine (m6A) is the most common and abundant covalent modification of messenger RNA, modulated by 'writers', 'erasers' and 'readers' of this mark (Meyer & Jaffrey 2014, Niu Y et al, 2013, Yue et al 2015). Approximately 0.1 to 0.5% of all mRNA adenosines are m6A modified (Li Y et al 2015). *In vitro* data have shown that m6A influences fundamental aspects of mRNA biology, mainly mRNA expression, splicing, stability, localisation and translation (Meyer et al, 2015; Sledz & Jinek 2016). M6A modifications are tissue specific and there is significant variability in their occurrence profiles in non-diseased tissues (eg brain, heart, kidney) and diseased tissues and cells (lung, renal, breast, and leukaemic cancer cells) (Meyer et al 2012).

[0003] The m6A modifications and its erasers and writers such as FTO, ALKBH5, methyltransferase like 3 (METTL3) and METTL14 are associated with major diseases such as solid organ cancers, leukaemia, type 2 diabetes, neuropsychiatric behavioural and depressive disorders (Chandola et al 2015; Koranda et al 2018).

[0004] The RNA methyltransferase, METTL3, is the major, but not the sole enzyme, that catalyses m6A modification of RNA. It exists as a hetero-trimeric complex with METTL14 (Liu et al 2014, Wang et al 2016) and Wilm's Tumour Associated Protein (WTAP) (Ping et al 2014). Catalytic activity resides in METTL3, which transfers a methyl group from the co-factor S-adenosyl methionine to the substrate RNA and METTL14 facilitates substrate RNA binding. WTAP localises the complex in specific nuclear regions and also localises RNA substrates to the complex (Wang X et al 2016).

[0005] METTL3 has been reported to play a role in many aspects of the development of cancer (Fry et al 2018). Genetic knockdown of METTL3 in lung cancer cell lines (A549, H1299 and H1792) and HeLa cells leads to decreased growth, survival and invasion of human lung

cancer cells (Lin S et al 2016). METTL3 is significantly up-regulated in human bladder cancer (Cheng et al 2019). Knockdown of METTL3 drastically reduced bladder cancer cell proliferation, invasion, and survival in vitro and tumorigenicity in vivo. AF4/FMR2 family member 4 (AFF4), two key regulators of NF- κ B pathway (IKBKB and RELA) and MYC were further identified as direct targets of METTL3-mediated m6A modification. In renal carcinoma cell lines (CAK-1, CAK-2 and ACHN), genetic knockdown reduced cell proliferation via the phosphatidylinositol 3-kinase (PI3K)/AKT/mammalian target of rapamycin (mTOR) signalling pathway (Li X et al 2017).

[0006] Recently Barbieri et al (2017), defined a set of RNA-modifying enzymes that are necessary for AML leukaemia and identified a key leukaemic pathway for the METTL3 RNA methyltransferase. In this pathway, METTL3 is stably recruited by the CCAAT-box binding transcription factor CEBPZ to promoters of a specific set of active genes, resulting in m6A methylation of the respective mRNAs and increased translation. One important target is *SP1*, an oncogene in several cancers, which regulates *c-MYC* expression. Consistent with these findings, it has been reported that METTL3 can methylate its targets co-transcriptionally.

[0007] The pathway described by Barbieri et al., is critical for AML leukaemia, as three of its components are required for AML cell growth: (i) the m6A RNA methyltransferase METTL3; (ii) the transcription factor CEBPZ, which targets this enzyme to promoters; and (iii) *SP1*, whose translation is dependent upon the m6A modification by METTL3. Together, the observations of Barbieri et al define METTL3 enzymatic activity as a new candidate target for the treatment of AML.

[0008] In separate, independent studies it has been reported that METTL3 plays an essential role in controlling myeloid differentiation of mammalian normal hematopoietic and leukemic cells (Vu et al 2017). Forced expression of wild type METTL3, but not a mutant METTL3 (with defect in catalytic activity), significantly promotes cell proliferation and inhibits cell differentiation of human cord blood-derived CD34+ haematopoietic stem/progenitor cells (HSPCs). Genetic knockdown of METTL3 has the opposite effects. METTL3 is highly expressed in AML compared to normal HSPCs or other types of cancers. Knockdown of METTL3 in human AML cell lines significantly induces cell differentiation and apoptosis and inhibits leukemia progression in mice xeno-transplanted with MOLM-13 AML cells. The biological function of METTL3 is likely attributed to the promotion of translation of its mRNA targets such as MYC, BCL-2, and PTEN in an m6A-dependent manner.

[0009] Recently, METTL3 mediated m6A modification has been demonstrated to play an important role in T cell homeostasis and signal dependent induction of mRNA degradation in CD4 positive T cell lineages (Li et al 2017). Deletion of METTL3 in mouse T cells disrupts T cell homeostasis and differentiation. In a lymphopenic mouse adoptive transfer model, naive *Mettl3*-deficient T cells failed to undergo homeostatic expansion and remained in the naive

state for up to 12 weeks, thereby preventing colitis. Consistent with these observations, the mRNAs of SOCS family genes encoding the STAT signalling inhibitory proteins SOCS1, SOCS3 and CISH were marked by m6A, exhibited slower mRNA decay and showed increased mRNAs and levels of protein expression in *Mettl3*-deficient naive T cells. This increased SOCS family activity consequently inhibited IL-7-mediated STAT5 activation and T cell homeostatic proliferation and differentiation. Thus METTL3 mediated m6A methylation has important roles for inducible degradation of Socs mRNAs in response to IL-7 signalling in order to reprogram naive T cells for proliferation and differentiation, pointing to a role in auto-immunity.

[0010] Recent studies have revealed that depletion of METTL3 leads to alterations in the propagation of diverse viruses (Winkler et al). Following viral infection or stimulation of cells with an inactivated virus, deletion of the m6A 'writer' METTL3 led to an increase in the induction of interferon-stimulated genes. Consequently, propagation of different viruses was suppressed in an interferon-signaling-dependent manner. Significantly, the mRNA of IFNB, was m6A modified and was stabilized following repression of METTL3. m6A serves as a negative regulator of interferon response by dictating the fast turnover of interferon mRNAs and consequently facilitating viral propagation. Therefore METTL3 inhibitors may provide a novel therapeutic approach to a range of infectious and inflammatory diseases.

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[0032] An object of this invention is to provide inhibitors of METTL3 activity.

SUMMARY OF THE INVENTION

[0033] In one aspect, the present invention provides a compound as defined herein, or a pharmaceutically acceptable salt thereof.

[0034] In another aspect, the present invention provides a pharmaceutical composition as defined herein which comprises a compound as defined herein, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable excipients.

5 [0035] In another aspect, the present invention provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in therapy.

[0036] In another aspect, the present invention provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of a proliferative condition.

10 [0037] In another aspect, the present invention provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of cancer. In a particular embodiment, the cancer is a human cancer.

[0038] In another aspect, the present invention provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein,
15 for use in the inhibition of METTL3 activity.

[0039] In another aspect, the present invention provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of an autoimmune disease.

[0040] In another aspect, the present invention provides a compound as defined herein, or a
20 pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of a neurological disease.

[0041] In another aspect, the present invention provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of an infectious disease.

25 [0042] In another aspect, the present invention provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein, for use in the treatment of an inflammatory disease.

[0043] In another aspect, the present invention provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for
30 use in the treatment of a proliferative condition.

[0044] In another aspect, the present invention provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for

use in the treatment of cancer. In a particular embodiment, the medicament is for use in the treatment of human cancers.

[0045] In another aspect, the present invention provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the inhibition of METTL3 activity.

[0046] In another aspect, the present invention provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of an autoimmune disease.

[0047] In another aspect, the present invention provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of a neurological disease.

[0048] In another aspect, the present invention provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of an infectious disease.

[0049] In another aspect, the present invention provides the use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of an inflammatory disease.

[0050] In another aspect, the present invention provides a method of inhibiting METTL3 activity *in vitro* or *in vivo*, said method comprising contacting a cell with an effective amount of a compound as defined herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[0051] In another aspect, the present invention provides a method of inhibiting cell proliferation *in vitro* or *in vivo*, said method comprising contacting a cell with an effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[0052] In another aspect, the present invention provides a method of inhibiting metastasis *in vitro* or *in vivo*, said method comprising contacting a cell with an effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[0053] In another aspect, the present invention provides a method of treating a proliferative disorder, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[0054] In another aspect, the present invention provides a method of treating cancer, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

5 [0055] In another aspect, the present invention provides a method of treating an autoimmune disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

10 [0056] In another aspect, the present invention provides a method of treating a neurological disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

15 [0057] In another aspect, the present invention provides a method of treating an infectious disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

20 [0058] In another aspect, the present invention provides a method of treating an inflammatory disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt, or a pharmaceutical composition as defined herein.

[0059] In one aspect, the present invention provides a combination comprising a compound as defined herein, or a pharmaceutically acceptable salt thereof, with one or more additional therapeutic agents.

25 [0060] The present invention further provides a method of synthesising a compound, or a pharmaceutically acceptable salt, as defined herein.

[0061] In another aspect, the present invention provides a compound as defined herein, or a pharmaceutically acceptable salt, obtainable by, or obtained by, or directly obtained by a method of synthesis as defined herein.

30 [0062] In another aspect, the present invention provides novel intermediates as defined herein which are suitable for use in any one of the synthetic methods as set out herein.

[0063] Preferred, suitable, and optional features of any one particular aspect of the present invention are also preferred, suitable, and optional features of any other aspect.

BRIEF DESCRIPTION OF THE DRAWINGS

[0064] For a better understanding of the invention, and to show how embodiments of the same are put into effect, reference is now made, by way of example, to the following figures, in which:

5 Figure 1: Schematic of the MOLM13 AML proliferation assay with measurement of m6A levels

Figure 2: m6A levels in total RNA from MOLM13 (+IFN γ) day 4

Figure 3: Inhibition of MOLM13 proliferation 6 days

Figure 4: Inhibition of MOLM13 CD14 expression 6 days

Figure 5: Inhibition of MOLM14, Kasumi-1, NOMO-1 and THP.1 proliferation 7 days (IFN γ treated)

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Figure 6: Inhibition of KCL-22 proliferation 6 days (IFN γ treated)

DETAILED DESCRIPTION OF THE INVENTION**Definitions**

[0065] Unless otherwise stated, the following terms used in the specification and claims have the following meanings set out below.

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[0066] It is to be appreciated that references to “treating” or “treatment” include prophylaxis as well as the alleviation of established symptoms of a condition. “Treating” or “treatment” of a state, disorder or condition therefore includes: (1) preventing or delaying the appearance of clinical symptoms of the state, disorder or condition developing in a human that may be afflicted with or predisposed to the state, disorder or condition but does not yet experience or display clinical or subclinical symptoms of the state, disorder or condition, (2) inhibiting the state, disorder or condition, i.e., arresting, reducing or delaying the development of the disease or a relapse thereof (in case of maintenance treatment) or at least one clinical or subclinical symptom thereof, or (3) relieving or attenuating the disease, i.e., causing regression of the state, disorder or condition or at least one of its clinical or subclinical symptoms.

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[0067] A “therapeutically effective amount” means the amount of a compound that, when administered to a mammal for treating a disease, is sufficient to effect such treatment for the disease. The “therapeutically effective amount” will vary depending on the compound, the disease and its severity and the age, weight, etc., of the mammal to be treated.

[0068] In this specification the term “alkyl” includes both straight and branched chain alkyl groups. References to individual alkyl groups such as “propyl” are specific for the straight chain version only and references to individual branched chain alkyl groups such as “isopropyl” are specific for the branched chain version only. For example, “C₁₋₆alkyl” includes C₁₋₄alkyl,

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C₁₋₃alkyl, propyl, isopropyl and *t*-butyl. A similar convention applies to other radicals, for example "phenyl(C₁₋₆alkyl)" includes phenyl(C₁₋₄alkyl), benzyl, 1-phenylethyl and 2-phenylethyl.

[0069] The term "(m-nC)" or "C_{m-n}", or "(m-nC) group" or "C_{m-n}" used alone or as a prefix, refers to any group having m to n carbon atoms.

[0070] The term "alkenyl", as used herein, refers to an aliphatic group containing at least one double bond and is intended to include both "unsubstituted alkenyls" and "substituted alkenyls", the latter of which refers to alkenyl moieties having substituents replacing a hydrogen on one or more carbons of the alkenyl group. Such substituents may occur on one or more carbons that are included or not included in one or more double bonds. Moreover, such substituents include all those contemplated for alkyl groups, as discussed below, except where stability is prohibitive. For example, substitution of alkenyl groups by one or more alkyl, carbocyclyl, aryl, heterocyclyl, or heteroaryl groups is contemplated.

[0071] The term "alkynyl", as used herein, refers to an aliphatic group containing at least one triple bond and is intended to include both "unsubstituted alkynyls" and "substituted alkynyls", the latter of which refers to alkynyl moieties having substituents replacing a hydrogen on one or more carbons of the alkynyl group. Such substituents may occur on one or more carbons that are included or not included in one or more triple bonds. Moreover, such substituents include all those contemplated for alkyl groups, as discussed above, except where stability is prohibitive. For example, substitution of alkynyl groups by one or more alkyl, carbocyclyl, aryl, heterocyclyl, or heteroaryl groups is contemplated.

[0072] An "alkylene" group is an alkyl group that is positioned between and serves to connect two other chemical groups. Thus, "C₁₋₃alkylene" means a linear saturated divalent hydrocarbon radical of one to three carbon atoms or a branched saturated divalent hydrocarbon radical of three atoms, for example, methylene, ethylene, propylene, and the like.

[0073] The term "C_{m-n}cycloalkyl" means a hydrocarbon ring containing from m to n carbon atoms, for example "C₃₋₆cycloalkyl" means a hydrocarbon ring containing from 3 to 6 carbon atoms, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl. The term "C_{m-n}cycloalkyl" also encompasses non-aromatic saturated or partially saturated monocyclic, fused, bridged, or spiro bicyclic carbocyclic ring system(s). The term "C_{m-n}cycloalkyl" includes both monovalent species and divalent species. Monocyclic "C_{m-n}cycloalkyl" rings contain from about 3 to 12 (suitably from 3 to 8, most suitably from 5 to 6) ring carbon atoms. Bicyclic "C_{m-n}cycloalkyl" contain from 7 to 17 ring carbon atoms, suitably 7 to 12 ring carbon atoms. Bicyclic "C_{m-n}cycloalkyl" rings may be fused, spiro (e.g. spiro[3,3]heptane), or bridged ring systems (e.g. bicyclo[2.2.1]hept-2-ene and bicyclo[1.1.1]pentanyl).

[0074] The term “halo” or “halogeno” refers to fluoro, chloro, bromo and iodo.

[0075] The term “heterocyclyl”, “heterocyclic” or “heterocycle” means a non-aromatic saturated or partially saturated monocyclic, fused, bridged, or spiro bicyclic heterocyclic ring system(s). The term heterocyclyl includes both monovalent species and divalent species.

5 Monocyclic heterocyclic rings contain from about 3 to 12 (suitably from 3 to 7, most suitably from 5 to 6) ring atoms, with from 1 to 5 (suitably 1, 2 or 3) heteroatoms selected from nitrogen, oxygen or sulfur in the ring. Bicyclic heterocycles contain from 7 to 17 member atoms, suitably 7 to 12 member atoms, in the ring. Bicyclic heterocycles contain from about 7 to about 17 ring atoms, suitably from 7 to 12 ring atoms. Bicyclic heterocyclic(s) rings may be fused, spiro, or
10 bridged ring systems. Examples of heterocyclic groups include cyclic ethers such as oxiranyl, oxetanyl, tetrahydrofuranyl, dioxanyl, and substituted cyclic ethers. Heterocycles containing nitrogen include, for example, azetidiny, pyrrolidiny, piperidiny, piperaziny, tetrahydrotriaziny, tetrahydropyrazoly, and the like. Typical sulfur containing heterocycles include tetrahydrothienyl, dihydro-1,3-dithiol, tetrahydro-2*H*-thiopyran, and
15 hexahydrothiepine. Other heterocycles include dihydro-oxathiolyl, tetrahydro-oxazolyl, tetrahydro-oxadiazolyl, tetrahydrodioxazolyl, tetrahydro-oxathiazolyl, hexahydrotriaziny, tetrahydro-oxaziny, morpholiny, thiomorpholiny, tetrahydropyrimidiny, dioxoliny, octahydrobenzofuranyl, octahydrobenzimidazolyl, and octahydrobenzothiazolyl. For heterocycles containing sulfur, the oxidized sulfur heterocycles containing SO or SO₂ groups
20 are also included. Examples include the sulfoxide and sulfone forms of tetrahydrothienyl and thiomorpholiny such as tetrahydrothiene 1,1-dioxide and thiomorpholiny 1,1-dioxide. A suitable value for a heterocyclyl group which bears 1 or 2 oxo (=O) or thioxo (=S) substituents is, for example, 2-oxopyrrolidiny, 2-thioxopyrrolidiny, 2-oxoimidazolidiny, 2-thioxoimidazolidiny, 2-oxopiperidiny, 2,5-dioxopyrrolidiny, 2,5-dioxoimidazolidiny or
25 2,6-dioxopiperidiny. Particular heterocyclyl groups are saturated monocyclic 3 to 7 membered heterocyclyls containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen or sulfur, for example azetidiny, tetrahydrofuranyl, tetrahydropyranyl, pyrrolidiny, morpholiny, tetrahydrothienyl, tetrahydrothienyl 1,1-dioxide, thiomorpholiny, thiomorpholiny 1,1-dioxide, piperidiny, homopiperidiny, piperaziny or homopiperaziny. As the skilled person would
30 appreciate, any heterocycle may be linked to another group via any suitable atom, such as via a carbon or nitrogen atom. However, reference herein to piperidino or morpholino refers to a piperidin-1-yl or morpholin-4-yl ring that is linked via the ring nitrogen.

[0076] By “bridged ring systems” is meant ring systems in which two rings share more than two atoms, see for example *Advanced Organic Chemistry*, by Jerry March, 4th Edition, Wiley
35 Interscience, pages 131-133, 1992. Examples of bridged heterocyclyl ring systems include, aza-bicyclo[2.2.1]heptane, 2-oxa-5-azabicyclo[2.2.1]heptane, aza-bicyclo[2.2.2]octane, aza-

bicyclo[3.2.1]octane, quinuclidine, 6-azabicyclo[3.1.1]heptane, 8-azabicyclo[3.2.1]octane, bicyclo[3.2.1]octane, 7-oxabicyclo[2.2.1]hept-2-ene and 3-oxa-8-azabicyclo[3.2.1]octane .

[0077] The term “heteroaryl” or “heteroaromatic” means an aromatic mono-, bi-, or polycyclic ring incorporating one or more (for example 1-4, particularly 1, 2 or 3) heteroatoms selected from nitrogen, oxygen or sulfur. The term heteroaryl includes both monovalent species and divalent species. Examples of heteroaryl groups are monocyclic and bicyclic groups containing from five to twelve ring members, and more usually from five to ten ring members. The heteroaryl group can be, for example, a 5- or 6-membered monocyclic ring or a 9- or 10-membered bicyclic ring, for example a bicyclic structure formed from fused five and six membered rings or two fused six membered rings. Each ring may contain up to about four heteroatoms typically selected from nitrogen, sulfur and oxygen. Typically the heteroaryl ring will contain up to 3 heteroatoms, more usually up to 2, for example a single heteroatom. In one embodiment, the heteroaryl ring contains at least one ring nitrogen atom. The nitrogen atoms in the heteroaryl rings can be basic, as in the case of an imidazole or pyridine, or essentially non-basic as in the case of an indole or pyrrole nitrogen. In general the number of basic nitrogen atoms present in the heteroaryl group, including any amino group substituents of the ring, will be less than five.

[0078] Examples of heteroaryl include furyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, 1,3,5-triazenyl, benzofuranyl, indolyl, isoindolyl, benzothienyl, benzoxazolyl, benzimidazolyl, benzothiazolyl, benzothiazolyl, indazolyl, purinyl, benzofurazanyl, quinolyl, isoquinolyl, quinazolinyl, quinoxalinyl, cinnolinyl, pteridinyl, naphthyridinyl, carbazolyl, phenazinyl, benzisoquinolinyl, pyridopyrazinyl, thieno[2,3-*b*]furanyl, 2H-furo[3,2-*b*]pyranyl, 5H-pyrido[2,3-*d*]-o-oxazinyl, 1H-pyrazolo[4,3-*d*]-oxazolyl, 4H-imidazo[4,5-*d*]thiazolyl, pyrazino[2,3-*d*]pyridazinyl, imidazo[2,1-*b*]thiazolyl, imidazo[1,2-*b*][1,2,4]triazinyl. “Heteroaryl” also covers partially aromatic bi- or polycyclic ring systems wherein at least one ring is an aromatic ring and one or more of the other ring(s) is a non-aromatic, saturated or partially saturated ring, provided at least one ring contains one or more heteroatoms selected from nitrogen, oxygen or sulfur. Examples of partially aromatic heteroaryl groups include for example, tetrahydroisoquinolinyl, tetrahydroquinolinyl, 2-oxo-1,2,3,4-tetrahydroquinolinyl, dihydrobenzthienyl, dihydrobenzfuranyl, 2,3-dihydrobenzo[1,4]dioxinyl, benzo[1,3]dioxolyl, 2,2-dioxo-1,3-dihydro-2-benzothienyl, 4,5,6,7-tetrahydrobenzofuranyl, indolinyl, 1,2,3,4-tetrahydro-1,8-naphthyridinyl, 1,2,3,4-tetrahydropyrido[2,3-*b*]pyrazinyl and 3,4-dihydro-2H-pyrido[3,2-*b*][1,4]oxazinyl.

[0079] Examples of five membered heteroaryl groups include but are not limited to pyrrolyl, furanyl, thienyl, imidazolyl, furazanyl, oxazolyl, oxadiazolyl, oxatriazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, triazolyl and tetrazolyl groups.

5 **[0080]** Examples of six membered heteroaryl groups include but are not limited to pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl and triazinyl.

[0081] A bicyclic heteroaryl group may be, for example, a group selected from:

- a benzene ring fused to a 5- or 6-membered ring containing 1, 2 or 3 ring heteroatoms;
- a pyridine ring fused to a 5- or 6-membered ring containing 1, 2 or 3 ring heteroatoms;
- a pyrimidine ring fused to a 5- or 6-membered ring containing 1 or 2 ring heteroatoms;
- 10 a pyrrole ring fused to a 5- or 6-membered ring containing 1, 2 or 3 ring heteroatoms;
- a pyrazole ring fused to a 5- or 6-membered ring containing 1 or 2 ring heteroatoms;
- a pyrazine ring fused to a 5- or 6-membered ring containing 1 or 2 ring heteroatoms;
- an imidazole ring fused to a 5- or 6-membered ring containing 1 or 2 ring heteroatoms;
- an oxazole ring fused to a 5- or 6-membered ring containing 1 or 2 ring heteroatoms;
- 15 an isoxazole ring fused to a 5- or 6-membered ring containing 1 or 2 ring heteroatoms;
- a thiazole ring fused to a 5- or 6-membered ring containing 1 or 2 ring heteroatoms;
- an isothiazole ring fused to a 5- or 6-membered ring containing 1 or 2 ring heteroatoms;
- a thiophene ring fused to a 5- or 6-membered ring containing 1, 2 or 3 ring heteroatoms;
- a furan ring fused to a 5- or 6-membered ring containing 1, 2 or 3 ring heteroatoms;
- 20 a cyclohexyl ring fused to a 5- or 6-membered heteroaromatic ring containing 1, 2 or 3 ring heteroatoms; and
- a cyclopentyl ring fused to a 5- or 6-membered heteroaromatic ring containing 1, 2 or 3 ring heteroatoms.

25 **[0082]** Particular examples of bicyclic heteroaryl groups containing a six membered ring fused to a five membered ring include but are not limited to benzfuranyl, benzthiophenyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzthiazolyl, benzisothiazolyl, isobenzofuranyl, indolyl, isoindolyl, indoliziny, indoliny, isoindoliny, puriny (e.g., adeniny, guaniny), indazolyl, benzodioxolyl and pyrazolopyridiny groups.

30 **[0083]** Particular examples of bicyclic heteroaryl groups containing two fused six membered rings include but are not limited to quinoliny, isoquinoliny, chromanyl, thiochromanyl, chromenyl, isochromenyl, chromanyl, isochromanyl, benzodioxanyl, quinoliziny,

benzoxazinyl, benzodiazinyl, pyridopyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, phthalazinyl, naphthyridinyl and pteridinyl groups.

[0084] The term “aryl” means a cyclic or polycyclic aromatic ring having from 5 to 12 carbon atoms. The term aryl includes both monovalent species and divalent species. Examples of aryl groups include, but are not limited to, phenyl, biphenyl, naphthyl and the like. In particular embodiment, an aryl is phenyl.

[0085] The term “optionally substituted” refers to either groups, structures, or molecules that are substituted and those that are not substituted.

[0086] Where optional substituents are chosen from “one or more” groups it is to be understood that this definition includes all substituents being chosen from one of the specified groups or the substituents being chosen from two or more of the specified groups.

[0087] The phrase “compound of the invention” means those compounds which are disclosed herein, both generically and specifically.

Compounds of the invention

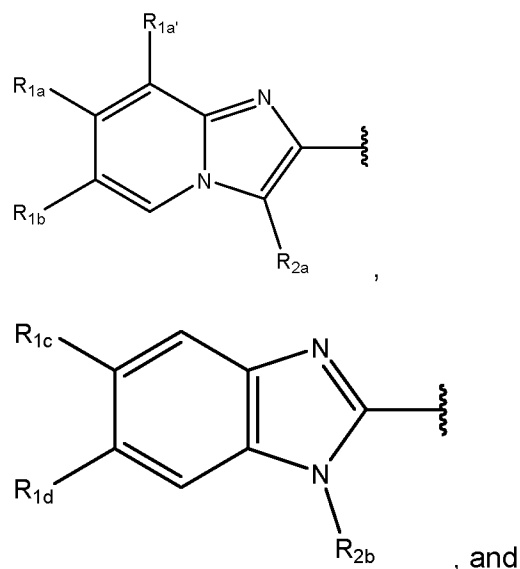
[0088] In one aspect, the present invention relates to compounds of the formula (I), or a pharmaceutically acceptable salt thereof,

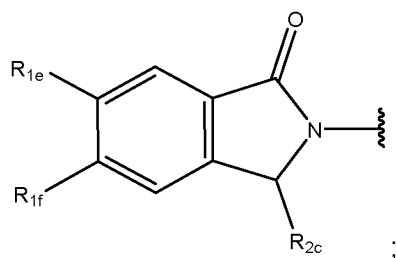


(I)

wherein:

X is selected from:





wherein:

R_{1a}, R_{1b}, R_{1c}, R_{1d}, R_{1e} and R_{1f} are independently selected from hydrogen, cyano, halo or a group of the formula:



wherein

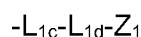
L_{1a} is absent or selected from C₁₋₃alkylene and C₃₋₅cycloalkylene, wherein C₁₋₃alkylene and C₃₋₅cycloalkylene are optionally substituted by one or more substituents selected from aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl, C₁₋₃alkyl, cyano, C₁₋₃alkoxy, halo, hydroxy, C₁₋₃haloalkoxy, -O-C₃₋₄cycloalkyl, NH₂ or oxo; wherein any -O-C₃₋₆cycloalkyl aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl or C₁₋₃alkyl is optionally further substituted by one or more substituents selected from cyano, hydroxy, C₁₋₃alkoxy, halo, C₁₋₃haloalkoxy, -O-C₃₋₄cycloalkyl, or NH₂; wherein -O-C₃₋₆cycloalkyl is optionally further substituted with halo, cyano or hydroxy; ; or C₁₋₃alkylene is optionally spiro-fused to a 3- to 5-membered cycloalkyl or heterocyclic ring, or a spirocyclic ring system, each of which is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo or C₁₋₂haloalkoxy;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₃alkyl, wherein C₁₋₃alkyl is optionally further substituted by cyano, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, NH₂, C₃₋₆cycloalkyl or a 3 to 6 membered heterocyclyl, wherein the C₃₋₆cycloalkyl or a 3 to 6 membered heterocyclyl in turn are optionally further substituted by halo, hydroxy, C₁₋₂alkoxy or C₁₋₂haloalkoxy; and

Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl), C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system) or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl,

trifluoromethoxy, amino, oxo, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, -S(O)₀₋₂R_tR_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u, N(R_t)SO₂R_u or (CH₂)_zNR_tR_u (where z is 1, 2 or 3), wherein C₁₋₄alkyl is in turn optionally substituted by one more substituents selected from cyano, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, -O-C₃cycloalkyl, wherein -O-C₃cycloalkyl is optionally substituted with halo, cyano or hydroxy; and wherein R_t and R_u are each independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



wherein

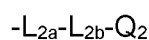
L_{1c} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

L_{1d} is absent or selected from C(O), O, C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl), heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system), aryl or heteroaryl, ; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, cyano, hydroxyl, NR_{t1}R_{u1}, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, C(O)N(R_{t1})R_{u1}, N(R_{t1})C(O)R_{u1}, -S(O)₀₋₂R_{t1}R_{u1}, S(O)_yR_{t1} (where y is 0, 1 or 2), SO₂N(R_{t1})R_{u1}, N(R_{t1})SO₂R_{u1} or (CH₂)_zNR_{t1}R_{u1} (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C₁₋₄alkyl; and when Z₁ is C₃₋₈cycloalkyl or heterocyclyl, Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclyl ring;

R_{1a'} is selected from hydrogen, halo and methyl;

R_{2a}, R_{2b} and R_{2c} are selected from hydrogen, halo or a group of the formula:



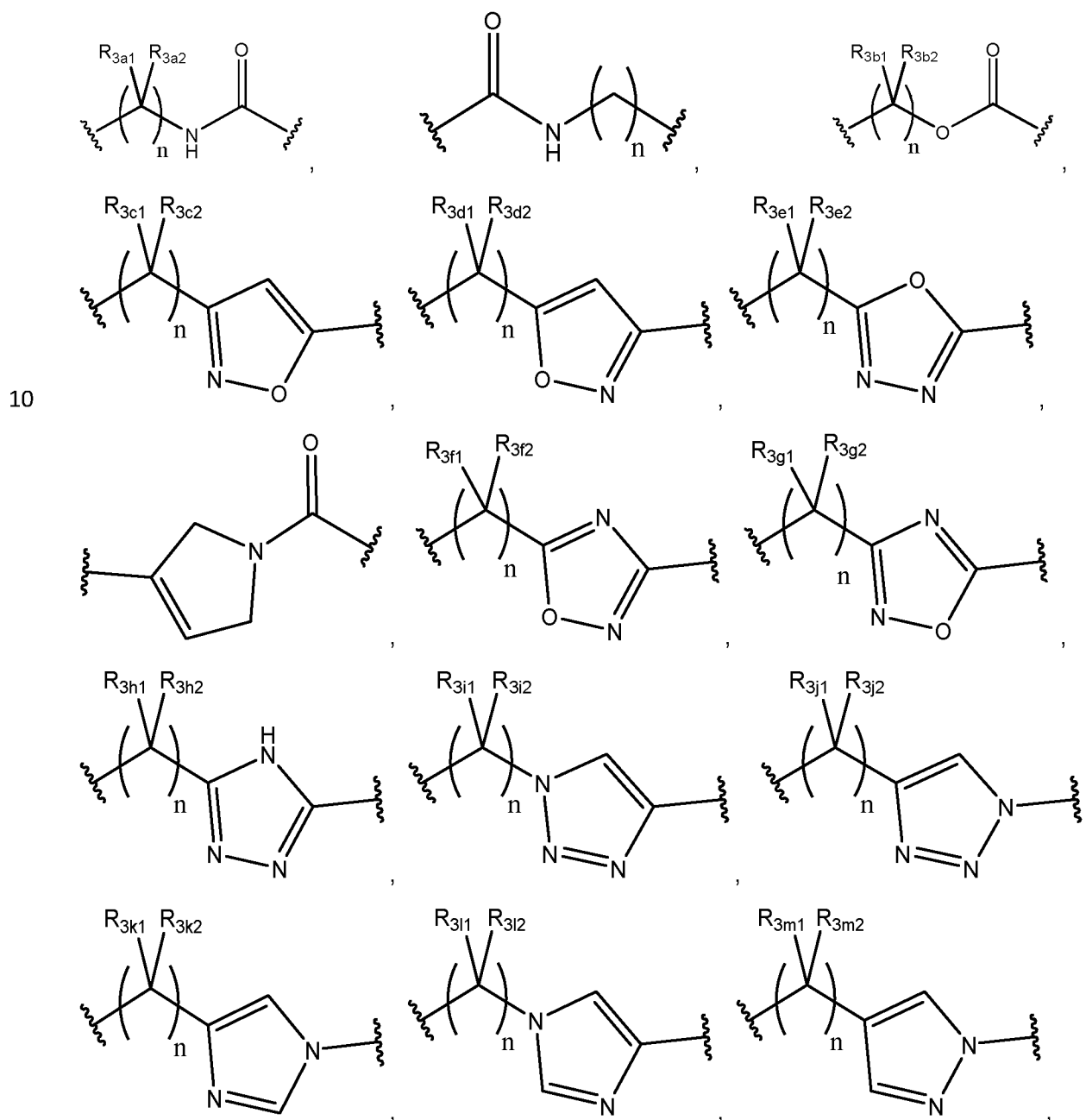
wherein

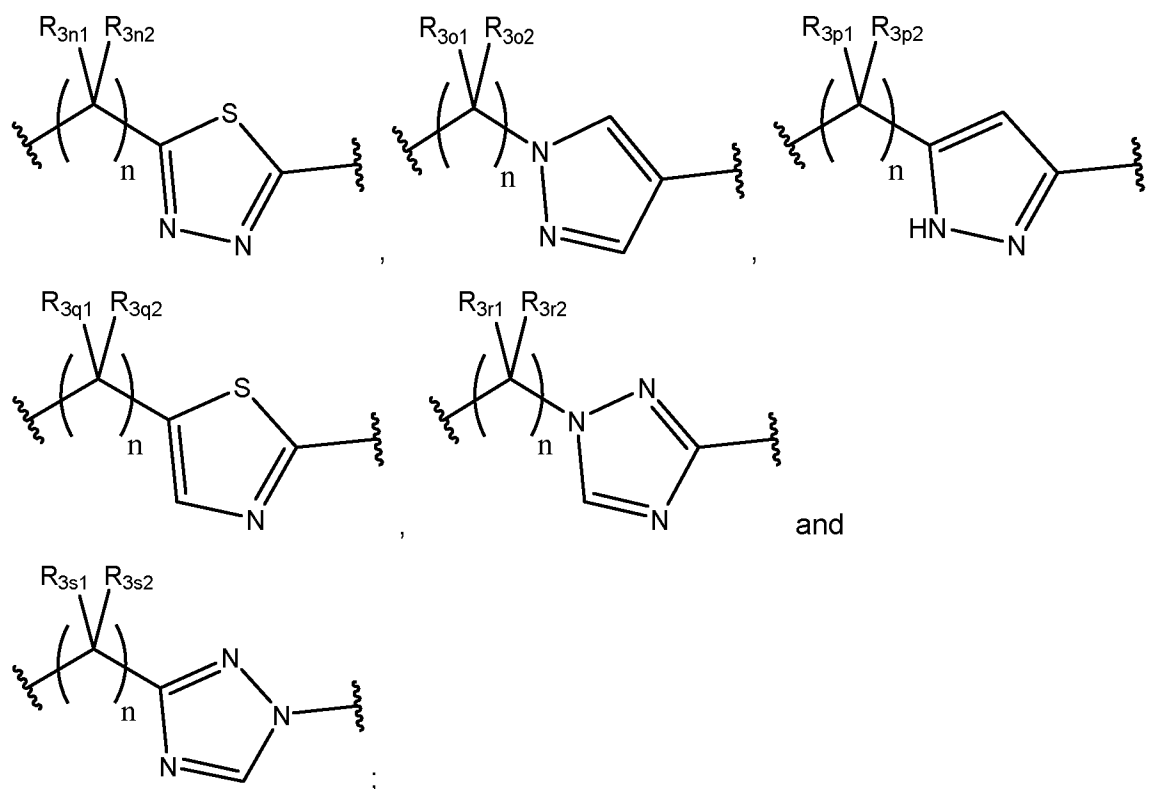
L_{2a} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

L_{2b} is absent or selected from O, S, SO, SO₂, N(R_n), C(O), C(O)O, OC(O), C(O)N(R_n), N(R_n)C(O), N(R_n)C(O)N(R_o), S(O)₂N(R_n), or N(R_n)SO₂, wherein R_n and R_o are each independently selected from hydrogen or C₁₋₂alkyl; and

Q₂ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₆cycloalkyl, aryl, heterocyclyl or heteroaryl, each of which is optionally substituted by one or more substituents selected from halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, amino, carboxy, carbamoyl, sulphamoyl, C₁₋₄alkyl, NR_pR_q, OR_p, C(O)R_p, C(O)OR_p, OC(O)R_p, C(O)N(R_p)R_q,
 5 N(R_r)C(O)R_p, S(O)_yR_p (where y is 0, 1 or 2), SO₂N(R_p)R_q, N(R_r)SO₂R_p or (CH₂)_zNR_pR_q (where z is 1, 2 or 3), wherein R_p and R_q are each independently selected from hydrogen or C₁₋₄alkyl;

Y is selected from:

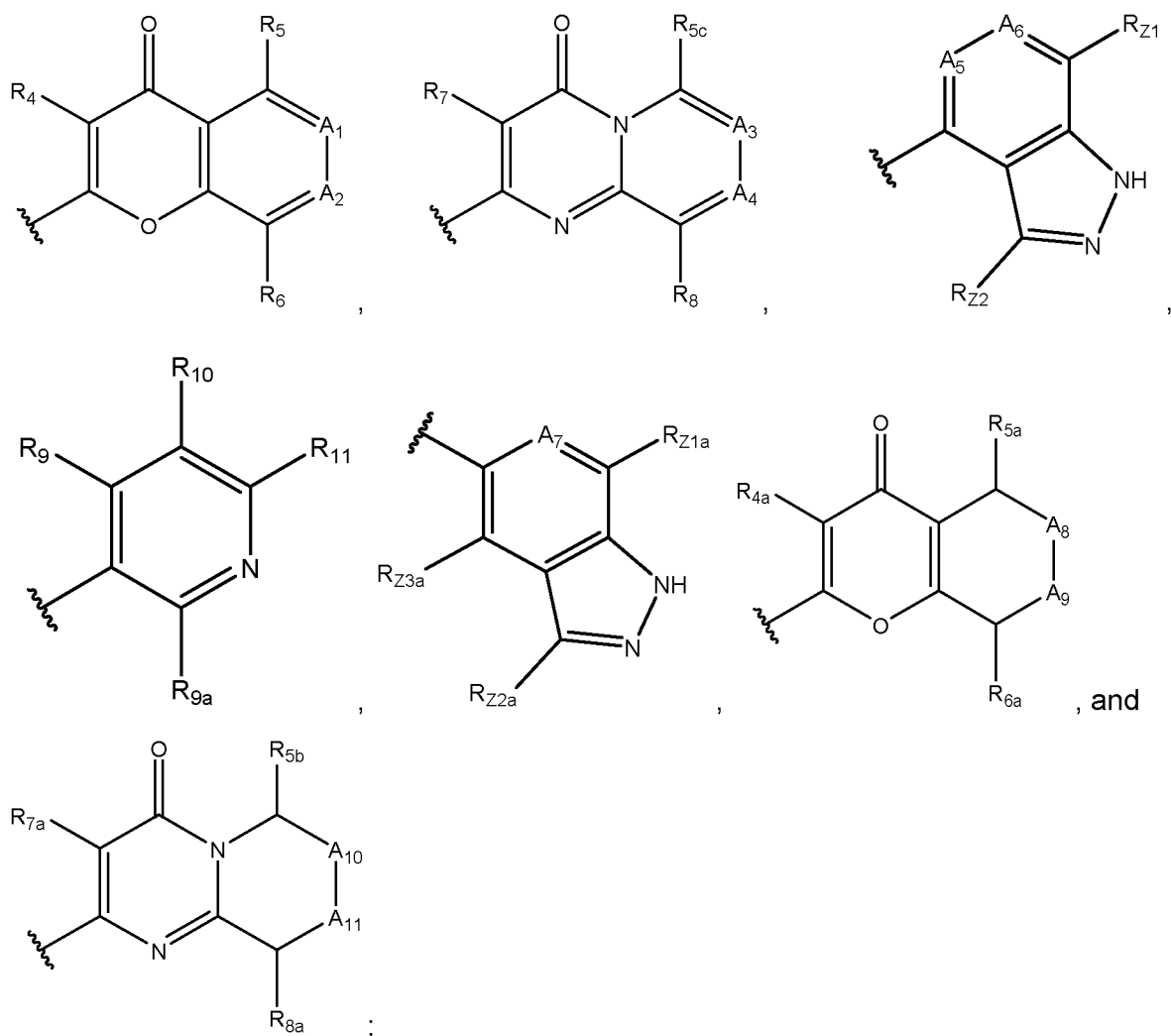




wherein:

- 5 R_{3a1}, R_{3b1}, R_{3c1}, R_{3d1}, R_{3e1}, R_{3f1}, R_{3g1}, R_{3h1}, R_{3i1}, R_{3j1}, R_{3k1}, R_{3l1}, R_{3m1}, R_{3n1}, R_{3o1}, R_{3p1}, R_{3q1}, R_{3r1} and R_{3s1} are independently selected from hydrogen (including deuterium), C₁₋₆alkyl, C₃₋₄ cycloalkyl, hydroxy, and halo; and wherein C₁₋₆alkyl, or C₃₋₄ cycloalkyl is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;
- 10 R_{3a2}, R_{3b2}, R_{3c2}, R_{3d2}, R_{3e2}, R_{3f2}, R_{3g2}, R_{3h2}, R_{3i2}, R_{3j2}, R_{3k2}, R_{3l2}, R_{3m2}, R_{3n2}, R_{3o2}, R_{3p2}, R_{3q2}, R_{3r2} and R_{3s2} are hydrogen or halo;
- with the proviso that R_{3a1}, R_{3b1}, R_{3i1}, R_{3l1}, R_{3o1}, R_{3r1}, R_{3a2}, R_{3b2}, R_{3i2}, R_{3l2}, R_{3o2} and R_{3s1} cannot be halo when n=1 or when n=2 and the carbon atom to which they are attached is linked to an oxygen or nitrogen atom;
- 15 or R_{3a1} and R_{3a2}, R_{3b1} and R_{3b2}, R_{3c1} and R_{3c2}, R_{3d1} and R_{3d2}, R_{3e1} and R_{3e2}, R_{3f1} and R_{3f2}, R_{3g1} and R_{3g2}, R_{3h1} and R_{3h2}, R_{3i1} and R_{3i2}, R_{3j1} and R_{3j2}, R_{3k1} and R_{3k2}, R_{3l1} and R_{3l2}, R_{3m1} and R_{3m2}, R_{3n1} and R_{3n2}, R_{3o1} and R_{3o2}, R_{3p1} and R_{3p2}, R_{3q1} and R_{3q2}, or R_{3r1} and R_{3r2} or R_{3s1} and R_{3s2} may be linked such that, together with the carbon atom to which they are attached, they form a spiro-fused C₃₋₄cycloalkyl which is optionally
- 20 substituted with one or more substituents selected from halo, methyl, amino, cyano, and hydroxy;

Z is selected from:



wherein:

- 5 R₄, R₇, R_{4a} and R_{7a} are independently selected from hydrogen, halo, cyano and methyl;
- R₅, R_{5a}, R_{5b} and R_{5c} are independently selected from hydrogen, halo, cyano and methyl;
- 10 R₆, R₈, R_{6a} and R_{8a} are independently selected from hydrogen, halo, cyano and methyl;
- R₉, R_{9a}, R₁₀ and R₁₁ are independently selected from hydrogen, NH₂, halo, cyano, and C₁₋₆ alkyl; or
- 15 R₉ and R₁₀ may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system or R₁₀ and R₁₁ may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system; wherein either of the fused 5- or 6-membered saturated or unsaturated ring system may be optionally substituted by one or more substituents selected from C₁₋₂alkyl, cyano, C₁₋₂haloalkyl, hydroxy, C₁₋

$_2$ alkoxy, halo, C_{1-2} haloalkoxy, $NR_{1ia}R_{1ja}$ or $-S(O)_{0-2}R_{1ia}R_{1ja}$, wherein R_{1ia} and R_{1ja} are H or C_{1-2} alkyl;

R_{Z1} and R_{Z1a} are selected from hydrogen, C_{1-4} alkyl, cyano, halo, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, C_{3-6} cycloalkyl and $-O-C_{3-6}$ cycloalkyl, wherein C_{3-6} cycloalkyl and $-O-C_{3-6}$ cycloalkyl are optionally substituted by one or more of halo, methyl or methoxy;

R_{Z2} and R_{Z2a} are selected from hydrogen, C_{1-4} alkyl, cyano, halo, NH_2 and C_{1-4} alkoxy;

R_{Z3a} is selected from hydrogen, C_{1-4} alkyl, cyano, halo, NH_2 and C_{1-4} alkoxy

A_1 is selected from CR_{12} and N;

A_2 is selected from CR_{13} and N;

A_3 is selected from CR_{14} and N;

A_4 is selected from CR_{15} and N;

A_5 is selected from CR_{16} and N;

A_6 is selected from CR_{17} and N;

A_7 is selected from CR_{18} and N;

A_8 is selected from $CR_{19}R_{20}$ and NR_{21} ;

A_9 is selected from $CR_{22}R_{23}$ and NR_{24} ;

A_{10} is selected from $CR_{25}R_{26}$ and NR_{27} ;

A_{11} is selected from $CR_{28}R_{29}$ and NR_{30} ;

R_{12} and R_{14} are independently selected from hydrogen, halo, cyano and C_{1-4} alkyl;

R_{13} is selected from hydrogen, halo, cyano, methoxy and methyl;

R_{15} is selected from hydrogen, halo, cyano methoxy and methyl;

R_{16} is selected from hydrogen, halo, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, a 3- to 4-membered heterocyclyl and C_{3-4} cycloalkoxy;

R_{17} is selected from hydrogen, hydroxy, halo, cyano, C_{1-5} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, a 5- or 6-membered or heteroaryl, C_{3-6} cycloalkyl, $-O-C_{3-6}$ cycloalkyl, heterocyclyl, $-O$ -heterocyclyl (carbon-linked), $-(OCH_2CH_2)_m-NR_qR_r$, $-(OCH_2CH_2)_m-OCH_3$ wherein m is an integer from 1 to 6, NR_qR_r , $-C(O)-NR_qR_r$, $-C(O)OR_q$;

wherein R_q and R_r are each independently hydrogen, C_{1-5} alkyl, C_{3-6} cycloalkyl, a 3- to 6- membered carbon-linked heterocyclyl, wherein C_{1-5} alkyl, C_{3-6} cycloalkyl, a 3- to 6- membered carbon-linked heterocyclyl may be optionally substituted by one or more substituents selected from C_{1-2} alkyl, cyano, C_{1-2} haloalkyl, hydroxy, C_{1-2} alkoxy, halo, C_{1-2} haloalkoxy, $NR_{1ea}R_{1fa}$ or $-S(O)_{0-2}R_{1ea}R_{1fa}$, wherein R_{1ea} and R_{1fa} are H or C_{1-2} alkyl; or R_q and R_r are linked together such that, together with the nitrogen atom to which they are attached, they form a 3- to 6-membered heterocyclic ring, which may be optionally substituted by one or more substituents selected from C_{1-2} alkyl, cyano, C_{1-2} haloalkyl, hydroxy, C_{1-2} alkoxy, halo, C_{1-2} haloalkoxy;

wherein any C_{1-5} alkyl, C_{1-4} alkoxy, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5- or 6-membered or heteroaryl, C_{3-6} cycloalkyl, $-O-C_{3-6}$ cycloalkyl, heterocyclyl or $-O$ -heterocyclyl (carbon-linked) is optionally further substituted by one or more substituents selected from C_{1-2} alkyl, cyano, C_{1-2} haloalkyl, hydroxy, C_{1-2} alkoxy, halo, C_{1-2} haloalkoxy, $NR_{1ea}R_{1fa}$ or $-S(O)_{0-2}R_{1ea}R_{1fa}$, wherein R_{1ea} and R_{1fa} are H or C_{1-2} alkyl;

R_{18} is selected from hydrogen, halo, cyano, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, a 5- or 6-membered heteroaryl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, a 3- to 4-membered heterocyclyl and C_{3-4} cycloalkoxy;

R_{19} , R_{20} , R_{25} and R_{26} are selected from hydrogen, halo, cyano and C_{1-4} alkyl;

R_{22} and R_{23} are selected from hydrogen, halo, cyano and methyl;

R_{28} and R_{29} are selected from hydrogen, methoxy and methyl;

R_{21} , R_{24} , R_{27} and R_{30} are hydrogen; and

n is 0, 1 or 2;

with the proviso that the compound is not:

2-((1H-benzo[d]imidazol-2-yl)methyl)-5-(pyridin-3-yl)-1,3,4-oxadiazole;

2-((6-chloro-1-phenyl-1H-benzo[d]imidazol-2-yl)methyl)-5-(pyridin-3-yl)-1,3,4-oxadiazole;

N-({6-methylimidazo[1,2-a]pyridin- 2- yl}methyl)-1H-indazole-5-carboxamide.

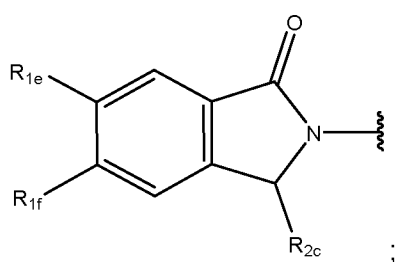
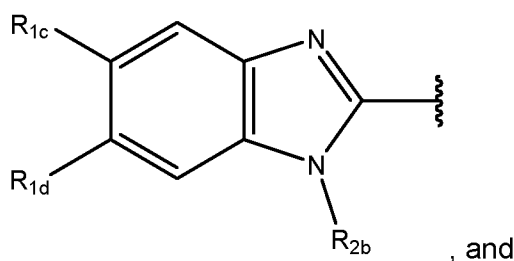
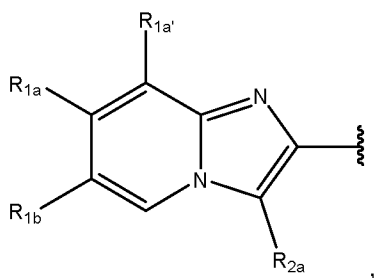
[0089] In one aspect, the present invention relates to compounds of the formula (I), or a pharmaceutically acceptable salt thereof,



(I)

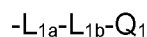
wherein:

X is selected from:



wherein:

R_{1a}, R_{1b}, R_{1c}, R_{1d}, R_{1e} and R_{1f} are independently selected from hydrogen, cyano, halo or a group of the formula:



wherein

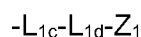
L_{1a} is absent or C₁₋₃alkylene, C₃₋₄cycloalkylene, optionally substituted by one or more substituents selected from aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl, C₁₋₂alkyl, cyano, halo, hydroxy, or oxo; wherein any aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl or C₁₋₂alkyl is optionally further substituted by one or more substituents selected from halo, cyano or hydroxy;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl, wherein C₁₋₂alkyl is optionally

further substituted by C₃₋₆cycloalkyl or a 3 to 6 membered heterocyclyl, which in turn are optionally further substituted by halo, hydroxy, C₁₋₂alkoxy or C₁₋₂haloalkoxy; and

Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₈cycloalkyl (e.g. C₃₋₆cycloalkyl), C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, oxo, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u, N(R_t)SO₂R_u or (CH₂)_zNR_tR_u (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



wherein

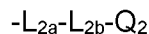
L_{1c} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

L_{1d} is absent or selected from C(O), O, C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

Z₁ is C₃₋₈cycloalkyl, heterocyclyl, phenyl or 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, cyano, hydroxyl, NR_{t1}R_{u1}, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, C(O)N(R_{t1})R_{u1}, N(R_{t1})C(O)R_{u1}, S(O)_yR_{t1} (where y is 0, 1 or 2), SO₂N(R_{t1})R_{u1}, N(R_{t1})SO₂R_{u1} or (CH₂)_zNR_{t1}R_{u1} (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C₁₋₄alkyl; and when Z₁ is C₃₋₈cycloalkyl or heterocyclyl, Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclyl ring;

R_{1a'} is selected from hydrogen, halo and methyl;

R_{2a}, R_{2b} and R_{2c} are selected from hydrogen, halo or a group of the formula:



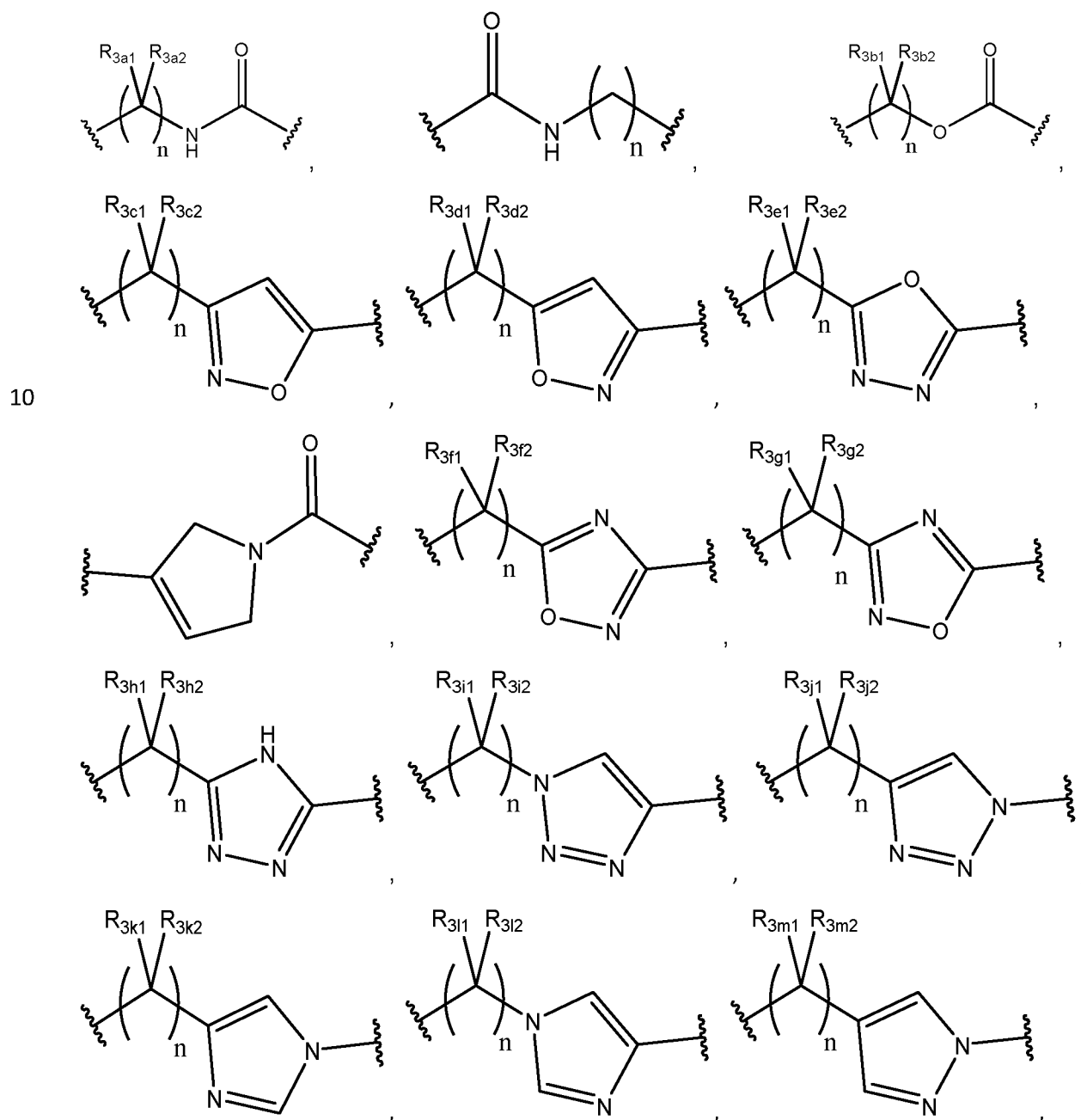
wherein

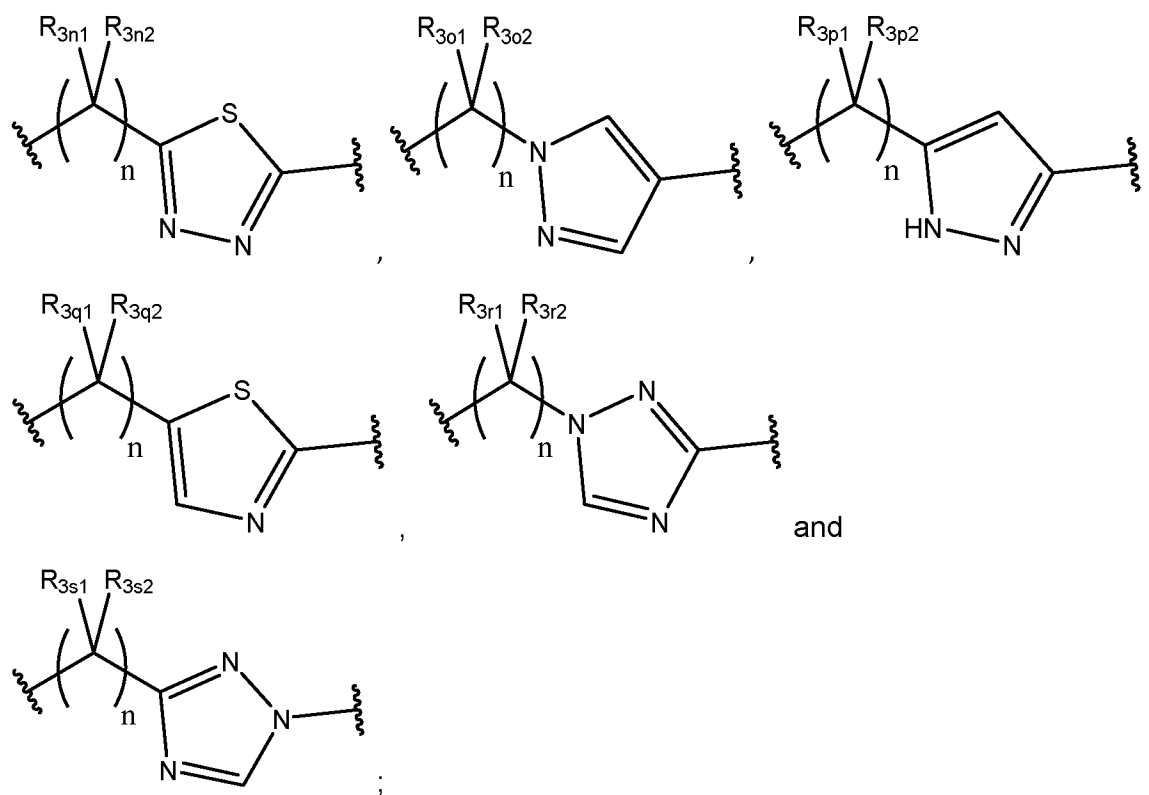
L_{2a} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

L_{2b} is absent or selected from O, S, SO, SO₂, N(R_n), C(O), C(O)O, OC(O), C(O)N(R_n), N(R_n)C(O), N(R_n)C(O)N(R_o), S(O)₂N(R_n), or N(R_n)SO₂, wherein R_n and R_o are each independently selected from hydrogen or C₁₋₂alkyl; and

Q₂ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₆cycloalkyl, aryl, heterocyclyl or heteroaryl, each of which is optionally substituted by one or more substituents selected from halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, amino, carboxy, carbamoyl, sulphamoyl, C₁₋₄alkyl, NR_pR_q, OR_p, C(O)R_p, C(O)OR_p, OC(O)R_p, C(O)N(R_p)R_q,
 5 N(R_r)C(O)R_p, S(O)_yR_p (where y is 0, 1 or 2), SO₂N(R_p)R_q, N(R_r)SO₂R_p or (CH₂)_zNR_pR_q (where z is 1, 2 or 3), wherein R_p and R_q are each independently selected from hydrogen or C₁₋₄alkyl;

Y is selected from:





;

5 wherein:

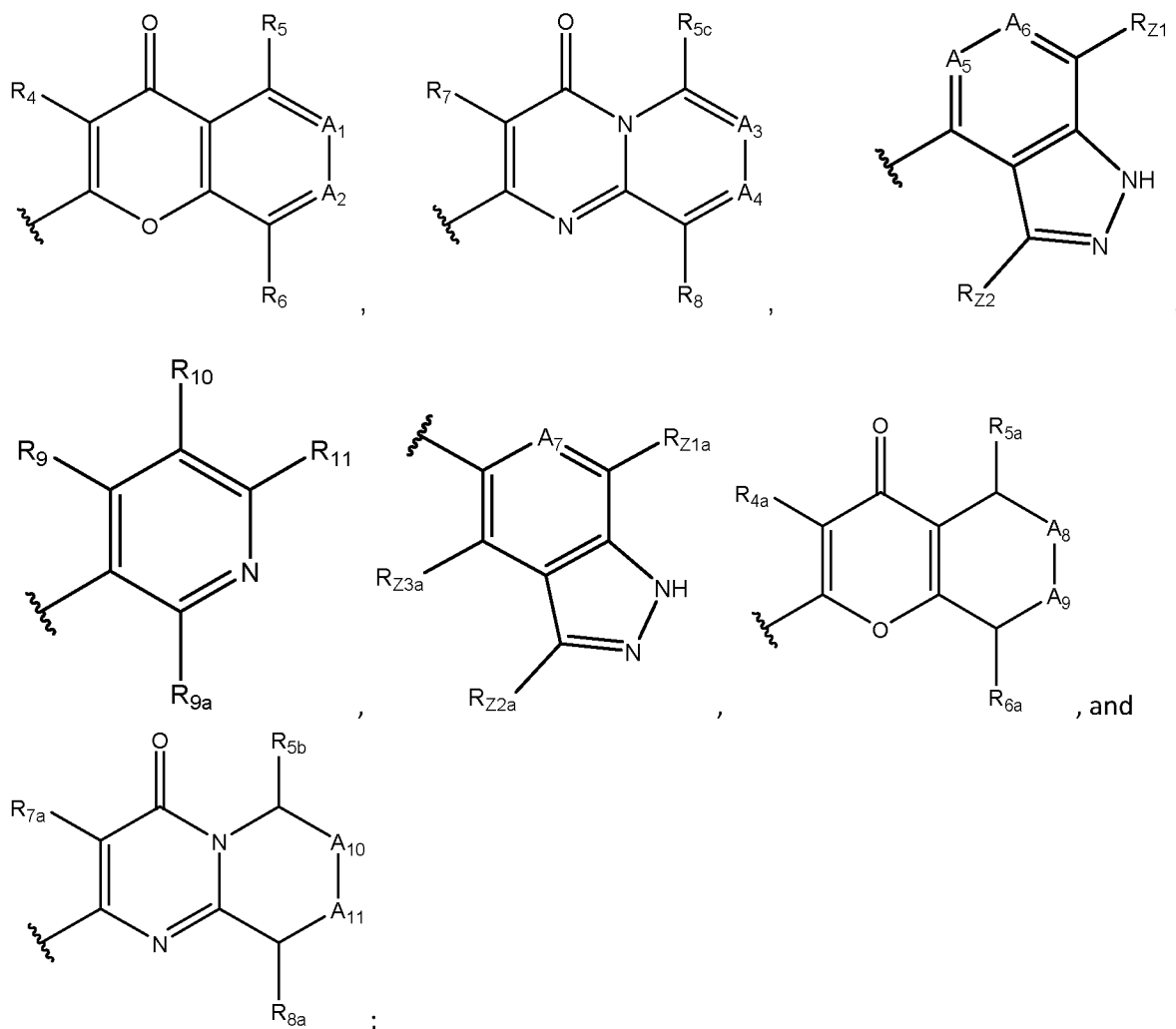
R_{3a1}, R_{3b1}, R_{3c1}, R_{3d1}, R_{3e1}, R_{3f1}, R_{3g1}, R_{3h1}, R_{3i1}, R_{3j1}, R_{3k1}, R_{3l1}, R_{3m1}, R_{3n1}, R_{3o1}, R_{3p1}, R_{3q1}, R_{3r1} and R_{3s1} are independently selected from hydrogen (including deuterium), C₁₋₆alkyl, C₃₋₄ cycloalkyl, hydroxy, and halo; and wherein C₁₋₆alkyl, or C₃₋₄ cycloalkyl is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

R_{3a2}, R_{3b2}, R_{3c2}, R_{3d2}, R_{3e2}, R_{3f2}, R_{3g2}, R_{3h2}, R_{3i2}, R_{3j2}, R_{3k2}, R_{3l2}, R_{3m2}, R_{3n2}, R_{3o2}, R_{3p2}, R_{3q2}, R_{3r2} and R_{3s2} are hydrogen or halo;

with the proviso that R_{3a1}, R_{3b1}, R_{3i1}, R_{3l1}, R_{3o1}, R_{3r1}, R_{3a2}, R_{3b2}, R_{3i2}, R_{3l2}, R_{3o2} and R_{3s2} cannot be halo when n=1 or when n=2 and the carbon atom to which they are attached is linked to an oxygen or nitrogen atom;

or R_{3a1} and R_{3a2}, R_{3b1} and R_{3b2}, R_{3c1} and R_{3c2}, R_{3d1} and R_{3d2}, R_{3e1} and R_{3e2}, R_{3f1} and R_{3f2}, R_{3g1} and R_{3g2}, R_{3h1} and R_{3h2}, R_{3i1} and R_{3i2}, R_{3j1} and R_{3j2}, R_{3k1} and R_{3k2}, R_{3l1} and R_{3l2}, R_{3m1} and R_{3m2}, R_{3n1} and R_{3n2}, R_{3o1} and R_{3o2}, R_{3p1} and R_{3p2}, R_{3q1} and R_{3q2}, R_{3r1} and R_{3r2} or R_{3s1} and R_{3s2} may be linked such that, together with the carbon atom to which they are attached, they form a spiro-fused C₃₋₄cycloalkyl which is optionally substituted with one or more substituents selected from halo, methyl, amino, cyano, and hydroxy;

Z is selected from:



5 wherein:

R₄, R₇, R_{4a} and R_{7a} are independently selected from hydrogen, halo, cyano and methyl;

R₅, R_{5a}, R_{5b} and R_{5c} are independently selected from hydrogen, halo, cyano and methyl;

R₆, R₈, R_{6a} and R_{8a} are independently selected from hydrogen, halo, cyano and methyl;

R₉, R_{9a}, R₁₀ and R₁₁ are independently selected from hydrogen, NH₂, halo, cyano, and
10 C₁₋₆ alkyl; or

R₉ and R₁₀ may be linked together to form a fused 5- or 6-membered saturated or
unsaturated ring system or R₁₀ and R₁₁ may be linked together to form a fused 5- or 6-
membered saturated or unsaturated ring system; wherein either of the fused 5- or 6-
membered saturated or unsaturated ring system may be optionally substituted by one
15 or more substituents selected from C₁₋₂alkyl, cyano, C₁₋₂haloalkyl, hydroxy, C₁₋₂alkoxy,
halo, C₁₋₂haloalkoxy, NR_{1ia}R_{1ja} or -S(O)₀₋₂R_{1ia}R_{1ja}, wherein R_{1ia} and R_{1ja} are H or C₁₋₂alkyl;

R_{Z1} and R_{Z1a} are selected from hydrogen, C₁₋₄alkyl, cyano, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, C₃₋₆cycloalkyl and -O-C₃₋₆cycloalkyl, wherein C₃₋₆cycloalkyl and -O-C₃₋₆cycloalkyl are optionally substituted by one or more of halo, methyl or methoxy;

R_{Z2} and R_{Z2a} are selected from hydrogen, C₁₋₄alkyl, cyano, halo, NH₂ and C₁₋₄alkoxy;

5 R_{Z3a} is selected from hydrogen, C₁₋₄alkyl, cyano, halo, NH₂ and C₁₋₄alkoxy

A₁ is selected from CR₁₂ and N;

A₂ is selected from CR₁₃ and N;

A₃ is selected from CR₁₄ and N;

A₄ is selected from CR₁₅ and N;

10 A₅ is selected from CR₁₆ and N;

A₆ is selected from CR₁₇ and N;

A₇ is selected from CR₁₈ and N;

A₈ is selected from CR₁₉R₂₀ and NR₂₁;

A₉ is selected from CR₂₂R₂₃ and NR₂₄;

15 A₁₀ is selected from CR₂₅R₂₆ and NR₂₇;

A₁₁ is selected from CR₂₈R₂₉ and NR₃₀;

R₁₂ and R₁₄ are independently selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₁₃ is selected from hydrogen, halo, cyano, methoxy and methyl;

R₁₅ is selected from hydrogen, halo, cyano methoxy and methyl;

20 R₁₆ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₃₋₄cycloalkyl, a 3- to 4-membered heterocyclyl and C₃₋₄cycloalkoxy;

R₁₇ is selected from hydrogen, hydroxy, halo, cyano, C₁₋₅ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, C₂₋₄ alkenyl, C₂₋₄ alkynyl, phenyl, a 5- or 6-membered or heteroaryl, C₃₋₆cycloalkyl, -O-C₃₋₆cycloalkyl, heterocyclyl, -O-heterocyclyl (carbon-

25 linked), -(OCH₂CH₂)_m-NR_qR_r, -(OCH₂CH₂)_m-OCH₃ wherein m is an integer from 1 to 6, NR_qR_r, -C(O)-NR_qR_r, -C(O)OR_q;

wherein R_q and R_r are each independently hydrogen, C₁₋₅ alkyl, C₃₋₆cycloalkyl, a 3- to 6- membered carbon-linked heterocyclyl, wherein C₁₋₅ alkyl, C₃₋₆cycloalkyl, a 3- to 6-membered carbon-linked heterocyclyl may be optionally substituted by one or more substituents selected from C₁₋₂alkyl, cyano, C₁₋₂haloalkyl, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, NR_{1ea}R_{1fa} or -S(O)₀₋₂R_{1ea}R_{1fa}, wherein R_{1ea} and R_{1fa} are H or C₁₋₂alkyl;

30

or R_q and R_r are linked together such that, together with the nitrogen atom to which they are attached, they form a 3- to 6-membered heterocyclic ring, which may be optionally substituted by one or more substituents selected from C_{1-2} alkyl, cyano, C_{1-2} haloalkyl, hydroxy, C_{1-2} alkoxy, halo, C_{1-2} haloalkoxy;

wherein any C_{1-5} alkyl, C_{1-4} alkoxy, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl, 5- or 6-membered or heteroaryl, C_{3-6} cycloalkyl, $-O-C_{3-6}$ cycloalkyl, heterocyclyl or $-O$ -heterocyclyl (carbon-linked) is optionally further substituted by one or more substituents selected from C_{1-2} alkyl, cyano, C_{1-2} haloalkyl, hydroxy, C_{1-2} alkoxy, halo, C_{1-2} haloalkoxy, $NR_{1ea}R_{1fa}$ or $-S(O)_0-2R_{1ea}R_{1fa}$, wherein R_{1ea} and R_{1fa} are H or C_{1-2} alkyl;

R_{18} is selected from hydrogen, halo, cyano, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, a 5- or 6-membered heteroaryl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{3-4} cycloalkyl, a 3- to 4-membered heterocyclyl and C_{3-4} cycloalkoxy;

R_{19} , R_{20} , R_{25} and R_{26} are selected from hydrogen, halo, cyano and C_{1-4} alkyl;

R_{22} and R_{23} are selected from hydrogen, halo, cyano and methyl;

R_{28} and R_{29} are selected from hydrogen, methoxy and methyl;

R_{21} , R_{24} , R_{27} and R_{30} are hydrogen; and

n is 0, 1 or 2.

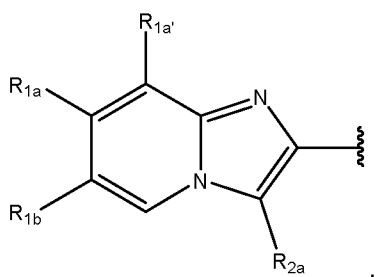
[0090] In one aspect, the present invention relates to compounds of the formula (I), or a pharmaceutically acceptable salt thereof,

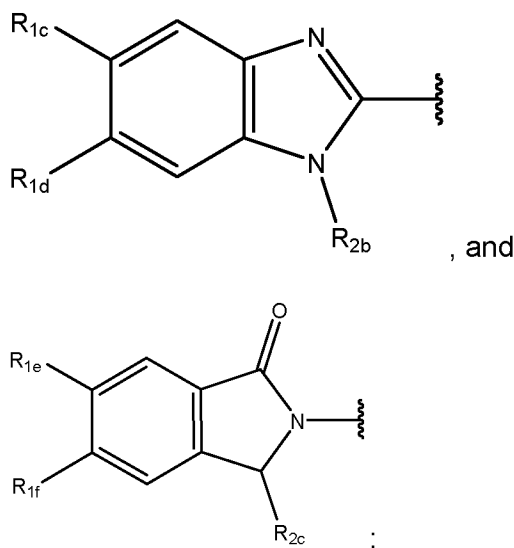


(I)

wherein:

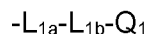
X is selected from:





wherein:

R_{1a} , R_{1b} , R_{1c} , R_{1d} , R_{1e} and R_{1f} are independently selected from hydrogen, cyano, halo
 5 or a group of the formula:



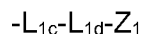
wherein

L_{1a} is absent or C_{1-3} alkylene, C_{3-4} cycloalkylene, optionally substituted by one or more
 substituents selected from C_{1-2} alkyl, halo, hydroxy, or oxo;

10 L_{1b} is absent or selected from O, S, SO, SO_2 , $N(R_r)$, $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_r)$,
 $N(R_r)C(O)$, $N(R_r)C(O)N(R_s)$, $S(O)_2N(R_r)$, or $N(R_r)SO_2$, wherein R_r and R_s are each
 independently selected from hydrogen or C_{1-2} alkyl; and

Q_1 is hydrogen, cyano, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl,
 heterocyclyl or heteroaryl; and wherein Q_1 is optionally substituted by one or more
 15 substituents selected from C_{1-4} alkyl, halo, trifluoromethyl, trifluoromethoxy, amino,
 cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u , OR_t , $C(O)R_t$, $C(O)OR_t$,
 $OC(O)R_t$, $C(O)N(R_t)R_u$, $N(R_t)C(O)R_u$, $S(O)_yR_t$ (where y is 0, 1 or 2), $SO_2N(R_t)R_u$,
 $N(R_t)SO_2R_u$ or $(CH_2)_zNR_tR_u$ (where z is 1, 2 or 3), wherein R_t and R_u are each
 independently selected from hydrogen or C_{1-4} alkyl; or

20 Q_1 is optionally substituted by one or more groups of the formula:



wherein

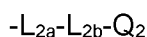
L_{1c} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

L_{1d} is absent or selected from $C(O)$, O , $C(O)O$, $OC(O)$, $C(O)N(R_v)$, $N(R_v)C(O)$, $N(R_v)C(O)N(R_w)$, $S(O)_2N(R_v)$, or $N(R_v)SO_2$, wherein R_v and R_w are each independently selected from hydrogen or C_{1-2} alkyl; and

Z_1 is C_{3-8} cycloalkyl, heterocyclyl, phenyl or 5-6 membered heteroaryl; wherein Z_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, C_{3-6} cycloalkyl, heterocyclyl, halo, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, cyano, hydroxyl, $NR_{t1}R_{u1}$, OR_{t1} , $C(O)R_{t1}$, $C(O)OR_{t1}$, $OC(O)R_{t1}$, $C(O)N(R_{t1})R_{u1}$, $N(R_{t1})C(O)R_{u1}$, $S(O)_yR_{t1}$ (where y is 0, 1 or 2), $SO_2N(R_{t1})R_{u1}$, $N(R_{t1})SO_2R_{u1}$ or $(CH_2)_zNR_{t1}R_{u1}$ (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C_{1-4} alkyl; and when Z_1 is C_{3-8} cycloalkyl or heterocyclyl, Z_1 is optionally spiro-fused to a C_{3-6} cycloalkyl or heterocyclyl ring;

$R_{1a'}$ is selected from hydrogen and methyl;

R_{2a} , R_{2b} and R_{2c} are selected from hydrogen or a group of the formula:



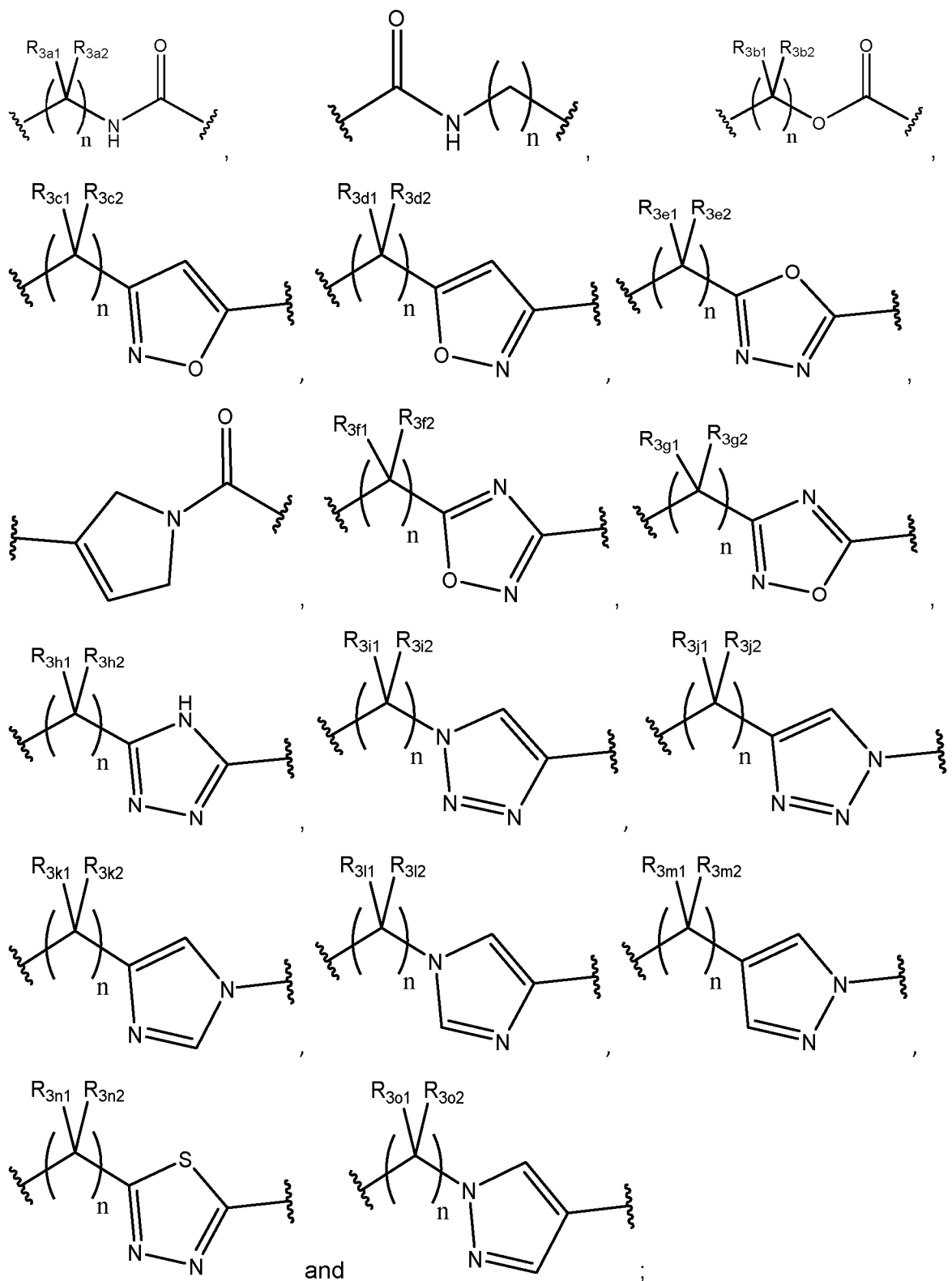
wherein

L_{2a} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

L_{2b} is selected from O , S , SO , SO_2 , $N(R_n)$, $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_n)$, $N(R_n)C(O)$, $N(R_n)C(O)N(R_o)$, $S(O)_2N(R_n)$, or $N(R_n)SO_2$, wherein R_n and R_o are each independently selected from hydrogen or C_{1-2} alkyl; and

Q_2 is hydrogen, cyano, C_{1-6} alkyl, C_{3-6} cycloalkyl, aryl, heterocyclyl or heteroaryl, each of which is optionally substituted by one or more substituents selected from halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, amino, carboxy, carbamoyl, sulphamoyl, C_{1-4} alkyl, NR_pR_q , OR_p , $C(O)R_p$, $C(O)OR_p$, $OC(O)R_p$, $C(O)N(R_p)R_q$, $N(R_r)C(O)R_p$, $S(O)_yR_p$ (where y is 0, 1 or 2), $SO_2N(R_p)R_q$, $N(R_r)SO_2R_p$ or $(CH_2)_zNR_pR_q$ (where z is 1, 2 or 3), wherein R_p and R_q are each independently selected from hydrogen or C_{1-4} alkyl;

Y is selected from:



wherein:

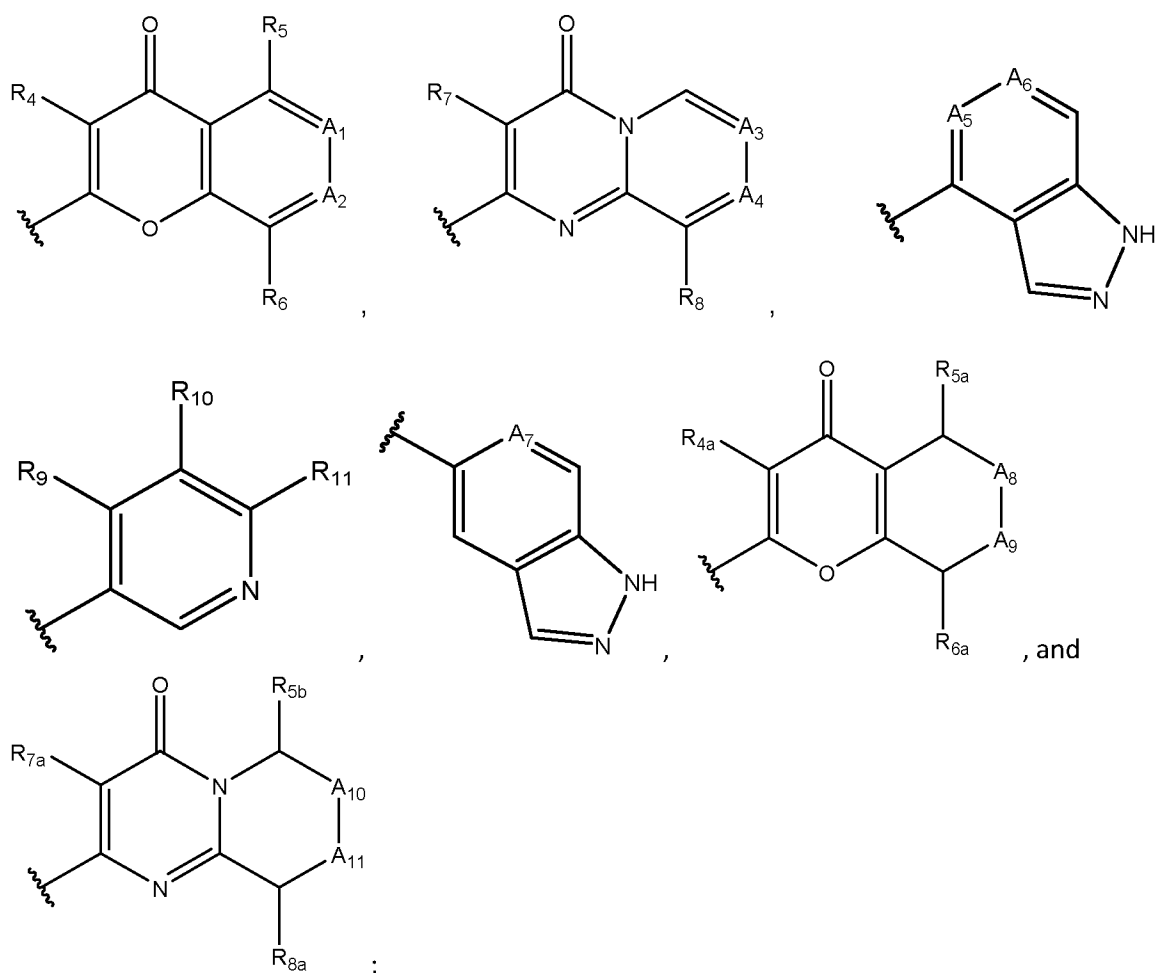
R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} and R_{3o1} are independently selected from hydrogen, C_{1-6} alkyl, C_{3-4} cycloalkyl, hydroxy, and halo; and

wherein C₁₋₆alkyl, or C₃₋₄ cycloalkyl is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

R_{3a2}, R_{3b2}, R_{3c2}, R_{3d2}, R_{3e2}, R_{3f2}, R_{3g2}, R_{3h2}, R_{3i2}, R_{3j2}, R_{3k2}, R_{3l2}, R_{3m2}, R_{3n2} and R_{3o2} are hydrogen;

- 5 or R_{3a1} and R_{3a2}, R_{3b1} and R_{3b2}, R_{3c1} and R_{3c2}, R_{3d1} and R_{3d2}, R_{3e1} and R_{3e2}, R_{3f1} and R_{3f2}, R_{3g1} and R_{3g2}, R_{3h1} and R_{3h2}, R_{3i1} and R_{3i2}, R_{3j1} and R_{3j2}, R_{3k1} and R_{3k2}, R_{3l1} and R_{3l2}, R_{3m1} and R_{3m2}, R_{3n1} and R_{3n2}, or R_{3o1} and R_{3o2} may be linked to form a spiro-fused C₃₋₄cycloalkyl which is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

- 10 Z is selected from:



wherein:

- 15 R₄, R₇, R_{4a} and R_{7a} are independently selected from hydrogen and methyl;
 R₅, R_{5a} and R_{5b} are independently selected from hydrogen and halo;
 R₆, R₈, R_{6a} and R_{8a} are independently selected from hydrogen, halo and methyl;

R₉, R₁₀ and R₁₁ are independently selected from hydrogen, NH₂, halo, cyano, and C₁₋₆ alkyl; or

R₉ and R₁₀ may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system or R₁₀ and R₁₁ may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system;

A₁ is selected from CR₁₂ and N;

A₂ is selected from CR₁₃ and N;

A₃ is selected from CR₁₄ and N;

A₄ is selected from CR₁₅ and N;

A₅ is selected from CR₁₆ and N;

A₆ is selected from CR₁₇ and N;

A₇ is selected from CR₁₈ and N;

A₈ is selected from CR₁₉R₂₀ and NR₂₁;

A₉ is selected from CR₂₂R₂₃ and NR₂₄;

A₁₀ is selected from CR₂₅R₂₆ and NR₂₇;

A₁₁ is selected from CR₂₈R₂₉ and NR₃₀;

R₁₂ and R₁₄ are independently selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₁₃ is selected from hydrogen, halo, cyano and methyl;

R₁₅ is selected from hydrogen, methoxy and methyl;

R₁₆ is selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₁₇ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl and a 5- or 6-membered heteroaryl;

R₁₈ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl and a 5- or 6-membered heteroaryl;

R₁₉, R₂₀, R₂₅ and R₂₆ are selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₂₂ and R₂₃ are selected from hydrogen, halo, cyano and methyl;

R₂₈ and R₂₉ are selected from hydrogen, methoxy and methyl;

R₂₁, R₂₄, R₂₇ and R₃₀ are hydrogen; and

n is 0, 1 or 2.

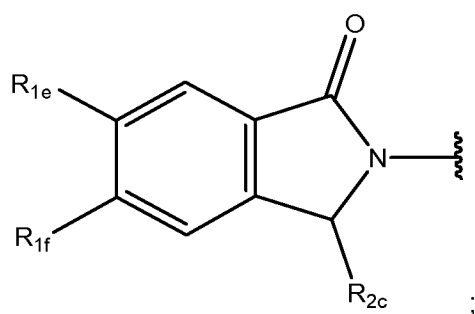
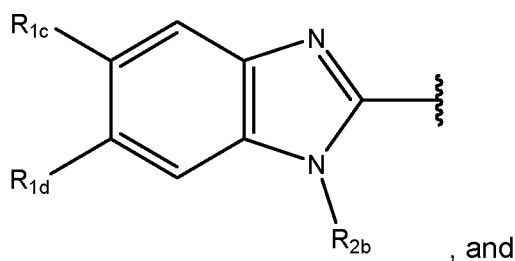
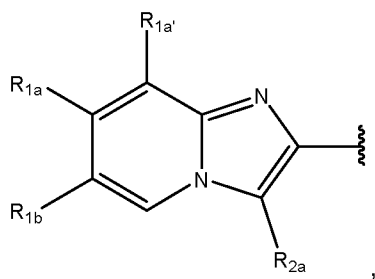
[0091] In one aspect, the present invention relates to compounds of formula (I) shown below, or a pharmaceutically acceptable salt thereof:



(I)

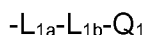
5 wherein:

X is selected from:



wherein:

- 10 R_{1a}, R_{1b}, R_{1c}, R_{1d}, R_{1e} and R_{1f} are independently selected from hydrogen, cyano, halo or a group of the formula:



wherein

- 15 L_{1a} is absent or C₁₋₃alkylene, C₃₋₄cycloalkylene, optionally substituted by one or more substituents selected from C₁₋₂alkyl, halo, hydroxy, or oxo;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl; and

- 20 Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₈cycloalkyl (e.g. C₃₋₆cycloalkyl), C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t,

$C(O)N(R_t)R_u$, $N(R_t)C(O)R_u$, $S(O)_yR_t$ (where y is 0, 1 or 2), $SO_2N(R_t)R_u$, $N(R_t)SO_2R_u$ or $(CH_2)_zNR_tR_u$ (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C_{1-4} alkyl; or

Q_1 is optionally substituted by one or more groups of the formula:



wherein

L_{1c} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

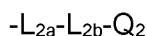
L_{1d} is absent or selected from $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_v)$, $N(R_v)C(O)$, $N(R_v)C(O)N(R_w)$, $S(O)_2N(R_v)$, or $N(R_v)SO_2$, wherein R_v and R_w are each independently selected from

10 hydrogen or C_{1-2} alkyl; and

Z_1 is phenyl or 5-6 membered heteroaryl; wherein Z_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, C_{1-4} alkylamino, amino, cyano, hydroxyl, carboxy, carbamoyl or sulphamoyl;

$R_{1a'}$ is selected from hydrogen and methyl;

15 R_{2a} , R_{2b} and R_{2c} are selected from hydrogen or a group of the formula:



wherein

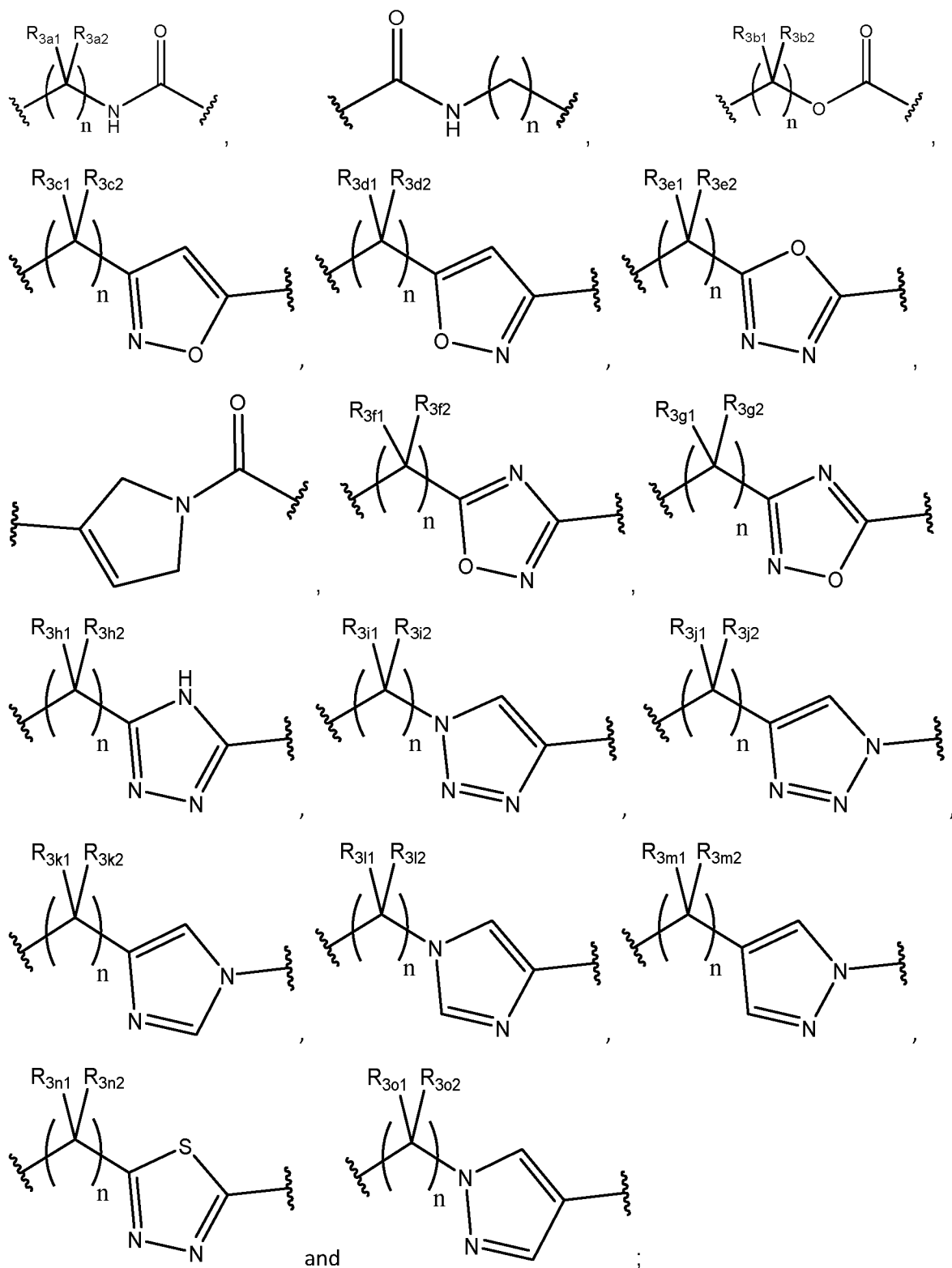
L_{2a} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

20 L_{2b} is selected from O, S, SO, SO_2 , $N(R_n)$, $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_n)$, $N(R_n)C(O)$, $N(R_n)C(O)N(R_o)$, $S(O)_2N(R_n)$, or $N(R_n)SO_2$, wherein R_n and R_o are each independently selected from hydrogen or C_{1-2} alkyl; and

Q_2 is hydrogen, cyano, C_{1-6} alkyl, C_{3-6} cycloalkyl, aryl, heterocyclyl or heteroaryl, each of which is optionally substituted by one or more substituents selected from halo,

25 trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, amino, carboxy, carbamoyl, sulphamoyl, C_{1-4} alkyl, NR_pR_q , OR_p , $C(O)R_p$, $C(O)OR_p$, $OC(O)R_p$, $C(O)N(R_p)R_q$, $N(R_r)C(O)R_p$, $S(O)_yR_p$ (where y is 0, 1 or 2), $SO_2N(R_p)R_q$, $N(R_r)SO_2R_p$ or $(CH_2)_zNR_pR_q$ (where z is 1, 2 or 3), wherein R_p and R_q are each independently selected from hydrogen or C_{1-4} alkyl;

Y is selected from:



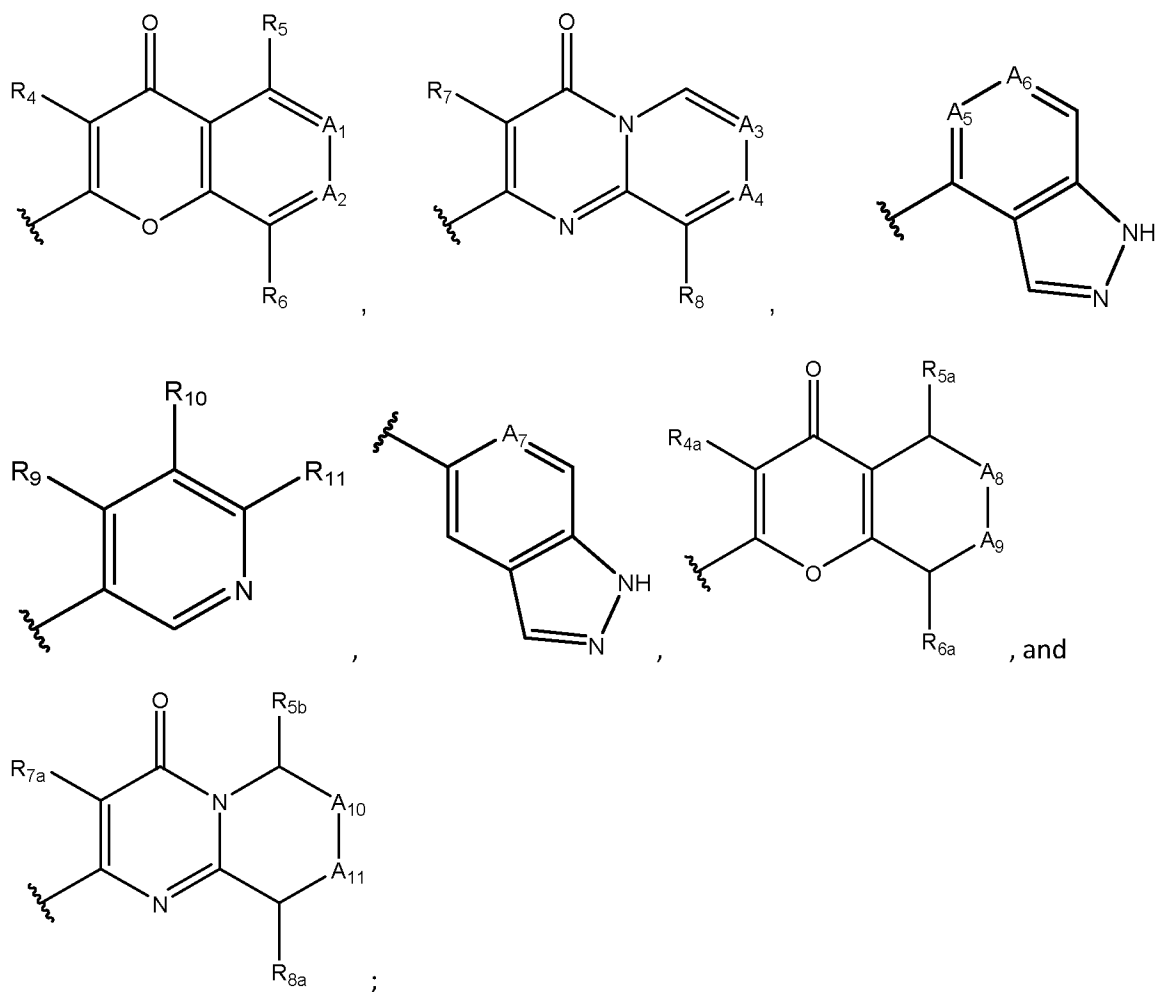
wherein:

R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} and R_{3o1} are independently selected from hydrogen, C_{1-6} alkyl, C_{3-4} cycloalkyl, hydroxy, and halo; and wherein C_{1-6} alkyl, or C_{3-4} cycloalkyl is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} and R_{3o2} are hydrogen;

or R_{3a1} and R_{3a2} , R_{3b1} and R_{3b2} , R_{3c1} and R_{3c2} , R_{3d1} and R_{3d2} , R_{3e1} and R_{3e2} , R_{3f1} and R_{3f2} , R_{3g1} and R_{3g2} , R_{3h1} and R_{3h2} , R_{3i1} and R_{3i2} , R_{3j1} and R_{3j2} , R_{3k1} and R_{3k2} , R_{3l1} and R_{3l2} , R_{3m1} and R_{3m2} ,
 5 R_{3n1} and R_{3n2} , and R_{3o1} and R_{3o2} may be linked to form a spiro-fused C_{3-4} cycloalkyl which is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

Z is selected from:



wherein:

R_4 , R_7 , R_{4a} and R_{7a} are independently selected from hydrogen and methyl;

R_5 , R_{5a} and R_{5b} are independently selected from hydrogen and halo;

15 R_6 , R_8 , R_{6a} and R_{8a} are independently selected from hydrogen, halo and methyl;

R_9 , R_{10} and R_{11} are independently selected from hydrogen, NH_2 , halo, cyano, and C_{1-6} alkyl;
 or

R₉ and R₁₀ may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system or R₁₀ and R₁₁ may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system;

A₁ is selected from CR₁₂ and N;

5 A₂ is selected from CR₁₃ and N;

A₃ is selected from CR₁₄ and N;

A₄ is selected from CR₁₅ and N;

A₅ is selected from CR₁₆ and N;

A₆ is selected from CR₁₇ and N;

10 A₇ is selected from CR₁₈ and N;

A₈ is selected from CR₁₉R₂₀ and NR₂₁;

A₉ is selected from CR₂₂R₂₃ and NR₂₄;

A₁₀ is selected from CR₂₅R₂₆ and NR₂₇;

A₁₁ is selected from CR₂₈R₂₉ and NR₃₀;

15 R₁₂ and R₁₄ are independently selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₁₃ is selected from hydrogen, halo, cyano and methyl;

R₁₅ is selected from hydrogen, methoxy and methyl;

R₁₆ is selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

20 R₁₇ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl and a 5- or 6-membered heteroaryl;

R₁₈ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl and a 5- or 6-membered heteroaryl;

R₁₉, R₂₀, R₂₅ and R₂₆ are selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₂₂ and R₂₃ are selected from hydrogen, halo, cyano and methyl;

25 R₂₈ and R₂₉ are selected from hydrogen, methoxy and methyl;

R₂₁, R₂₄, R₂₇ and R₃₀ are hydrogen; and

n is 0, 1 or 2.

[0092] Particular compounds of the invention include, for example, compounds of formula (I), or pharmaceutically acceptable salts thereof, wherein, unless otherwise stated, each of

X, Y, Z, R_{1a}, R_{1b}, R_{1c}, R_{1d}, R_{1e}, R_{1f}, R_{1a'}, R_{2a}, R_{2b}, R_{2c}, R_{3a1}, R_{3a2}, R_{3b1}, R_{3b2}, R_{3c1}, R_{3c2}, R_{3d1},
 R_{3d2}, R_{3e1}, R_{3e2}, R_{3f1}, R_{3f2}, R_{3g1}, R_{3g2}, R_{3h1}, R_{3h2}, R_{3i1}, R_{3i2}, R_{3j1}, R_{3j2}, R_{3k1}, R_{3k2}, R_{3l1}, R_{3l2},
 R_{3m1}, R_{3m2}, R_{3n1}, R_{3n2}, R_{3o1}, R_{3o2}, n, R₄, R_{4a}, R₅, R_{5a}, R_{5b}, R_{5c}, R₆, R_{6a}, R₇, R_{7a}, R₈, R_{8a}, R₉, R₁₀,
 R₁₁, R₁₂, R₁₃, R₁₄, R₁₅, R₁₆, R₁₇, R₁₈, R₁₉, R₂₀, R₂₁, R₂₂, R₂₃, R₂₄, R₂₅, R₂₆, R₂₇, R₂₈, R₂₉, R₃₀, A₁,

5 A₂, A₃, A₄, A₅, A₆, A₇, A₈, A₉, A₁₀ and A₁₁ and any associated substituent groups has any of the meanings defined hereinbefore or in any one of paragraphs (1) to (111b) hereinafter:-

(1) One of R_{1a} and R_{1b}, R_{1c} and R_{1d}, R_{1e} and R_{1f} is selected from hydrogen, halo, C₁₋₆-alkyl, C₂₋₃alkenyl or -O-C₁₋₆alkyl,

and the other is selected from hydrogen, cyano, halo or a group of the formula:

10
$$-L_{1a}-L_{1b}-Q_1$$

wherein

L_{1a} is absent or C₁₋₃alkylene, C₃₋₄cycloalkylene, optionally substituted by one or more substituents selected from C₁₋₂alkyl, halo, hydroxy, or oxo;

15 L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl; and

20 Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u, N(R_t)SO₂R_u or (CH₂)_zNR_tR_u (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:

25
$$-L_{1c}-L_{1d}-Z_1$$

wherein

L_{1c} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

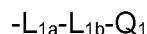
30 L_{1d} is absent or selected from C(O), C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

Z₁ is phenyl or 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy,

C₁₋₄alkoxy, C₁₋₄alkylamino, amino, cyano, hydroxyl, carboxy, carbamoyl or sulphamoyl;

(1a) One of R_{1a} and R_{1b}, R_{1c} and R_{1d}, R_{1e} and R_{1f} is selected from hydrogen, halo, C₁₋₆-alkyl, C₂₋₃alkenyl or -O-C₁₋₆alkyl,

5 and the other is selected from hydrogen, cyano, halo or a group of the formula:



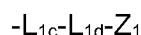
wherein

L_{1a} is absent or C₁₋₃alkylene, C₃₋₄cycloalkylene, optionally substituted by one or more substituents selected from C₁₋₂alkyl, halo, hydroxy, or oxo;

10 L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl; and

Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₈cycloalkyl (e.g. C₃₋₆cycloalkyl), C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by
15 one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u, N(R_t)SO₂R_u or (CH₂)_zNR_tR_u (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C₁₋₄alkyl; or

20 Q₁ is optionally substituted by one or more groups of the formula:



wherein

L_{1c} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

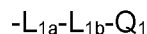
25 L_{1d} is absent or selected from C(O), O, C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl), heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system), phenyl or 5-6
30 membered heteroaryl; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, cyano, hydroxyl, NR_{t1}R_{u1}, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, C(O)N(R_{t1})R_{u1}, N(R_{t1})C(O)R_{u1}, S(O)_yR_{t1} (where y is 0, 1 or 2),

SO₂N(R_{t1})R_{u1}, N(R_{t1})SO₂R_{u1} or (CH₂)_zNR_{t1}R_{u1} (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C₁₋₄alkyl; and when Z₁ is C₃₋₈cycloalkyl or heterocyclyl, Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclyl ring;

- 5 (1b) One of R_{1a} and R_{1b}, R_{1c} and R_{1d}, R_{1e} and R_{1f} is selected from hydrogen, halo, C₁₋₆alkyl, C₂₋₃alkenyl or -O-C₁₋₆alkyl,

and the other is selected from hydrogen, cyano, halo or a group of the formula:



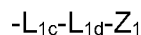
wherein

- 10 L_{1a} is absent or C₁₋₃alkylene, C₃₋₄cycloalkylene, optionally substituted by one or more substituents selected from aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl, C₁₋₂alkyl, cyano, halo, hydroxy, or oxo, wherein any aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl or C₁₋₂alkyl is optionally further substituted by one or more substituents selected from halo, cyano or hydroxy;

- 15 L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl, wherein C₁₋₂alkyl is optionally further substituted by C₃₋₆cycloalkyl or a 3 to 6 membered heterocyclyl, which in turn are optionally further substituted by halo, hydroxy, C₁₋₂alkoxy or C₁₋₂haloalkoxy; and

- 20 Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₈cycloalkyl (e.g. C₃₋₆cycloalkyl), C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, oxo cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u, N(R_t)SO₂R_u or (CH₂)_zNR_tR_u (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



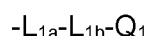
wherein

- 30 L_{1c} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;
- L_{1d} is absent or selected from C(O), O, C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl), heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system), phenyl or 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, cyano, hydroxyl, NR_{t1}R_{u1}, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, C(O)N(R_{t1})R_{u1}, N(R_{t1})C(O)R_{u1}, S(O)_yR_{t1} (where y is 0, 1 or 2), SO₂N(R_{t1})R_{u1}, N(R_{t1})SO₂R_{u1} or (CH₂)_zNR_{t1}R_{u1} (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C₁₋₄alkyl; and when Z₁ is C₃₋₈cycloalkyl or heterocyclyl, Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclyl ring;

(2) R_{1a}, R_{1c} and R_{1e} are selected from hydrogen, halo, C₁₋₆alkyl, C₂₋₃alkenyl or -O-C₁₋₆alkyl

and R_{1b}, R_{1d}, and R_{1f} are selected from hydrogen, cyano, halo or a group of the formula:



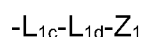
wherein

L_{1a} is absent or C₁₋₃alkylene, C₃₋₄cycloalkylene, optionally substituted by one or more substituents selected from C₁₋₂alkyl, halo, hydroxy, or oxo;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl; and

Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u, N(R_t)SO₂R_u or (CH₂)_zNR_tR_u (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



wherein

L_{1c} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

L_{1d} is absent or selected from C(O), C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

Z₁ is phenyl or 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, C₁₋₄alkylamino, amino, cyano, hydroxyl, carboxy, carbamoyl or sulphamoyl;

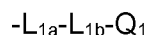
(3) R_{1a}, R_{1c} and R_{1e} are selected from hydrogen, halo, C₁₋₄alkyl, C₂₋₃alkenyl and -O-C₁₋₄alkyl;

(4) R_{1a}, R_{1c} and R_{1e} are selected from hydrogen, fluoro, bromo, chloro, methyl, ethyl, propyl, butyl, ethenyl, -O-methyl, -O-ethyl, -O-propyl and -O-butyl;

(5) R_{1a}, R_{1c} and R_{1e} are selected from hydrogen, fluoro, bromo, chloro, methyl, ethyl, -O-methyl, ethenyl and -O-ethyl;

(6) R_{1a}, R_{1c} and R_{1e} are selected from hydrogen, fluoro, bromo, methyl, ethenyl and -O-methyl;

(6a) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen, cyano, halo or a group of the formula:



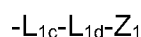
wherein

L_{1a} is absent or C₁₋₃alkylene, C₃₋₄cycloalkylene, optionally substituted by one or more substituents selected from C₁₋₂alkyl, halo, hydroxy, or oxo;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl; and

Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₈cycloalkyl (e.g. C₃₋₆cycloalkyl), C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u, N(R_t)SO₂R_u or (CH₂)_zNR_tR_u (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



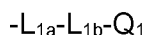
wherein

L_{1c} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

L_{1d} is absent or selected from C(O), O, C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl), heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system), phenyl or 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, cyano, hydroxyl, NR_{t1}R_{u1}, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, C(O)N(R_{t1})R_{u1}, N(R_{t1})C(O)R_{u1}, S(O)_yR_{t1} (where y is 0, 1 or 2), SO₂N(R_{t1})R_{u1}, N(R_{t1})SO₂R_{u1} or (CH₂)_zNR_{t1}R_{u1} (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C₁₋₄alkyl; and when Z₁ is C₃₋₈cycloalkyl or heterocyclyl, Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclyl ring;

(6b) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen, cyano, halo or a group of the formula:



wherein

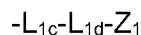
L_{1a} is absent or C₁₋₃alkylene, C₃₋₄cycloalkylene, optionally substituted by one or more substituents selected from aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl, C₁₋₂alkyl, cyano, halo, hydroxy, or oxo, wherein any aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl or C₁₋₂alkyl is optionally further substituted by one or more substituents selected from halo, cyano or hydroxy;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl, wherein C₁₋₂alkyl is optionally further substituted by C₃₋₆cycloalkyl or a 3 to 6 membered heterocyclyl, which in turn are optionally further substituted by halo, hydroxy, C₁₋₂alkoxy or C₁₋₂haloalkoxy; and

Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₈cycloalkyl (e.g. C₃₋₆cycloalkyl), C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, oxo, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1

or 2), $\text{SO}_2\text{N}(\text{R}_t)\text{R}_u$, $\text{N}(\text{R}_t)\text{SO}_2\text{R}_u$ or $(\text{CH}_2)_z\text{NR}_t\text{R}_u$ (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C_{1-4} alkyl; or

Q_1 is optionally substituted by one or more groups of the formula:



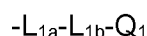
5 wherein

L_{1c} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

L_{1d} is absent or selected from $\text{C}(\text{O})$, O , $\text{C}(\text{O})\text{O}$, $\text{OC}(\text{O})$, $\text{C}(\text{O})\text{N}(\text{R}_v)$, $\text{N}(\text{R}_v)\text{C}(\text{O})$, $\text{N}(\text{R}_v)\text{C}(\text{O})\text{N}(\text{R}_w)$, $\text{S}(\text{O})_2\text{N}(\text{R}_v)$, or $\text{N}(\text{R}_v)\text{SO}_2$, wherein R_v and R_w are each independently selected from hydrogen or C_{1-2} alkyl; and

10 Z_1 is C_{3-8} cycloalkyl (including a spirocyclic carbocyclic and a bridged C_{3-8} cycloalkyl), heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system), phenyl or 5-6 membered heteroaryl; wherein Z_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, C_{3-6} cycloalkyl, heterocyclyl, halo, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, cyano, hydroxyl, $\text{NR}_{t1}\text{R}_{u1}$, OR_{t1} , $\text{C}(\text{O})\text{R}_{t1}$, $\text{C}(\text{O})\text{OR}_{t1}$, $\text{OC}(\text{O})\text{R}_{t1}$, $\text{C}(\text{O})\text{N}(\text{R}_{t1})\text{R}_{u1}$, $\text{N}(\text{R}_{t1})\text{C}(\text{O})\text{R}_{u1}$, $\text{S}(\text{O})_y\text{R}_{t1}$ (where y is 0, 1 or 2), $\text{SO}_2\text{N}(\text{R}_{t1})\text{R}_{u1}$, $\text{N}(\text{R}_{t1})\text{SO}_2\text{R}_{u1}$ or $(\text{CH}_2)_z\text{NR}_{t1}\text{R}_{u1}$ (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C_{1-4} alkyl; and when Z_1 is C_{3-8} cycloalkyl or heterocyclyl, Z_1 is optionally spiro-fused to a C_{3-6} cycloalkyl or heterocyclyl ring;

(7) R_{1b} , R_{1d} and R_{1f} are selected from hydrogen, cyano, halo or a group of the formula:



wherein

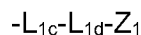
25 L_{1a} is absent or C_{1-3} alkylene, C_{3-4} cycloalkylene, optionally substituted by one or more substituents selected from C_{1-2} alkyl, halo, hydroxy, or oxo;

L_{1b} is absent or selected from O , S , SO , SO_2 , $\text{N}(\text{R}_r)$, $\text{C}(\text{O})$, $\text{C}(\text{O})\text{O}$, $\text{OC}(\text{O})$, $\text{C}(\text{O})\text{N}(\text{R}_r)$, $\text{N}(\text{R}_r)\text{C}(\text{O})$, $\text{N}(\text{R}_r)\text{C}(\text{O})\text{N}(\text{R}_s)$, $\text{S}(\text{O})_2\text{N}(\text{R}_r)$, or $\text{N}(\text{R}_r)\text{SO}_2$, wherein R_r and R_s are each independently selected from hydrogen or C_{1-2} alkyl; and

30 Q_1 is hydrogen, cyano, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u , OR_t , $\text{C}(\text{O})\text{R}_t$, $\text{C}(\text{O})\text{OR}_t$, $\text{OC}(\text{O})\text{R}_t$, $\text{C}(\text{O})\text{N}(\text{R}_t)\text{R}_u$, $\text{N}(\text{R}_t)\text{C}(\text{O})\text{R}_u$, $\text{S}(\text{O})_y\text{R}_t$ (where y is 0, 1 or 2), $\text{SO}_2\text{N}(\text{R}_t)\text{R}_u$,

$N(R_t)SO_2R_u$ or $(CH_2)_zNR_tR_u$ (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C_{1-4} alkyl; or

Q_1 is optionally substituted by one or more groups of the formula:



5 wherein

L_{1c} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

L_{1d} is absent or selected from $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_v)$, $N(R_v)C(O)$, $N(R_v)C(O)N(R_w)$, $S(O)_2N(R_v)$, or $N(R_v)SO_2$, wherein R_v and R_w are each independently selected from hydrogen or C_{1-2} alkyl; and

10 Z_1 is phenyl or 5-6 membered heteroaryl; wherein Z_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, C_{1-4} alkylamino, amino, cyano, hydroxyl, carboxy, carbamoyl or sulphamoyl;

(7a) R_{1b} , R_{1d} and R_{1f} are selected from hydrogen, cyano, halo or a group of the formula:



wherein

L_{1a} is absent or C_{1-3} alkylene, C_{3-4} cycloalkylene, optionally substituted by one or more substituents selected from C_{1-2} alkyl, halo, hydroxy, or oxo;

20 L_{1b} is absent or selected from O , S , SO , SO_2 , $N(R_r)$, $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_r)$, $N(R_r)C(O)$, $N(R_r)C(O)N(R_s)$, $S(O)_2N(R_r)$, or $N(R_r)SO_2$, wherein R_r and R_s are each independently selected from hydrogen or C_{1-2} alkyl; and

25 Q_1 is hydrogen, cyano, C_{1-6} alkyl, C_{3-8} cycloalkyl (e.g. C_{3-6} cycloalkyl), C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u , OR_t , $C(O)R_t$, $C(O)OR_t$, $OC(O)R_t$, $C(O)N(R_t)R_u$, $N(R_t)C(O)R_u$, $S(O)_yR_t$ (where y is 0, 1 or 2), $SO_2N(R_t)R_u$, $N(R_t)SO_2R_u$ or $(CH_2)_zNR_tR_u$ (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C_{1-4} alkyl; or

Q_1 is optionally substituted by one or more groups of the formula:



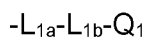
wherein

L_{1c} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

L_{1d} is absent or selected from C(O), O, C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl), heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system), phenyl or 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, cyano, hydroxyl, NR_{t1}R_{u1}, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, C(O)N(R_{t1})R_{u1}, N(R_{t1})C(O)R_{u1}, S(O)_yR_{t1} (where y is 0, 1 or 2), SO₂N(R_{t1})R_{u1}, N(R_{t1})SO₂R_{u1} or (CH₂)_zNR_{t1}R_{u1} (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C₁₋₄alkyl; and when Z₁ is C₃₋₈cycloalkyl or heterocyclyl, Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclyl ring;

(7b) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen, cyano, halo or a group of the formula:



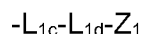
wherein

L_{1a} is absent or C₁₋₃alkylene, C₃₋₄cycloalkylene, optionally substituted by one or more substituents selected from aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl, C₁₋₂alkyl, cyano, halo, hydroxy, or oxo, wherein any aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl or C₁₋₂alkyl is optionally further substituted by one or more substituents selected from halo, cyano or hydroxy;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl, wherein C₁₋₂alkyl is optionally further substituted by C₃₋₆cycloalkyl or a 3 to 6 membered heterocyclyl, which in turn are optionally further substituted by halo, hydroxy, C₁₋₂alkoxy or C₁₋₂haloalkoxy; and

Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₈cycloalkyl (e.g. C₃₋₆cycloalkyl), C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, oxo, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u, N(R_t)SO₂R_u or (CH₂)_zNR_tR_u (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



wherein

L_{1c} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

5 L_{1d} is absent or selected from C(O), O, C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

10 Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl), heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system), phenyl or 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, cyano, hydroxyl, NR_{t1}R_{u1}, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, C(O)N(R_{t1})R_{u1}, N(R_{t1})C(O)R_{u1}, S(O)_yR_{t1} (where y is 0, 1 or 2), SO₂N(R_{t1})R_{u1}, N(R_{t1})SO₂R_{u1} or (CH₂)_zNR_{t1}R_{u1} (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C₁₋₄alkyl; and when Z₁ is C₃₋₈cycloalkyl or heterocyclyl, Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclyl ring;

(8) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen, halo, cyano or from a group of formula:



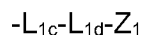
wherein

L_{1a} is absent or C₁₋₃alkylene, optionally substituted by one or more hydroxy;

L_{1b} is absent or N(R_r) wherein R_r is hydrogen; and

25 Q₁ is C₁₋₆alkyl, C₂₋₃alkenyl, C₃₋₈cycloalkyl (e.g. C₃₋₆cycloalkyl), aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from halo, carboxy, trifluoromethyl, NR_tR_u, OR_t wherein R_t and R_u are independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



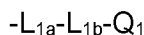
30 wherein

L_{1c} is absent;

L_{1d} is absent; and

Z₁ is phenyl or 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more C₁₋₄alkyl;

(8a) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen, halo, cyano or from a group of formula:



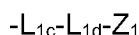
5 wherein

L_{1a} is absent or C₁₋₃alkylene, optionally substituted by one or more hydroxy;

L_{1b} is absent or N(R_r) wherein R_r is hydrogen or C₁₋₄alkyl; and

10 Q₁ is C₁₋₆alkyl, C₂₋₃alkenyl, C₃₋₆cycloalkyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from halo, carboxy, trifluoromethyl, NR_tR_u, OR_t wherein R_t and R_u are independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



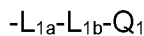
wherein

15 L_{1c} is absent;

L_{1d} is absent; and

20 Z₁ is is phenyl, 5-6 membered heteroaryl, C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl) or heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system); wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C₁₋₄alkyl; and Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclyl ring;

25 (8b) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen, halo, cyano or from a group of formula:



wherein

L_{1a} is C₁₋₃alkylene,;

L_{1b} is N(R_r) wherein R_r is hydrogen or C₁₋₄alkyl; and

Q₁ is C₁₋₆alkyl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from halo, carboxy, trifluoromethyl, NR_tR_u, OR_t wherein R_t and R_u are independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



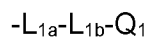
wherein

L_{1c} is absent;

L_{1d} is absent; and

10 Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl) or heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system); wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, wherein R_{t1} is selected from hydrogen or C₁₋₄alkyl; and Z₁ is optionally spiro-fused to
15 a C₃₋₆cycloalkyl or heterocyclyl ring;

(8c) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen or from a group of formula:



wherein

L_{1a} is C₁₋₃alkylene;

20 L_{1b} is N(R_r) wherein R_r is hydrogen or C₁₋₄alkyl; and

Q₁ is C₁₋₆alkyl; and wherein Q₁ is optionally substituted by one or more substituents selected from halo, carboxy, trifluoromethyl, NR_tR_u, OR_t wherein R_t and R_u are independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



wherein

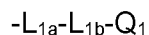
L_{1c} is absent;

L_{1d} is absent; and

30 Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl); wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, OR_{t1} or C(O)OR_{t1}, wherein R_{t1}

is selected from hydrogen or C₁₋₄alkyl; and Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclcyl ring;

(8d) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen or from a group of formula:



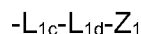
5 wherein

L_{1a} is C₁₋₃alkylene,;

L_{1b} is N(R_r) wherein R_r is hydrogen; and

10 Q₁ is C₁₋₆alkyl; and wherein Q₁ is optionally substituted by one or more substituents selected from halo, carboxy, trifluoromethyl, NR_tR_u, OR_t wherein R_t and R_u are independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



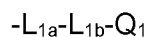
wherein

L_{1c} is absent;

15 L_{1d} is absent; and

Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl); wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl or halo, C₁₋₄haloalkyl, OR_{t1} or C(O)OR_{t1}, wherein R_{t1} is selected from hydrogen or C₁₋₄alkyl;

20 (8e) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen or from a group of formula:

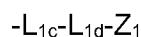


wherein

L_{1a} is C₁₋₃alkylene,;

L_{1b} is N(R_r) wherein R_r is hydrogen; and

25 Q₁ is C₁₋₆alkyl substituted by one or more groups of the formula:



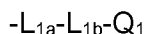
wherein

L_{1c} is absent;

L_{1d} is absent; and

Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl) that is optionally substituted by one or more substituents selected from C₁₋₄alkyl or halo;

- 5 (9) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen, halo, cyano or from a group of formula:



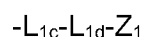
wherein

L_{1a} is absent or C₁₋₃alkylene;

L_{1b} is absent or N(R_r) wherein R_r is hydrogen; and

- 10 Q₁ is C₁₋₆alkyl, and wherein

Q₁ is substituted by a group of the formula:



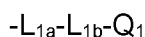
wherein

L_{1c} is absent;

- 15 L_{1d} is absent; and

Z₁ is phenyl;

- (9a) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen, halo, cyano or from a group of formula:



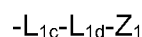
- 20 wherein

L_{1a} is absent or C₁₋₃alkylene, optionally substituted by one or more hydroxy;

L_{1b} is absent; and

- 25 Q₁ is a 5- or 6-membered aryl, a 5- or 6-membered heteroaryl, a 5- or 6-membered heterocyclyl or a 7, 8 or 9 membered bridged heterocycle, wherein Q₁ is optionally substituted by one or more substituents selected from halo, NR_tR_u, OR_t, wherein R_t and R_u are independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



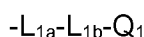
wherein

- 30 L_{1c} is absent;

L_{1d} is absent; and

Z₁ is 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more C₁₋₄alkyl;

- 5 (10) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen, halo, cyano or from a group of formula:



wherein

L_{1a} is absent or C₁₋₃alkylene, optionally substituted by one or more hydroxy;

L_{1b} is absent or N(R_r) wherein R_r is hydrogen; and

- 10 Q₁ is a 5- or 6-membered aryl, a 5- or 6-membered heteroaryl, or a 5- or 6-membered heterocyclyl, wherein Q₁ is optionally substituted by one or more substituents selected from halo, NR_tR_u, OR_t wherein R_t and R_u are independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:

- 15
$$-L_{1c}-L_{1d}-Z_1$$

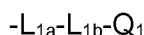
wherein

L_{1c} is absent;

L_{1d} is absent; and

- 20 Z₁ is 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more C₁₋₄alkyl;

- (11) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen, halo, cyano or from a group of formula:



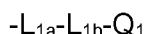
wherein

L_{1a} is absent or C₁₋₃alkylene optionally substituted by one hydroxy;

- 25 L_{1b} is absent or N(R_r) wherein R_r is hydrogen; and

Q₁ is phenyl, pyrazolyl, piperazinyl or pyridinyl, wherein Q₁ is optionally substituted by one or more substituents selected from chloro and methoxy;

- (12) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen, halo, cyano or from a group of formula:



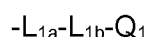
- 30 wherein

L_{1a} is absent;

L_{1b} is absent or N(R_r) wherein R_r is hydrogen; and

Q₁ is C₁₋₆alkyl optionally substituted with 5-6 membered heteroaryl; wherein 5-6 membered heteroaryl is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, C₁₋₄alkylamino, amino, cyano, hydroxyl, carboxy, carbamoyl or sulphamoyl;

(13) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen, halo, cyano or from a group of formula:



wherein

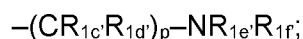
L_{1a} is absent;

L_{1b} is absent or N(R_r) wherein R_r is hydrogen; and

Q₁ is C₁₋₆alkyl optionally substituted with piperazinyl, imidazolyl or pyridyl, wherein the imidazolyl is optionally substituted with C₁₋₄alkyl;

(14) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen; halo; cyano; hydroxy; C₁₋₆alkyl optionally substituted with OH, NH₂, a 5-6 membered aryl, carboxy and/or a 5-6 membered heterocyclyl; C₁₋₆alkyloxy; C₂₋₃alkenyl; C₃₋₆cycloalkyl; -C₁₋₃alkylene-NH-C₁₋₆alkyl wherein the C₁₋₆alkyl is optionally substituted with OH, trifluoromethyl, carboxy or phenyl; -NH-heteroaryl wherein the heteroaryl is a 5- or 6-membered heteroaryl; 5- or 6-membered heteroaryl; 5- or 6-membered heterocyclic; 5- or 6-membered aryl optionally substituted with -OC₁₋₄alkyl or halo; and -NH-C₁₋₆alkyl wherein the C₁₋₆alkyl is optionally substituted with a 5- or 6-membered heteroaryl and wherein the 5- or 6-membered heteroaryl is optionally substituted with C₁₋₄alkyl;

(14a) R_{1b}, R_{1d} and R_{1f} are independently selected from hydrogen, halo, cyano, hydroxy, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkoxy, or a group of the formula:



wherein

p is an integer selected from 1 or 2;

R_{1c'} and R_{1d'} are independently selected from:

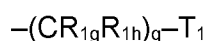
- (i) hydrogen (including deuterium),
- (ii) C₁₋₃alkyl which is optionally substituted by one more substituents selected from cyano, hydroxy, C₁₋₃alkoxy, halo, C₁₋₃haloalkoxy, -O-C₃₋₄cycloalkyl, or NH₂; wherein -O-C₃₋₆cycloalkyl is optionally substituted with halo, cyano or hydroxy,

- (iii) or $R_{1c'}$ and $R_{1d'}$ are linked together such that, together with the carbon atom to which they are attached, they form a 3- to 5-membered cycloalkyl or heterocyclic ring, or a spirocyclic ring system, each of which is optionally substituted by one or more substituents selected from C_{1-2} alkyl, C_{1-2} haloalkyl, cyano, hydroxy, C_{1-2} alkoxy, halo or C_{1-2} haloalkoxy;

$R_{1e'}$ is selected from:

- (i) hydrogen (including deuterium);
- (ii) C_{1-3} alkyl which is optionally substituted by one more substituents selected from cyano, hydroxy, C_{1-2} alkoxy, halo, C_{1-2} haloalkoxy and NH_2 ;

R_{1f} is a group with the formula:



wherein:

q is 0, 1 or 2 (e.g. q is 1 or 2);

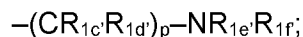
R_{1g} and R_{1h} are independently selected from:

- a) hydrogen (including deuterium); or
- b) C_{1-3} alkyl, which is optionally substituted by one more substituents selected from cyano, hydroxy, C_{1-2} alkoxy, halo, C_{1-2} haloalkoxy, -O- C_3 cycloalkyl, wherein -O- C_3 cycloalkyl is optionally substituted with halo, cyano or hydroxy;

and T_1 is selected from C_{3-8} cycloalkyl, aryl, heterocyclyl, heteroaryl, a spirocyclic carbocyclic or heterocyclic ring system, a bridged C_{3-8} cycloalkyl, or a bridged heterocyclic ring system, each of which is optionally substituted by one or more substituents selected from C_{1-2} alkyl, C_{1-2} haloalkyl, cyano, hydroxy, C_{1-2} alkoxy, halo or C_{1-2} haloalkoxy;

or $R_{1e'}$ and R_{1f} are linked such that, together with the nitrogen atom to which they are attached, they form a mono- or bicyclic-heterocyclic ring, which is optionally substituted by one or more substituents selected from C_{1-2} alkyl, C_{1-2} haloalkyl, cyano, hydroxy, C_{1-2} alkoxy, halo, C_{1-2} haloalkoxy, $NR_{1i}R_{1j}$ or $-S(O)_{0-2}R_{1i}R_{1j}$, wherein R_{1i} and R_{1j} are H or C_{1-2} alkyl, and/or the mono- or bicyclic heterocyclic ring formed by R_{1e} and R_{1f} is optionally spiro-fused to a C_{3-6} cycloalkyl or a heterocyclic ring, which in turn is optionally substituted by one or more substituents selected from C_{1-2} alkyl, cyano, hydroxy, C_{1-2} alkoxy, halo, C_{1-2} haloalkoxy, $NR_{1i}R_{1j}$ or $-S(O)_{0-2}R_{1i}R_{1j}$, wherein R_{1i} and R_{1j} are H or C_{1-2} alkyl.

(14b) R_{1d} and R_{1f} are independently selected from hydrogen, halo, cyano, hydroxy, C_{1-4} -alkyl, C_{1-4} alkoxy and C_{1-4} haloalkoxy; and R_{1b} is a group of the formula:



wherein

5 p is an integer selected from 1 or 2;

$R_{1c'}$ and $R_{1d'}$ are independently selected from:

- (i) hydrogen (including deuterium) or
- (ii) C_{1-3} alkyl which is optionally substituted by one more substituents selected from cyano, hydroxy, C_{1-2} alkoxy, halo, C_{1-2} haloalkoxy, $-O-C_3$ cycloalkyl;

10 $R_{1e'}$ is selected from hydrogen (including deuterium) or C_{1-2} alkyl; and

R_{1f} is a group with the formula:



wherein:

15 q is 0, 1 or 2 (e.g. q is 1 or 2); R_{1g} and R_{1h} are independently selected from:

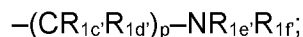
- a) hydrogen (including deuterium); or
- b) C_{1-2} alkyl, which is optionally substituted by one more substituents selected from cyano, hydroxy, C_{1-2} alkoxy, halo or C_{1-2} haloalkoxy;

20 and T_1 is selected from C_{3-8} cycloalkyl, aryl, heterocyclyl, heteroaryl, a spirocyclic carbocyclic or heterocyclic ring system, a bridged C_{3-8} cycloalkyl, or a bridged heterocyclic ring system, each of which is optionally substituted by one or more substituents selected from C_{1-2} alkyl, C_{1-2} haloalkyl, cyano, hydroxy, C_{1-2} alkoxy, halo or C_{1-2} haloalkoxy;

25 or $R_{1e'}$ and R_{1f} are linked such that, together with the nitrogen atom to which they are attached, they form a mono- or bicyclic-heterocyclic ring, which is optionally substituted by one or more substituents selected from C_{1-2} alkyl, C_{1-2} haloalkyl, cyano, hydroxy, C_{1-2} alkoxy, halo or C_{1-2} haloalkoxy, and/or the mono- or bicyclic heterocyclic ring formed by $R_{1e'}$ and R_{1f} is optionally spiro-fused to a C_{3-6} cycloalkyl or a heterocyclic ring, which in turn is optionally substituted by one or more substituents selected from C_{1-2} alkyl, C_{1-2} haloalkyl, cyano, hydroxy, C_{1-2} alkoxy, halo or C_{1-2} haloalkoxy.

30

- (14c) R_{1d} and R_{1f} are independently selected from hydrogen, halo, cyano, hydroxy, C_{1-4} -alkyl, C_{1-4} alkoxy and C_{1-4} haloalkoxy; and R_{1b} is a group of the formula:



wherein

5 p is an integer selected from 1 or 2;

$R_{1c'}$ and $R_{1d'}$ are independently selected from hydrogen (including deuterium) or C_{1-2} alkyl;

$R_{1e'}$ is selected from hydrogen (including deuterium) or C_{1-2} alkyl; and

R_{1f} is a group with the formula:



wherein:

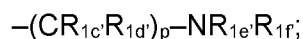
q is 0, 1 or 2 (e.g. q is 1 or 2); R_{1g} and R_{1h} are independently selected from hydrogen (including deuterium) or C_{1-2} alkyl;

15 and T_1 is selected from C_{3-4} cycloalkyl, heterocyclyl, a spirocyclic carbocyclic or heterocyclic ring system, a bridged C_{3-8} cycloalkyl, or a bridged heterocyclic ring system, each of which is optionally substituted by one or more substituents selected from C_{1-2} alkyl, C_{1-2} haloalkyl, cyano, hydroxy, C_{1-2} alkoxy, halo or C_{1-2} haloalkoxy;

20 or $R_{1e'}$ and R_{1f} are linked such that, together with the nitrogen atom to which they are attached, they form a mono- or bicyclic-heterocyclic ring, which is optionally substituted by one or more substituents selected from C_{1-2} alkyl, C_{1-2} haloalkyl, cyano, hydroxy, C_{1-2} alkoxy, halo or C_{1-2} haloalkoxy, and/or the mono- or bicyclic heterocyclic ring formed by R_{1e} and R_{1f} is optionally spiro-fused to a C_{3-6} cycloalkyl or a heterocyclic ring, which in turn is optionally substituted by one or more substituents selected from C_{1-2} alkyl, C_{1-2} haloalkyl, cyano, hydroxy, C_{1-2} alkoxy, halo or C_{1-2} haloalkoxy.

25

- (14d) R_{1d} and R_{1f} are independently selected from hydrogen, halo, cyano, hydroxy, methyl and methoxy; and R_{1b} is a group of the formula:



30 wherein

p is 1;

R_{1c'} and R_{1d'} are independently selected from hydrogen (including deuterium) or C₁₋₂alkyl;

R_{1e'} is selected from hydrogen (including deuterium) or C₁₋₂alkyl; and

R_{1f} is a group with the formula:



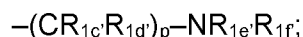
wherein:

q is 0, 1 or 2 (e.g. q is 1 or 2); R_{1g} and R_{1h} are independently selected from hydrogen (including deuterium) or C₁₋₂alkyl;

and T₁ is selected from C₃₋₄cycloalkyl, heterocyclyl, a spirocyclic carbocyclic or heterocyclic ring system, a bridged C₃₋₈cycloalkyl, or a bridged heterocyclic ring system, each of which is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo or C₁₋₂haloalkoxy;

or R_{1e'} and R_{1f} are linked such that, together with the nitrogen atom to which they are attached, they form a mono- or bicyclic-heterocyclic ring, which is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo or C₁₋₂haloalkoxy, and/or the mono- or bicyclic heterocyclic ring formed by R_{1e} and R_{1f} is optionally spiro-fused to a C₃₋₆cycloalkyl or a heterocyclic ring; which in turn is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo or C₁₋₂haloalkoxy.

(14e) R_{1d} and R_{1f} are independently selected from hydrogen, halo, cyano, hydroxy, methyl and methoxy; and R_{1b} is a group of the formula:



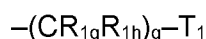
wherein

p is 1;

R_{1c'} and R_{1d'} are independently selected from hydrogen (including deuterium) or C₁₋₂alkyl;

R_{1e'} is selected from hydrogen (including deuterium) or C₁₋₂alkyl; and

R_{1f} is a group with the formula:



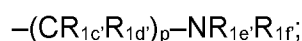
wherein:

q is 1;

R_{1g} and R_{1h} are independently selected from hydrogen (including deuterium) or C₁₋₂alkyl;

and T₁ is selected from C₃₋₄cycloalkyl, heterocyclyl, a spirocyclic carbocyclic or heterocyclic ring system, a bridged C₃₋₈cycloalkyl, or a bridged heterocyclic ring system, each of which is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo or C₁₋₂haloalkoxy.

(14f) R_{1d} and R_{1f} are independently selected from hydrogen, halo, cyano, hydroxy, methyl and methoxy; and R_{1b} is a group of the formula:



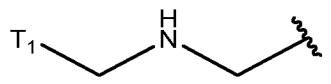
wherein

p is 1;

R_{1c'} and R_{1d'} are independently selected from hydrogen (including deuterium) or C₁₋₂alkyl; and

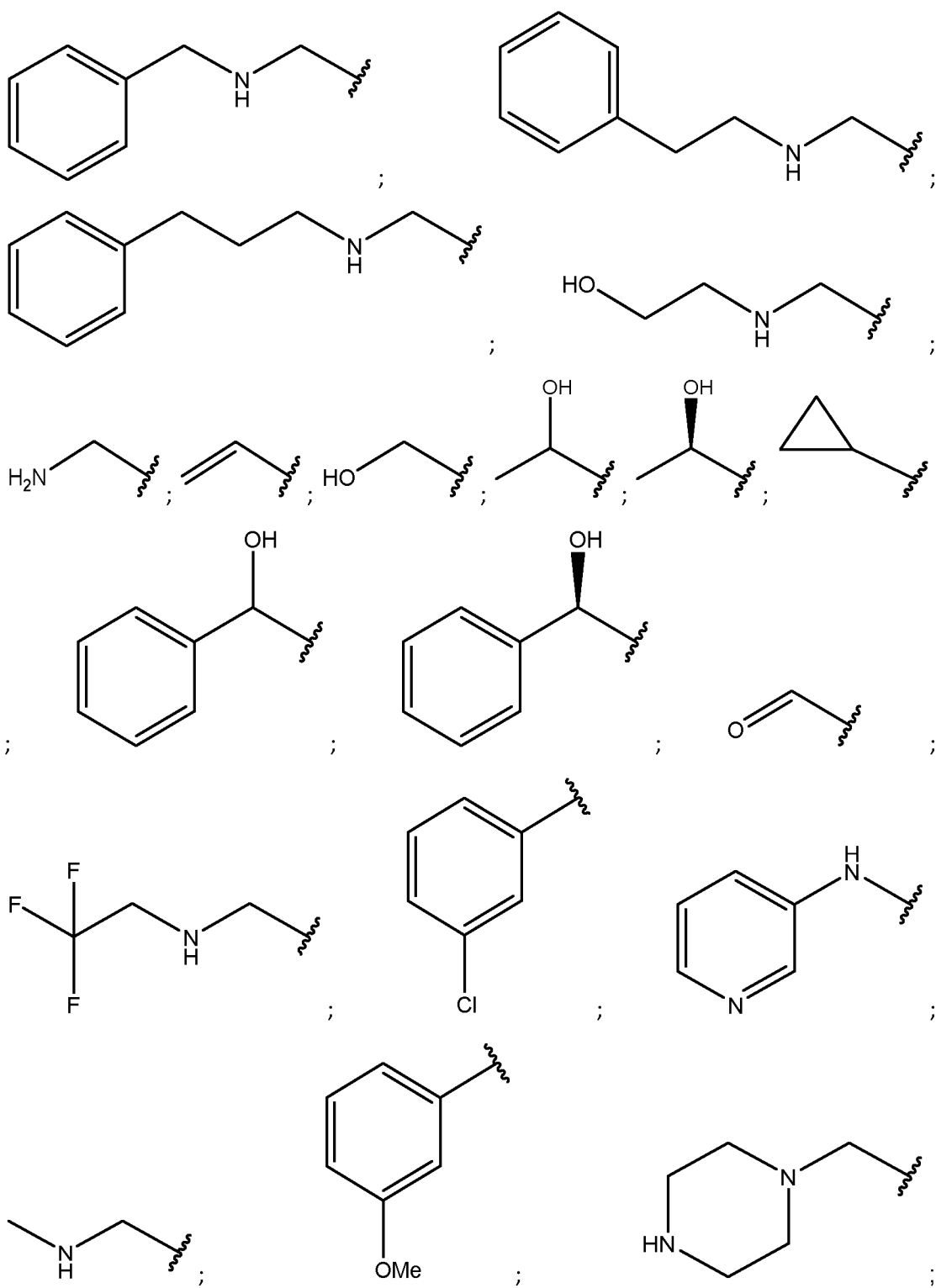
R_{1e'} and R_{1f'} are linked such that, together with the nitrogen atom to which they are attached, they form a mono- or bicyclic-heterocyclic ring, which is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo or C₁₋₂haloalkoxy, and/or the mono- or bicyclic heterocyclic ring formed by R_{1e'} and R_{1f'} is optionally spiro-fused to a C₃₋₆cycloalkyl or a heterocyclic ring, which in turn is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo or C₁₋₂haloalkoxy.

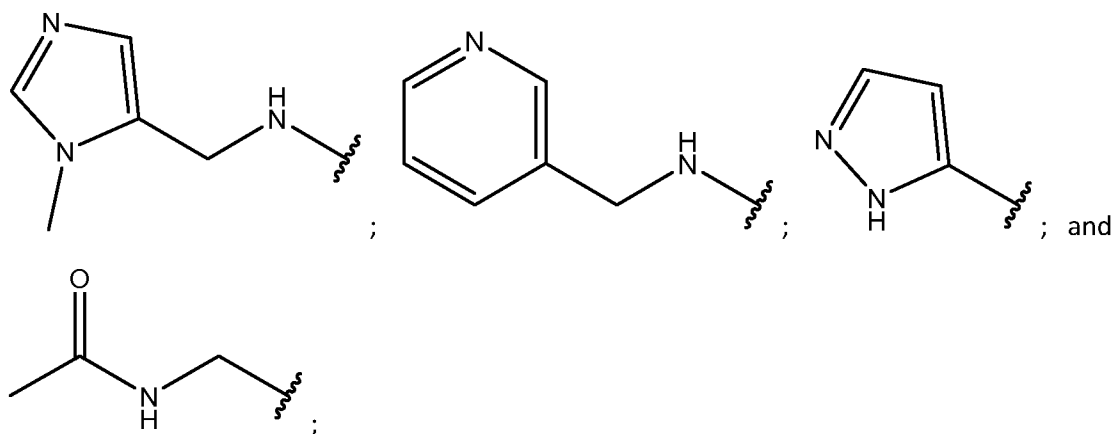
(14g) R_{1d} and R_{1f} are independently selected from hydrogen, halo, cyano, hydroxy, methyl and methoxy; and R_{1b} is a group of the formula



wherein T₁ is selected from C₃₋₄cycloalkyl, heterocyclyl, a spirocyclic carbocyclic or heterocyclic ring system, a bridged C₃₋₈cycloalkyl, or a bridged heterocyclic ring system, each of which is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo or C₁₋₂haloalkoxy.

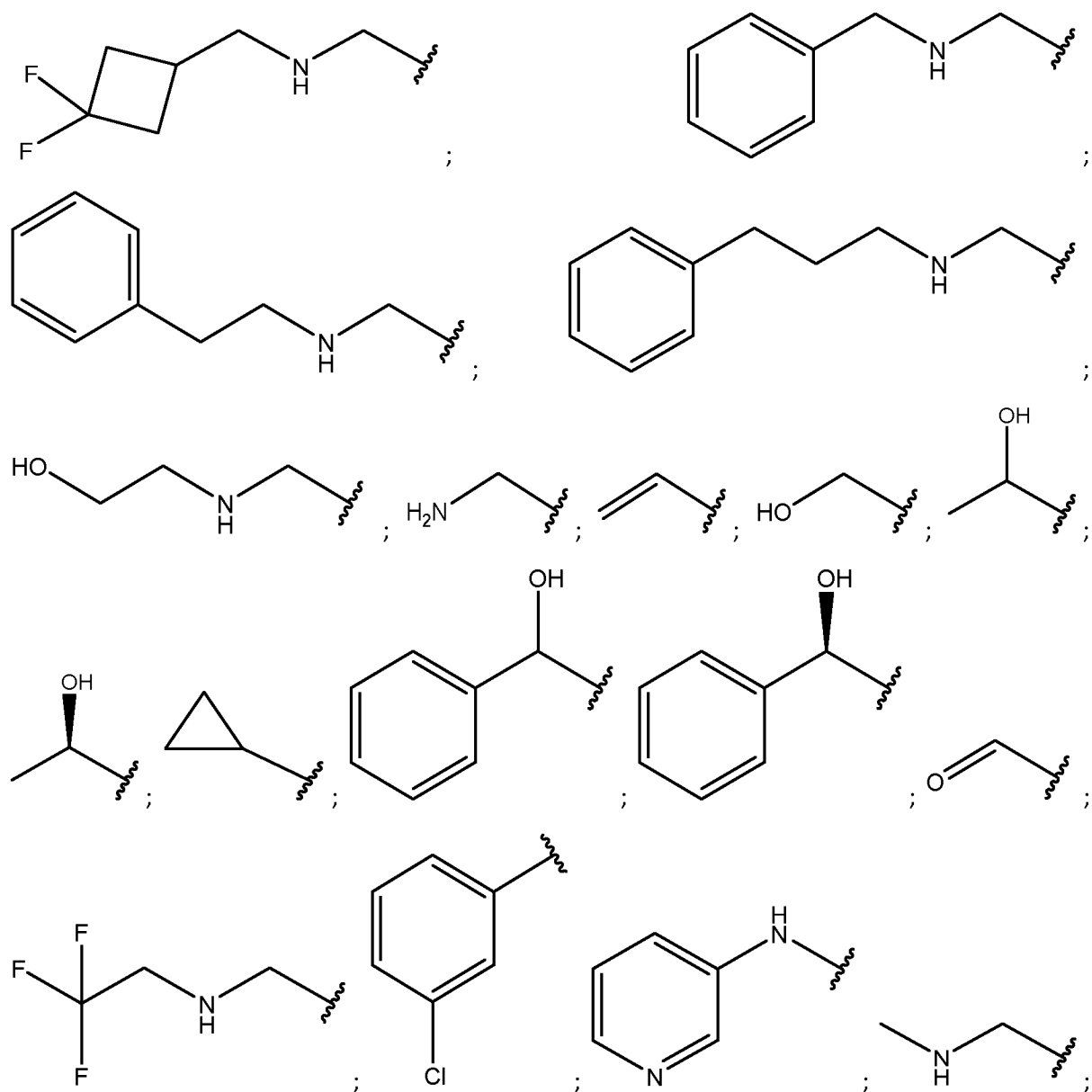
(15) R_{1b}, R_{1d} and R_{1f} are selected from hydrogen; bromo; chloro; fluoro; cyano; methyl; hydroxy; methoxy;



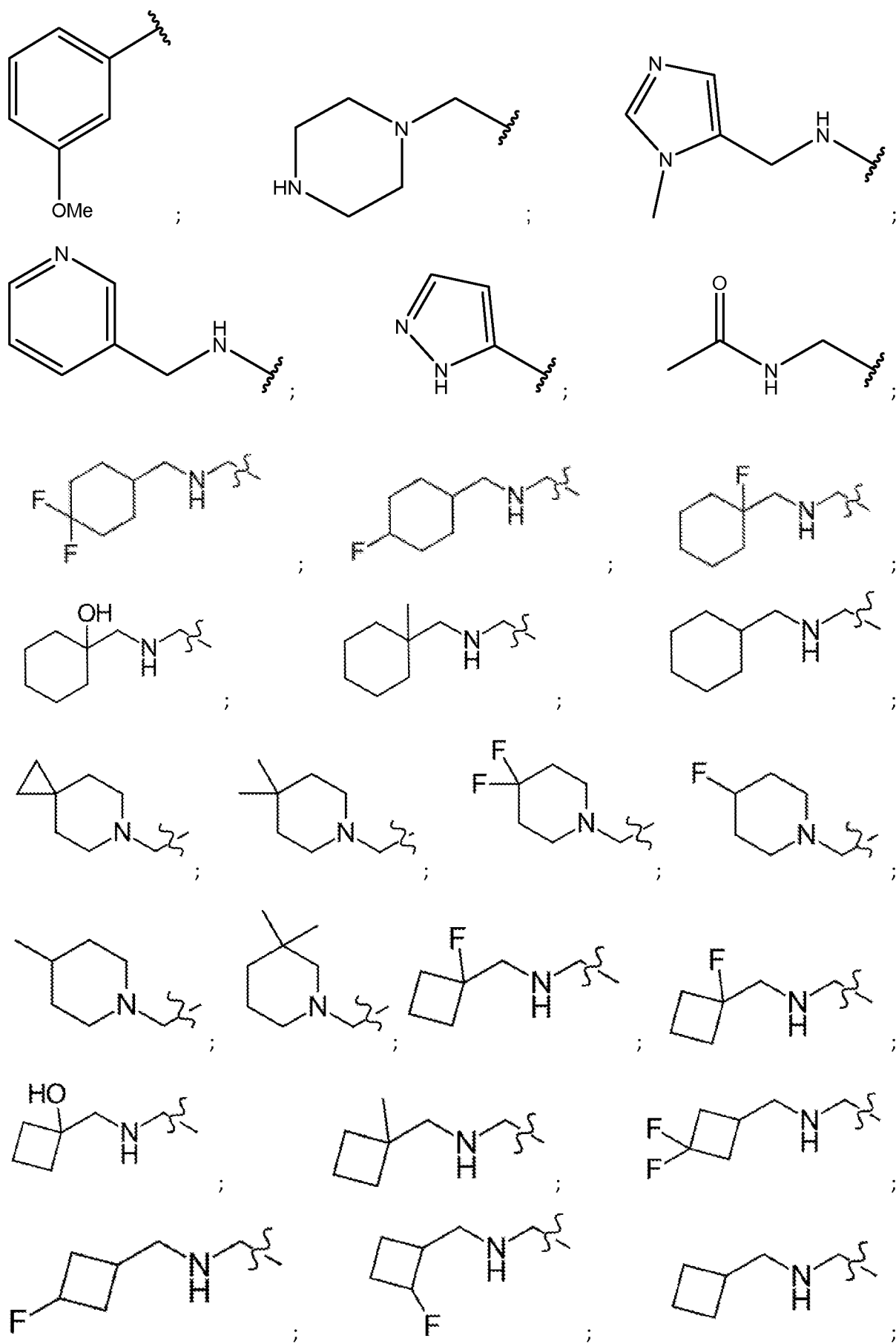


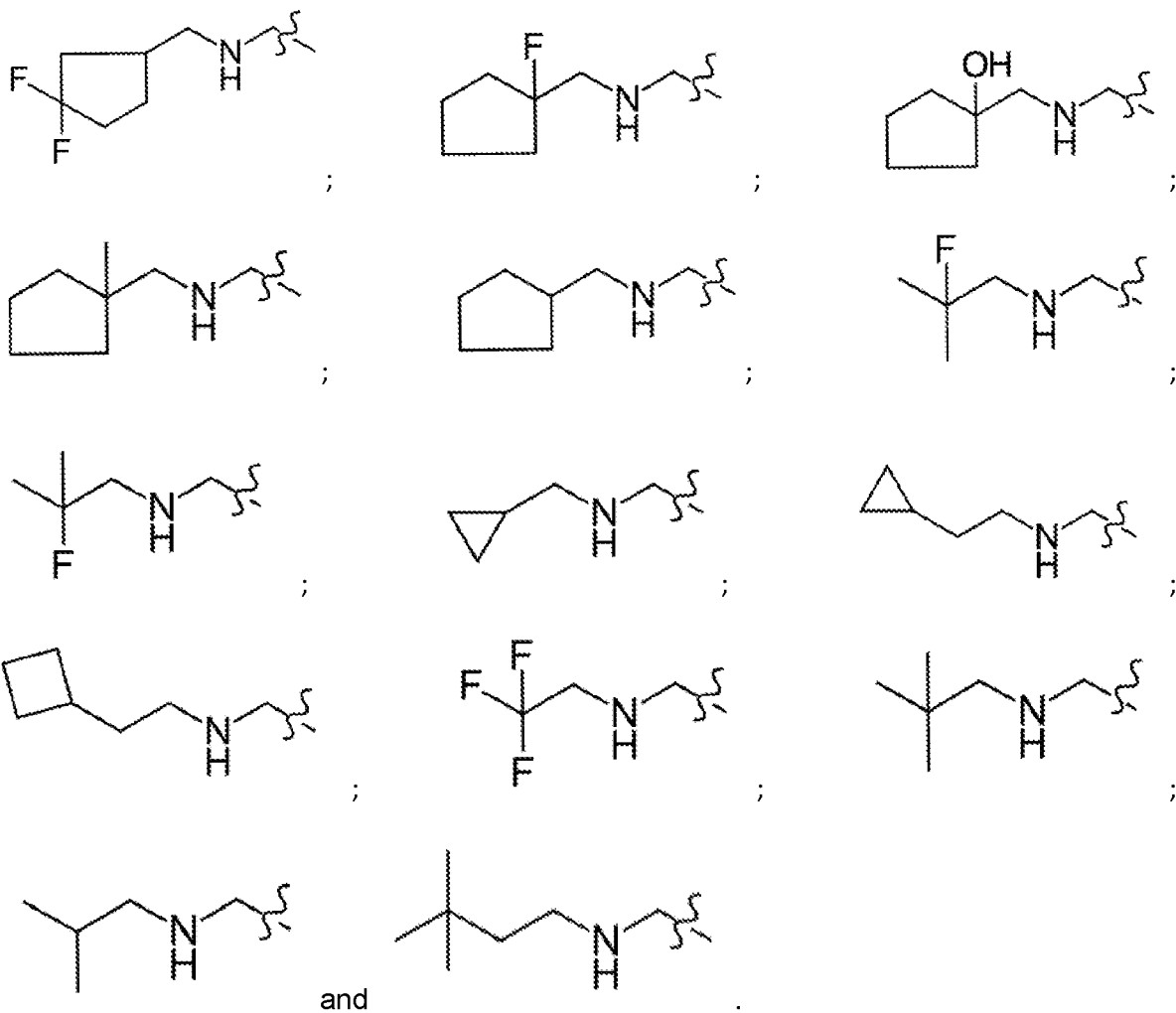
(15a) R_{1d} and R_{1f} are selected from hydrogen; bromo; chloro; fluoro; cyano; methyl; methoxy;

5 and R_{1b} is selected from:



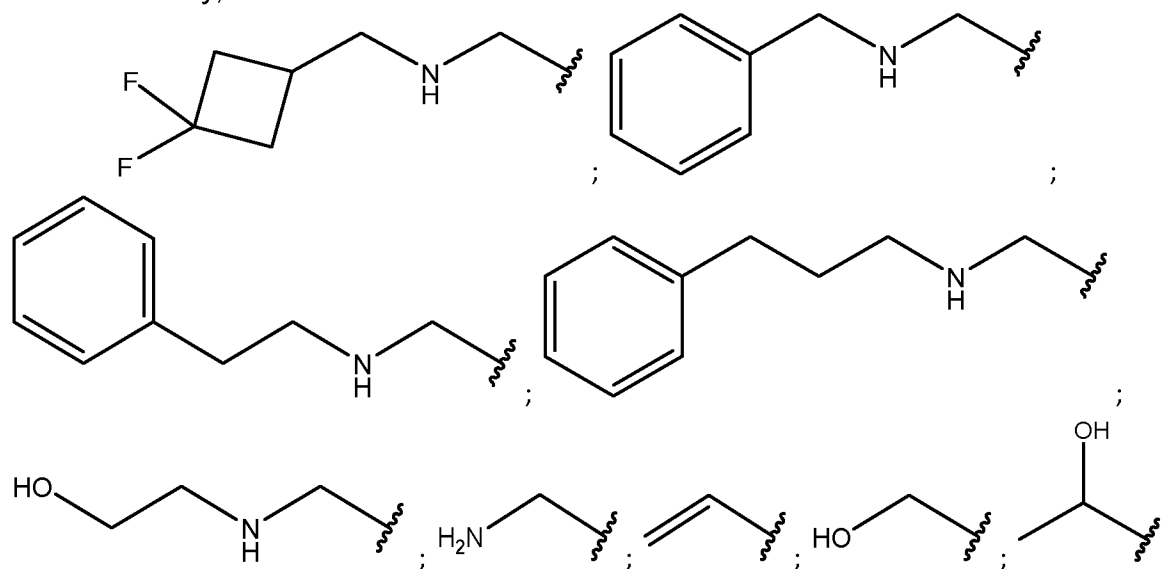
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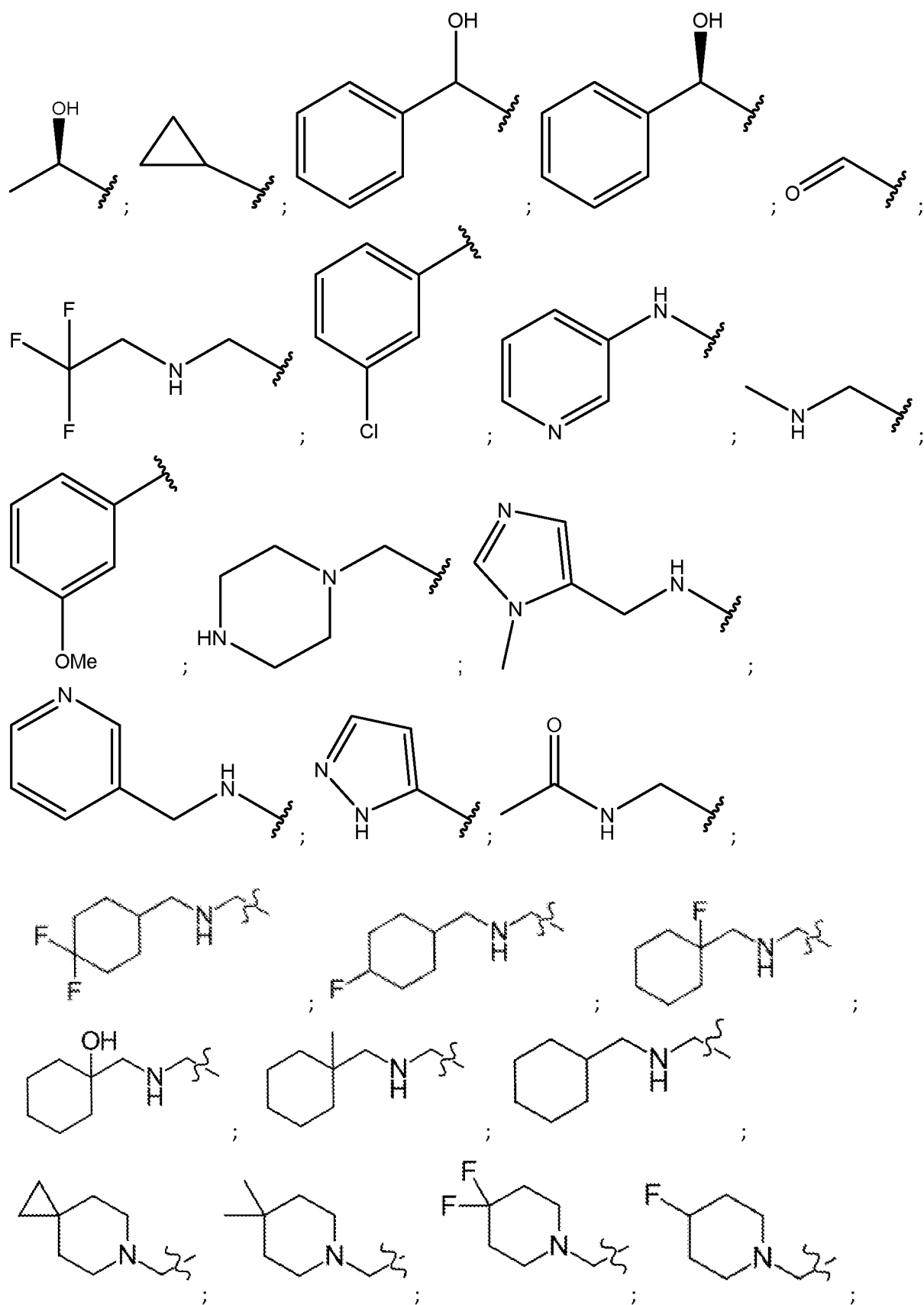


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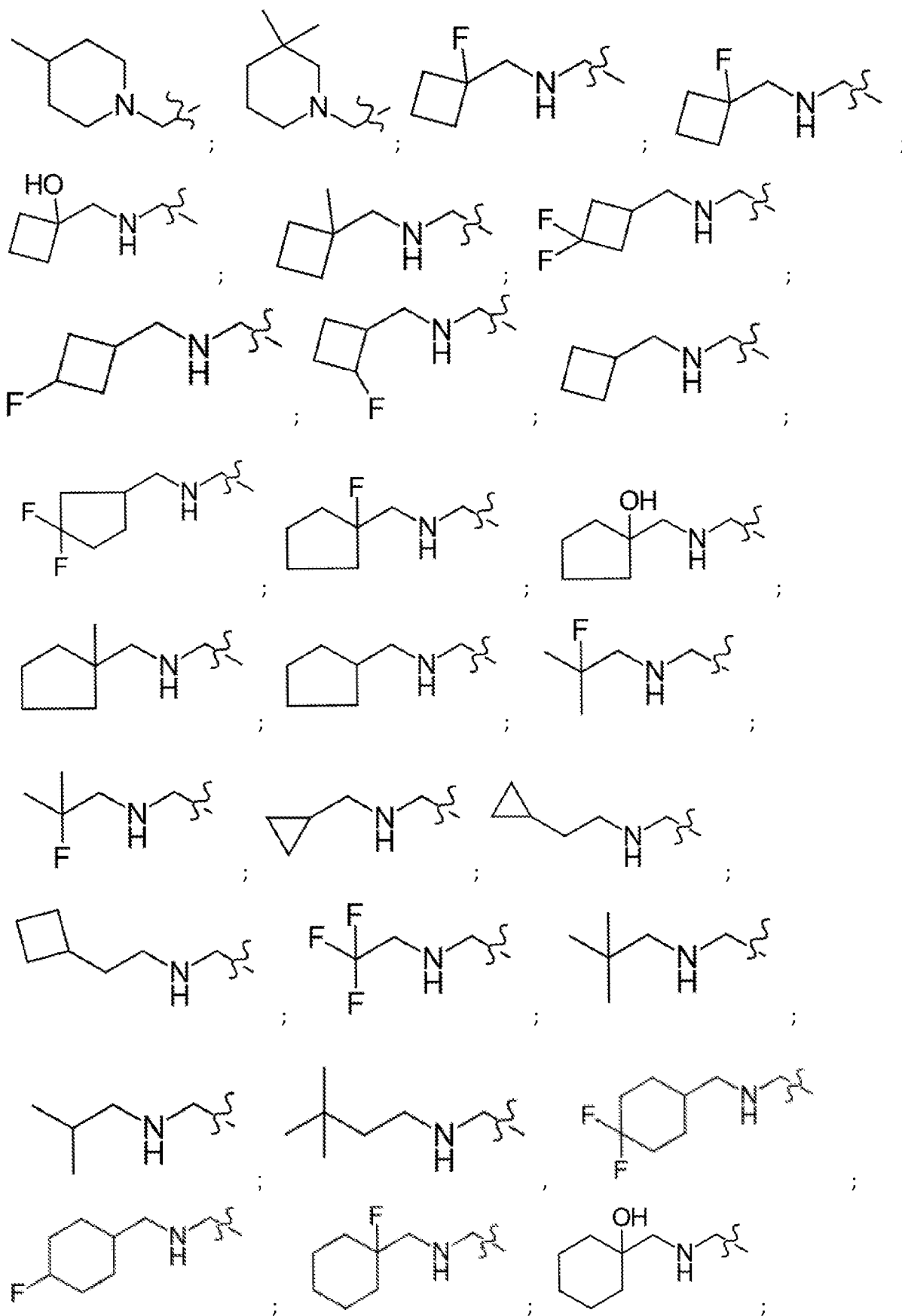
(15b) R_{1b} , R_{1d} and R_{1f} are selected from hydrogen; bromo; chloro; fluoro; cyano; methyl; methoxy,

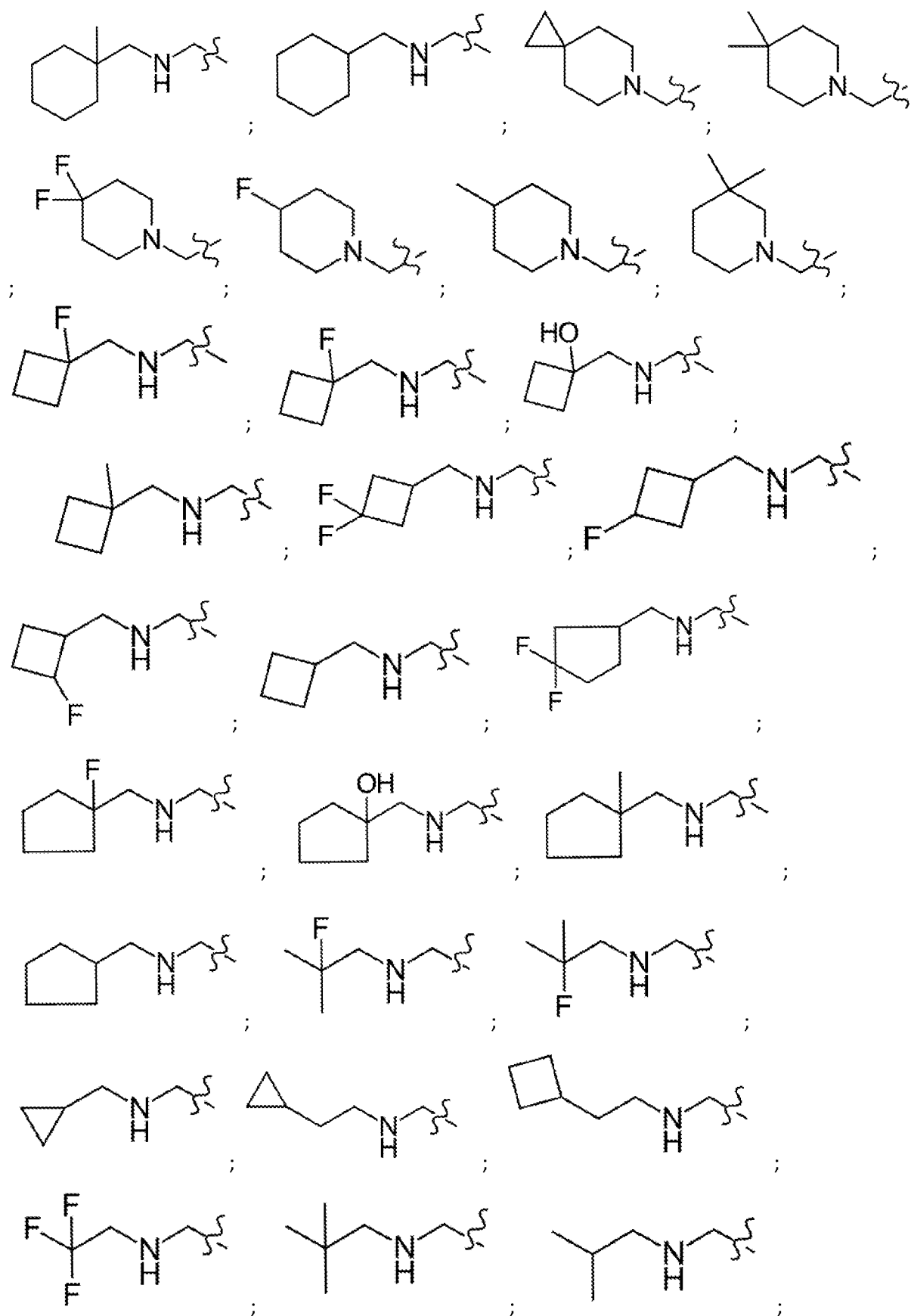


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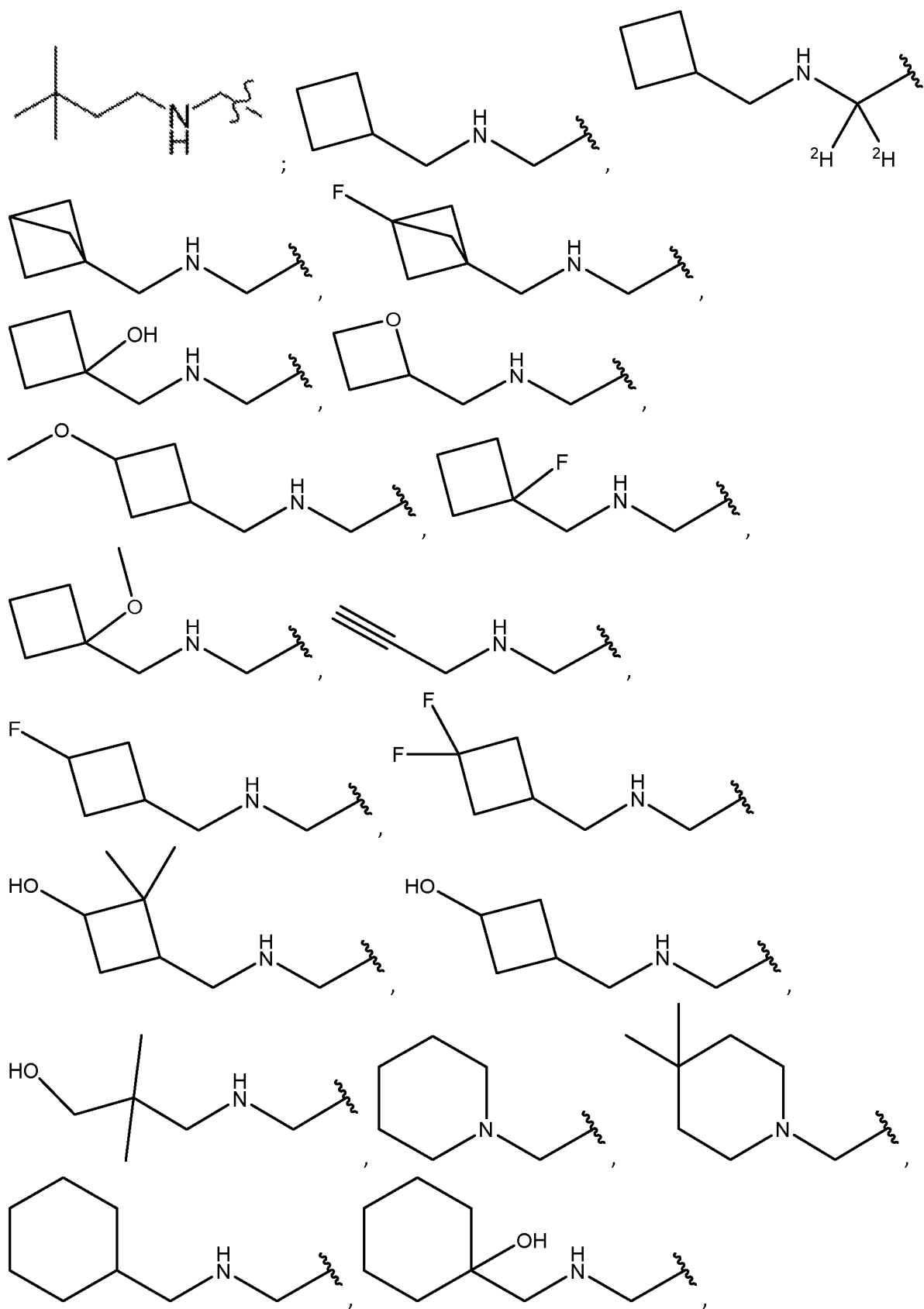


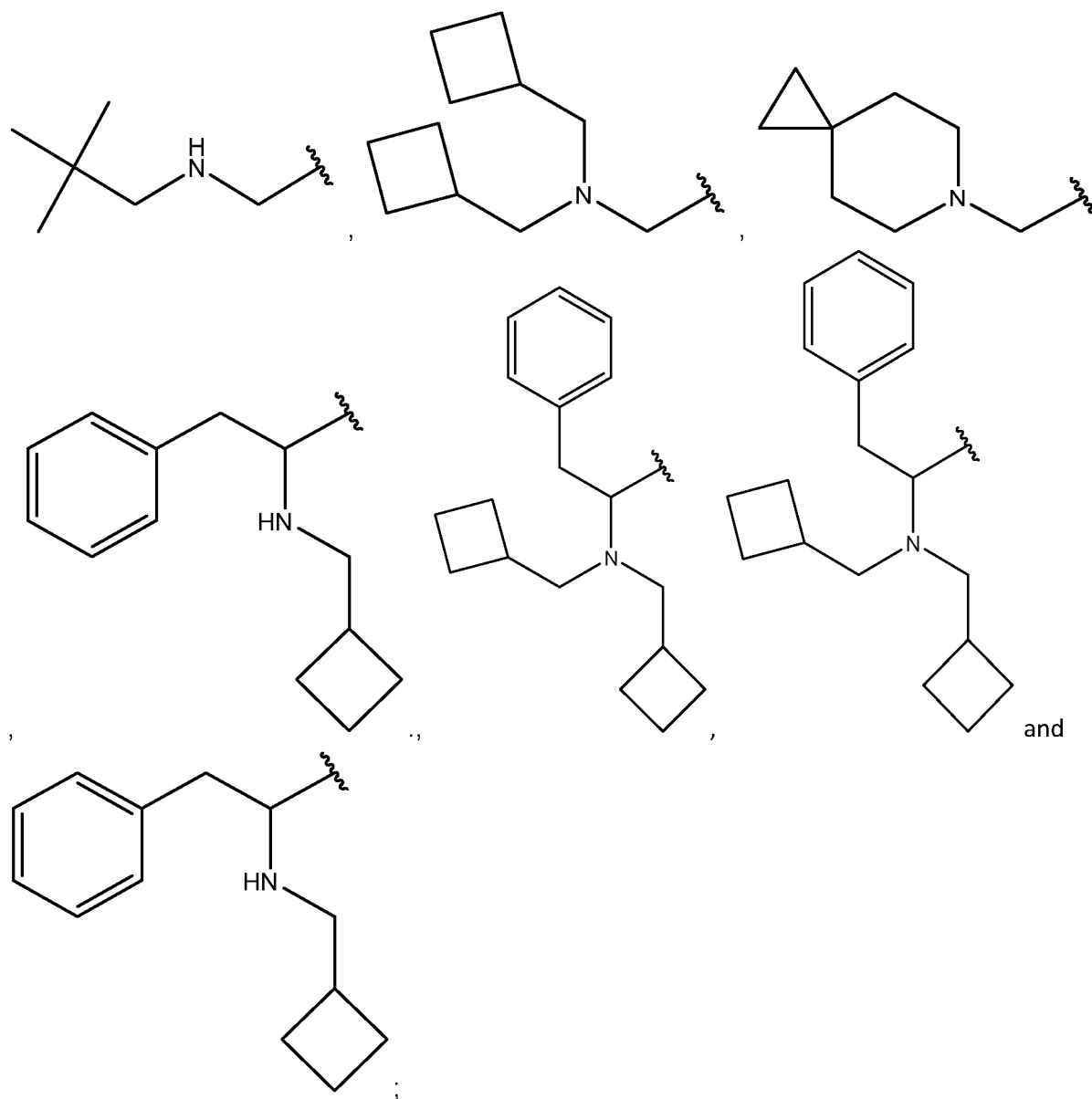
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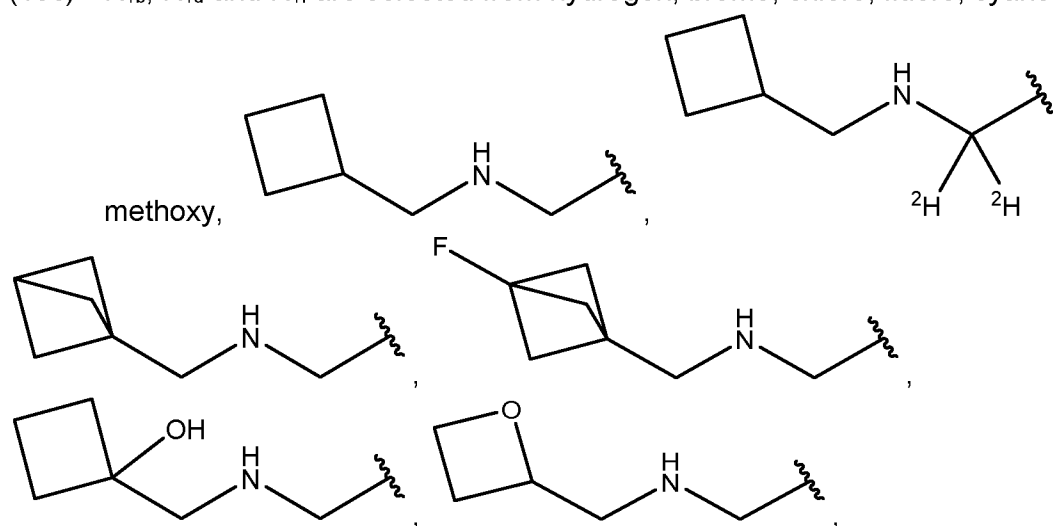


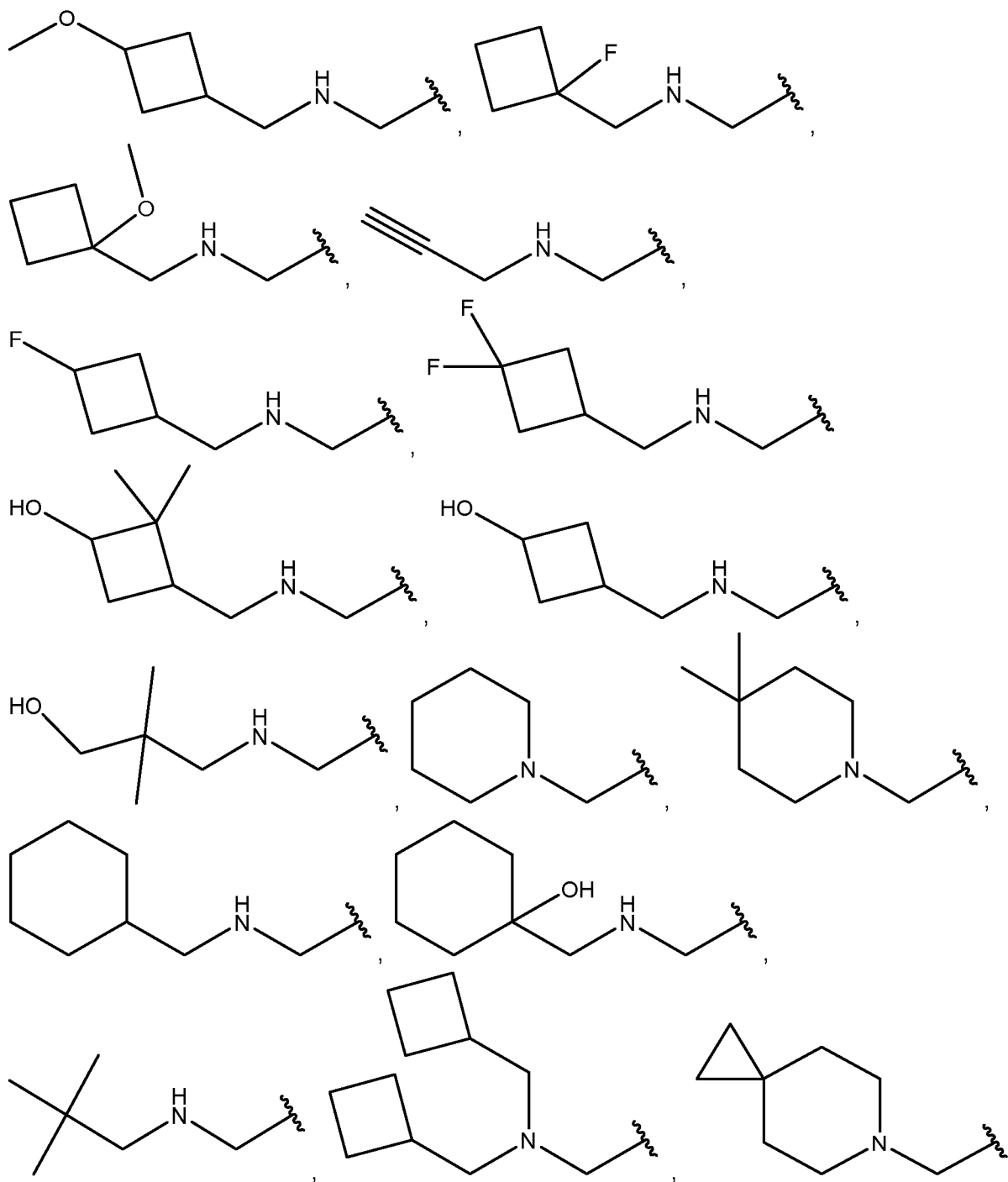
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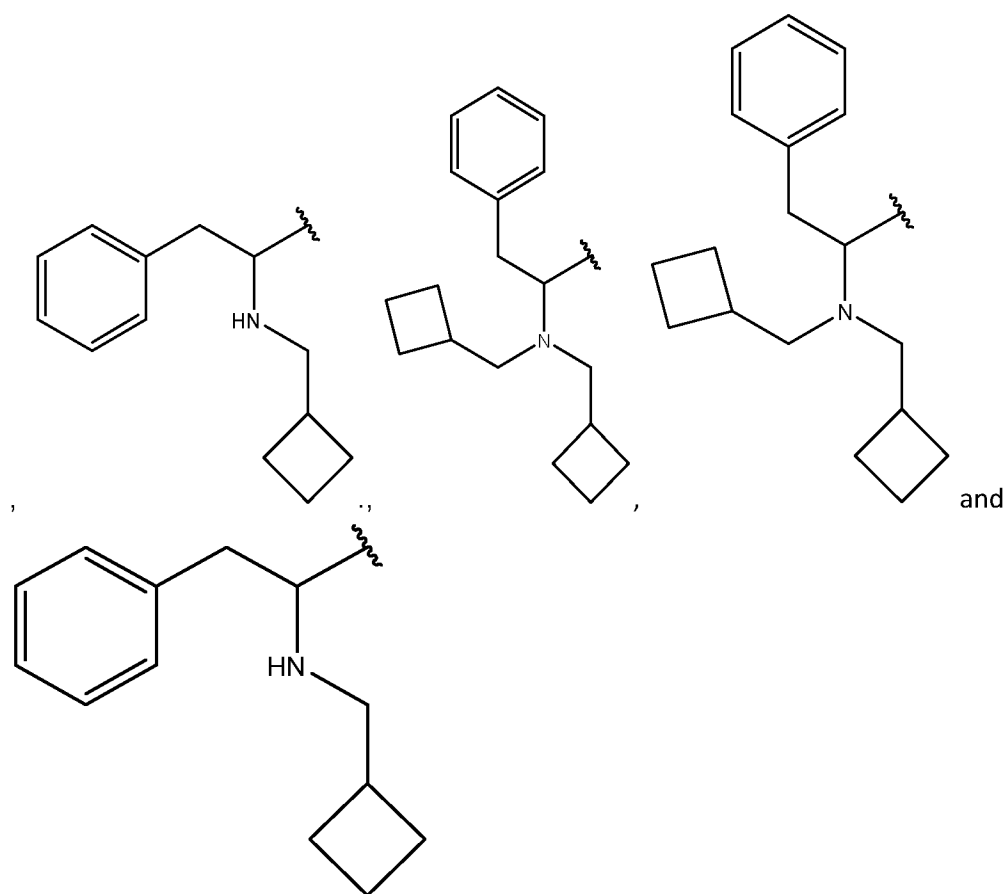


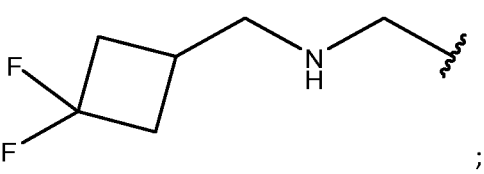
5 (15c) R_{1b} , R_{1d} and R_{1f} are selected from hydrogen; bromo; chloro; fluoro; cyano; methyl;



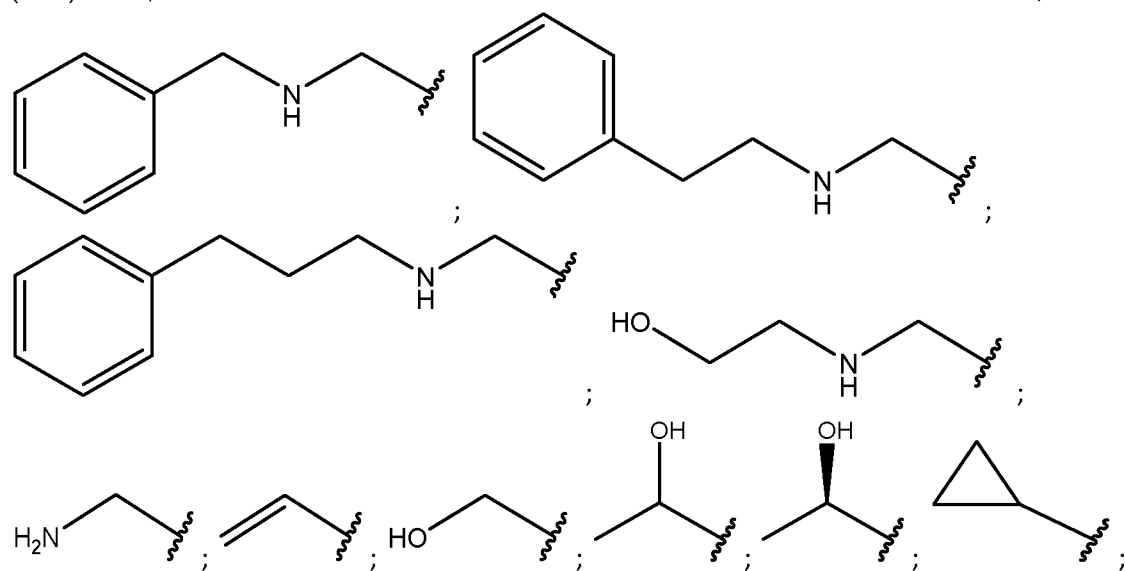


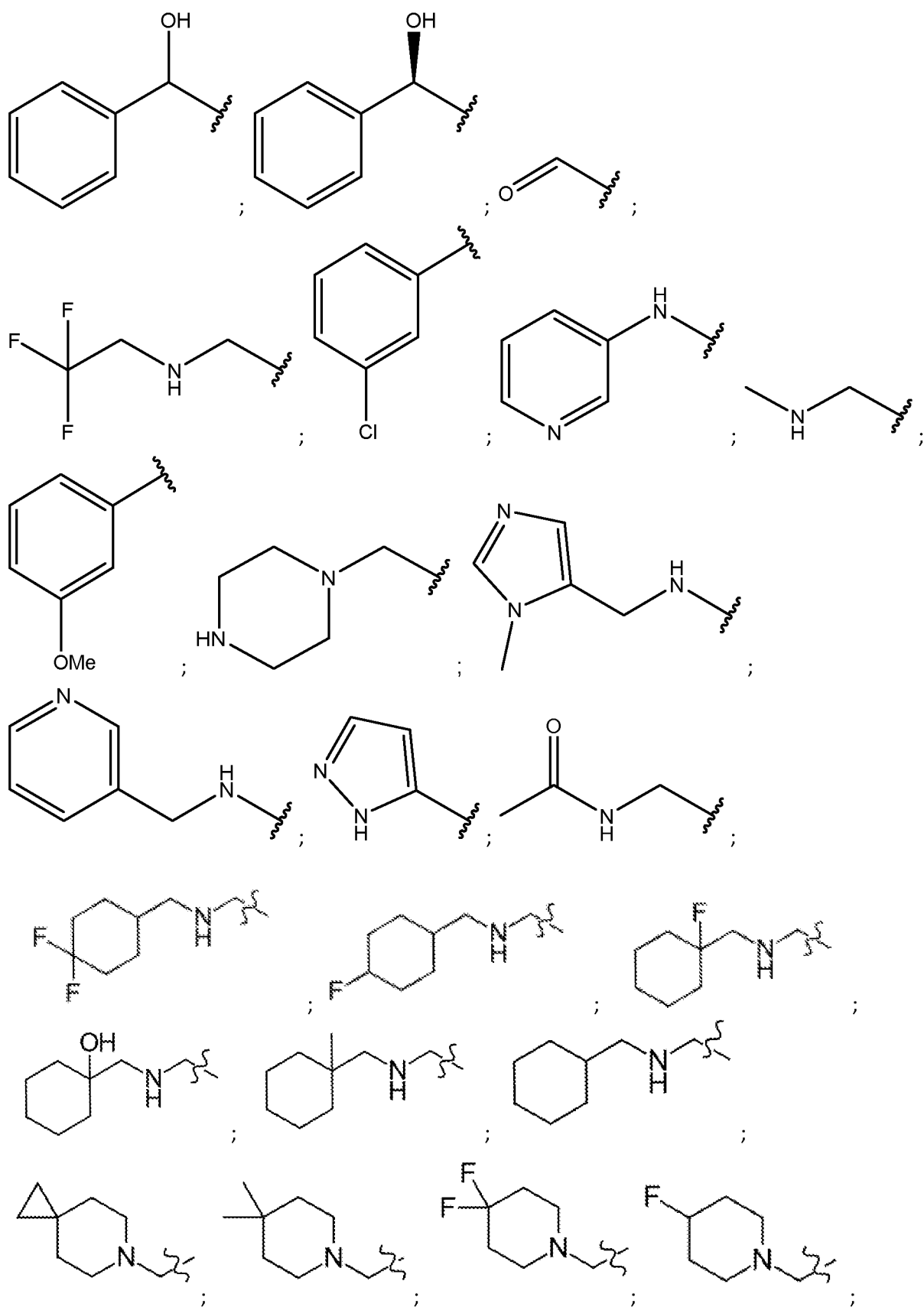
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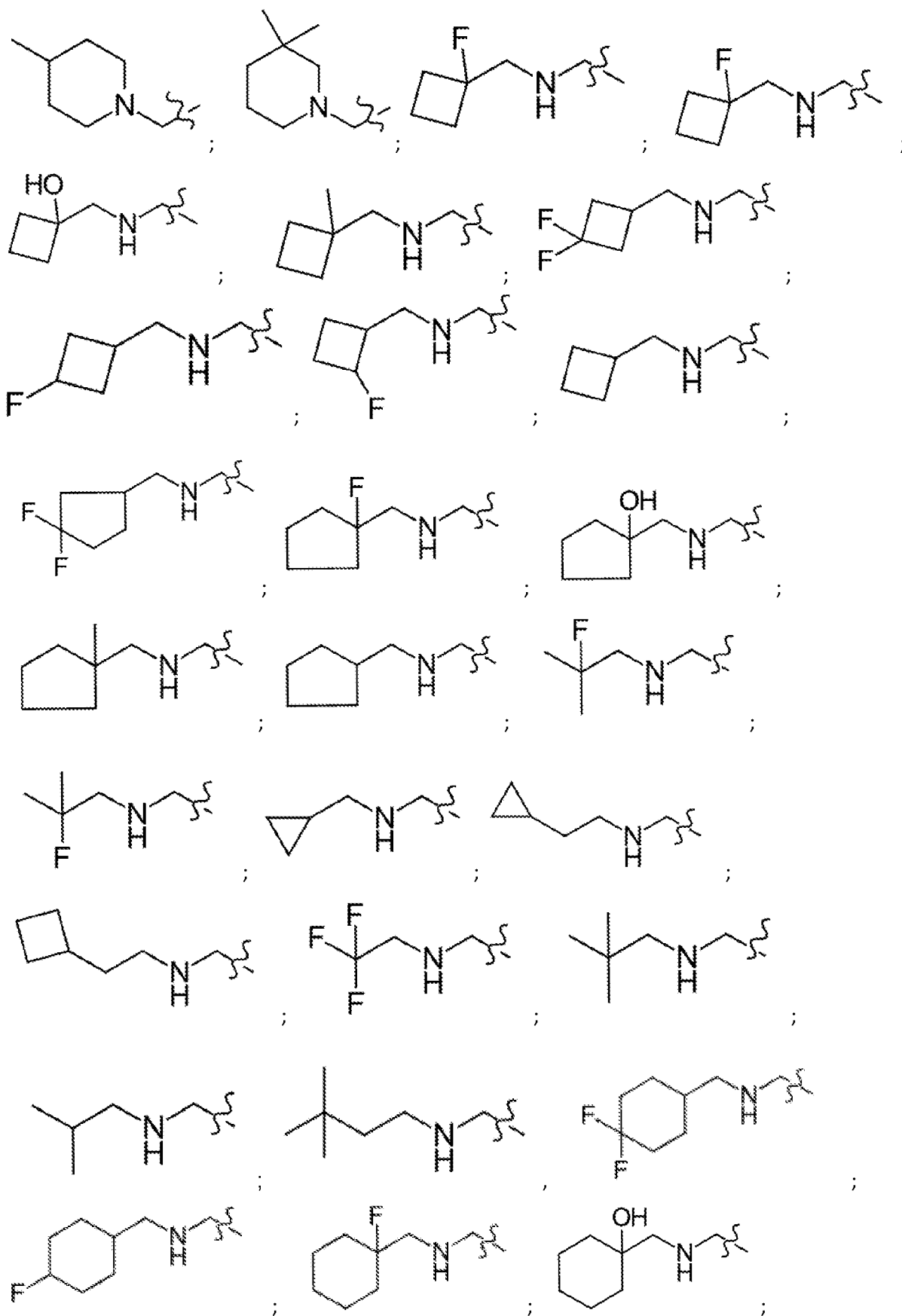


(15d) R_{1b} , R_{1d} and R_{1f} are selected from:  ;

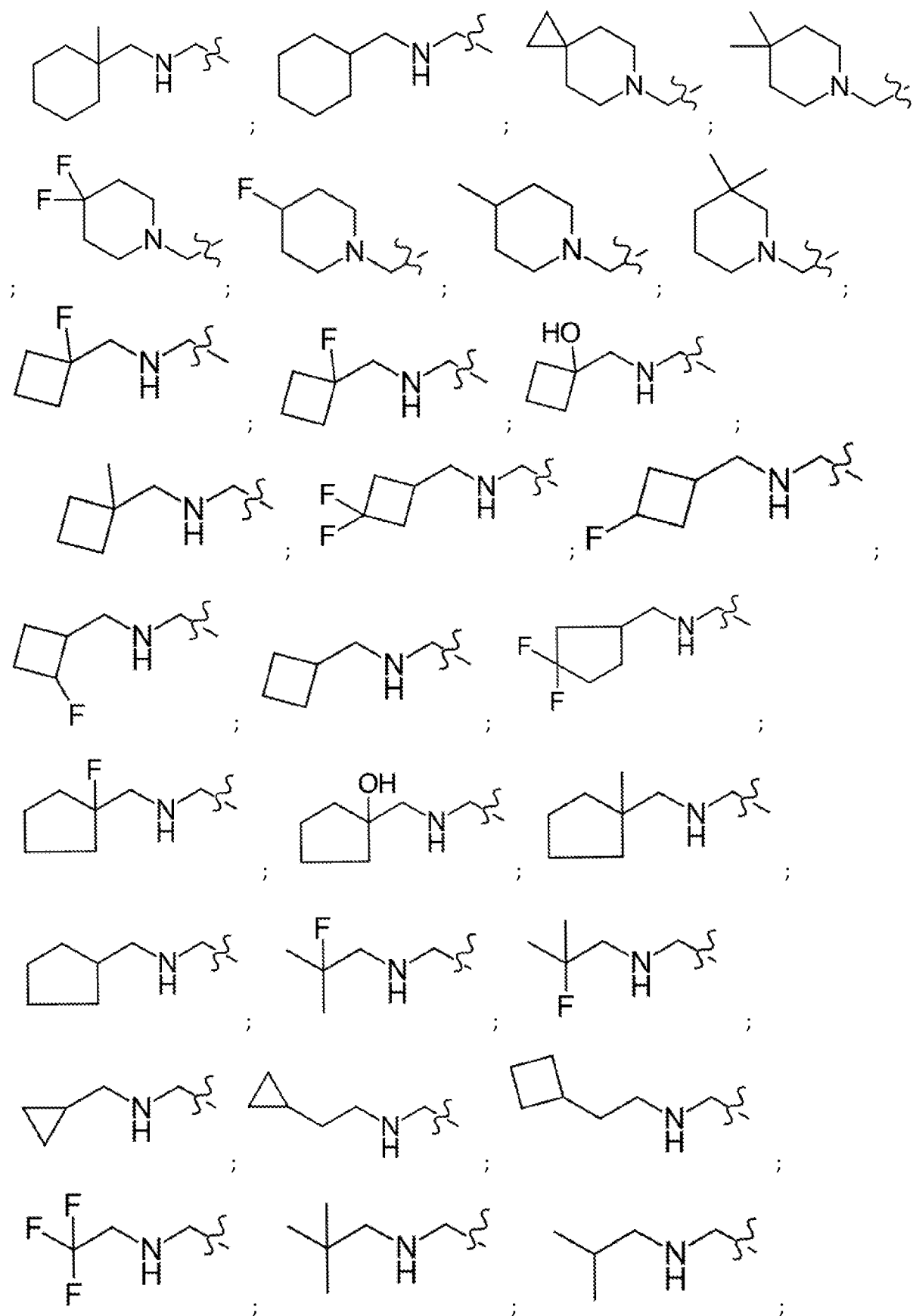
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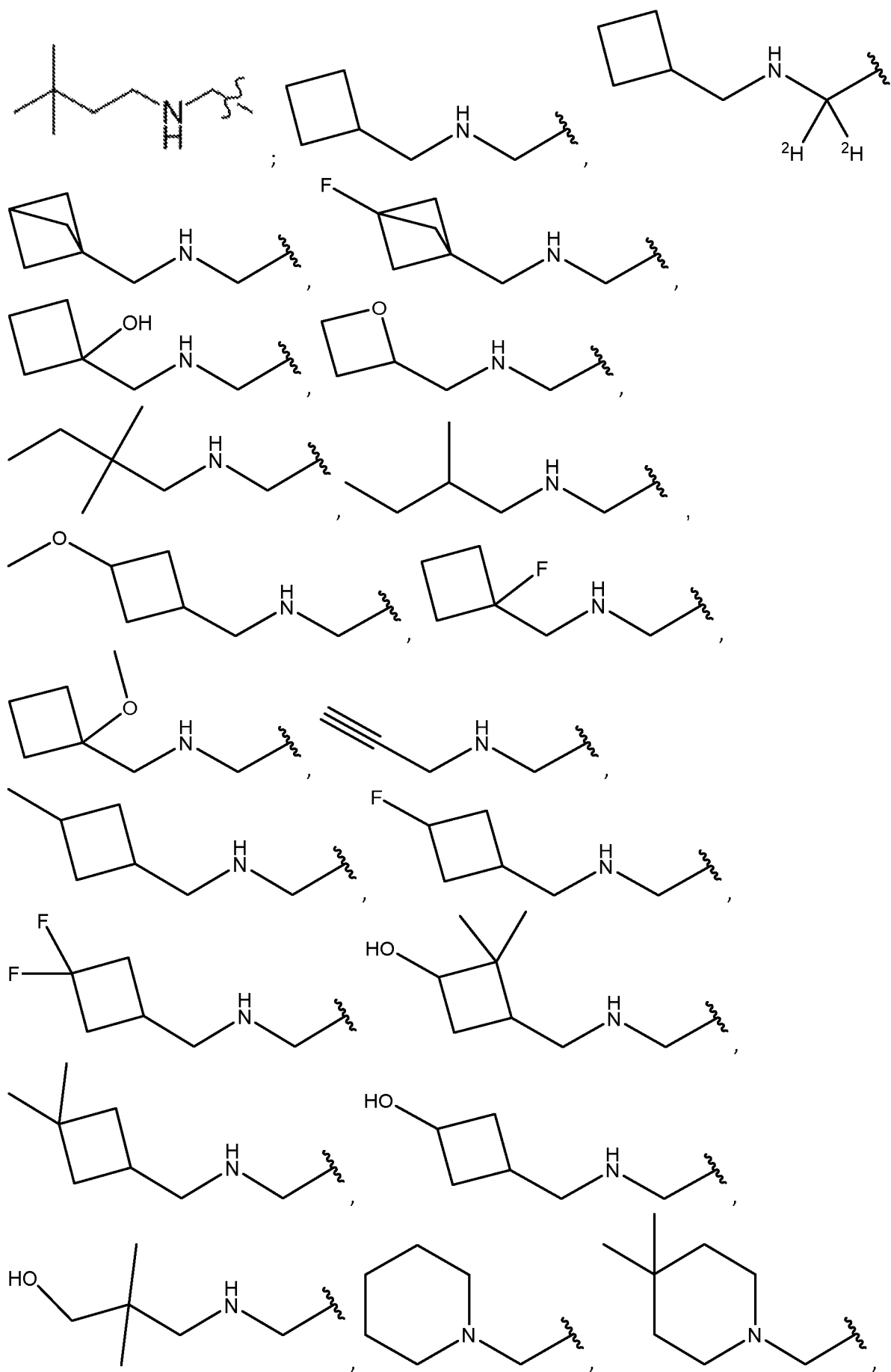






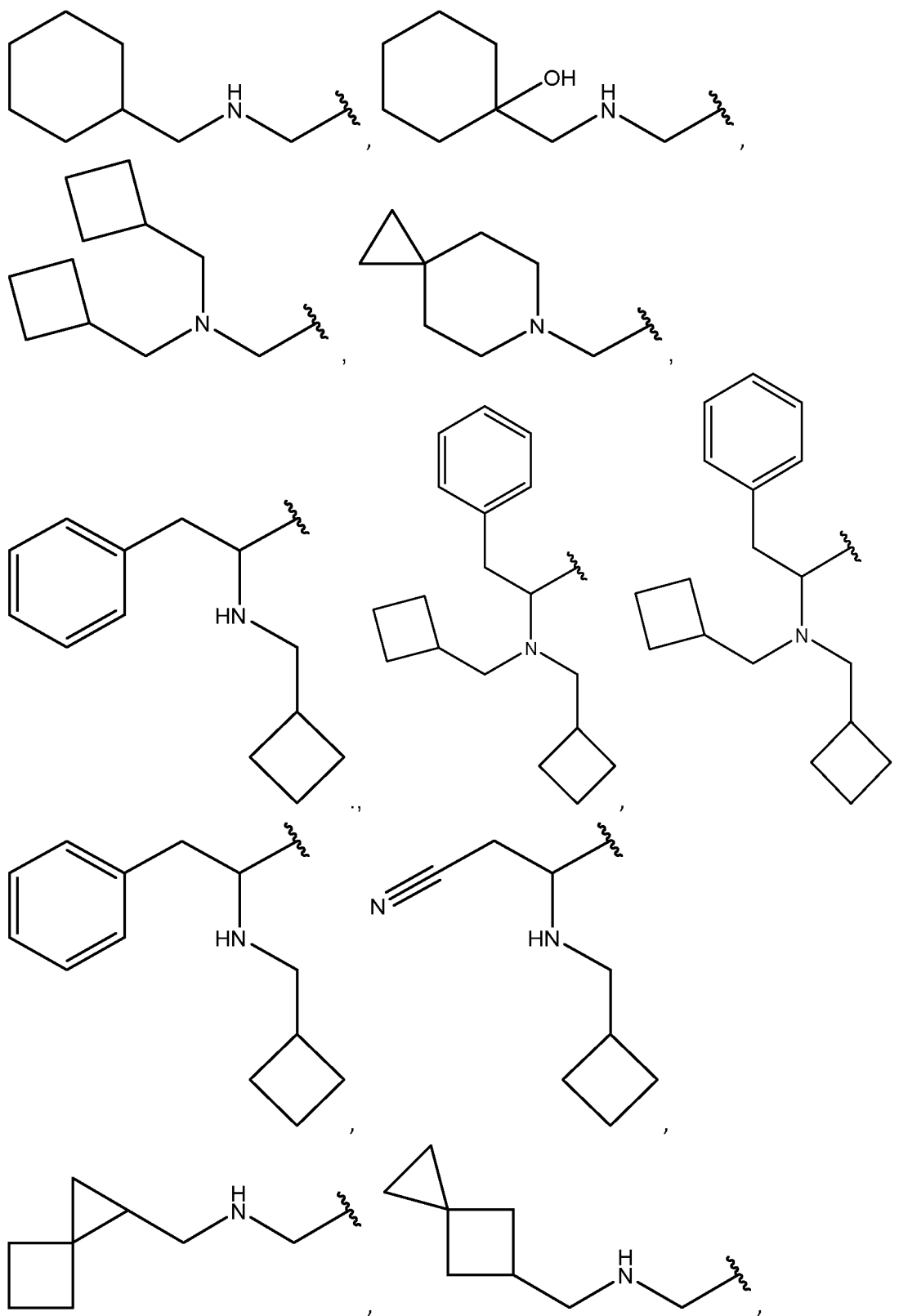
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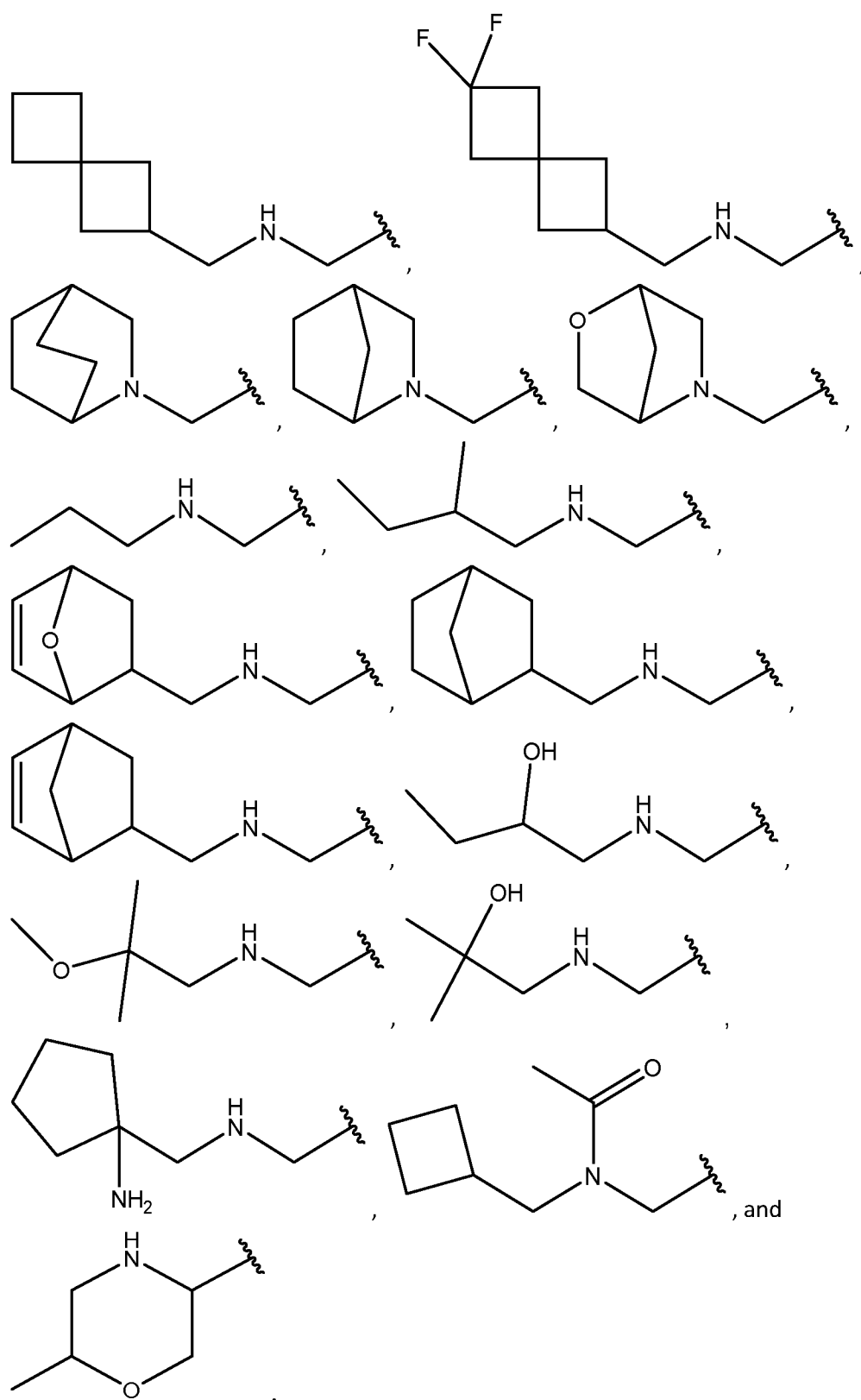


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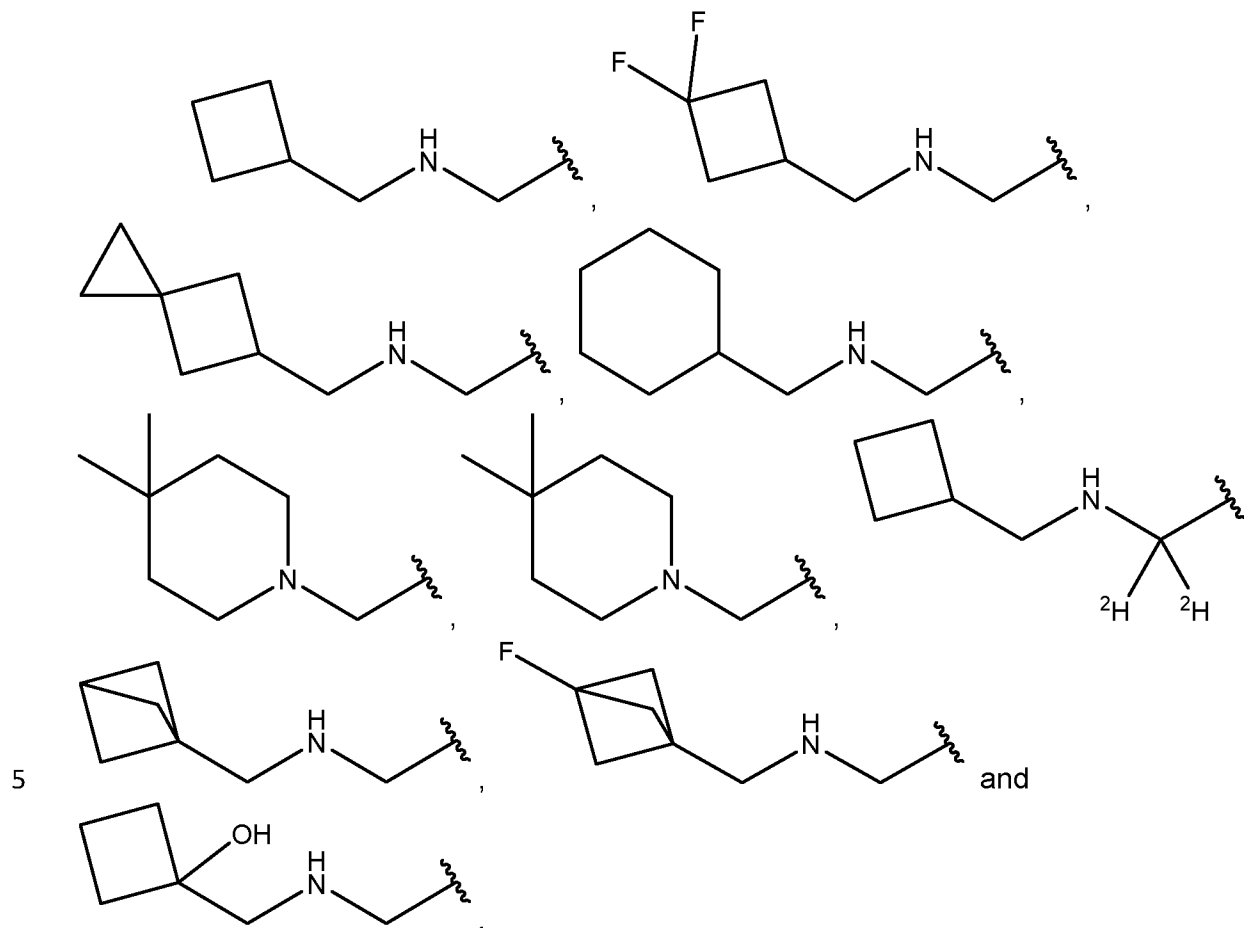


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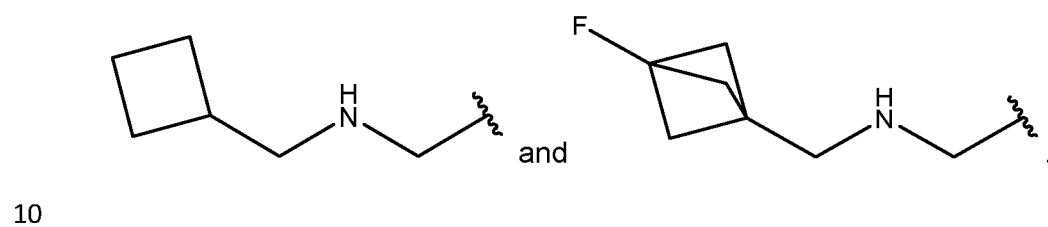


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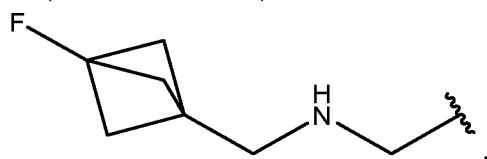
(15e) R_{1b} , R_{1d} and R_{1f} are selected from;



(15f) R_{1b} , R_{1d} and R_{1f} are selected from;



(15g) R_{1b} , R_{1d} and R_{1f} are;

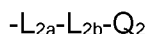


(16) $R_{1a'}$ is selected from hydrogen, halo and methyl;

(16a) $R_{1a'}$ is selected from hydrogen and methyl;

(17) $R_{1a'}$ is hydrogen;

(18) R_{2a} , R_{2b} and R_{2c} are selected from hydrogen, halo or a group of the formula:



wherein

L_{2a} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

L_{2b} is absent or selected from O, S, SO, SO_2 , $N(R_n)$, $C(O)$, $C(O)O$, $OC(O)$,

$C(O)N(R_n)$, $N(R_n)C(O)$, $N(R_n)C(O)N(R_o)$, $S(O)_2N(R_n)$, or $N(R_n)SO_2$, wherein R_n and R_o

are each independently selected from hydrogen or C_{1-2} alkyl; and

Q_2 is hydrogen, cyano, C_{1-6} alkyl, C_{3-6} cycloalkyl, aryl, heterocyclyl or heteroaryl, each of

which is optionally substituted by one or more substituents selected from halo,

trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, amino, carboxy, carbamoyl,

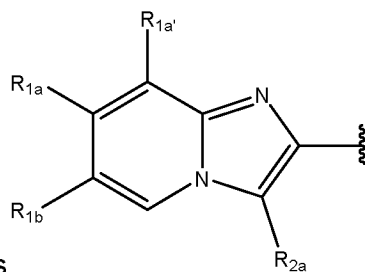
sulphamoyl, C_{1-4} alkyl, NR_pR_q , OR_p , $C(O)R_p$, $C(O)OR_p$, $OC(O)R_p$, $C(O)N(R_p)R_q$,

$N(R_r)C(O)R_p$, $S(O)_yR_p$ (where y is 0, 1 or 2), $SO_2N(R_p)R_q$, $N(R_r)SO_2R_p$ or $(CH_2)_zNR_pR_q$

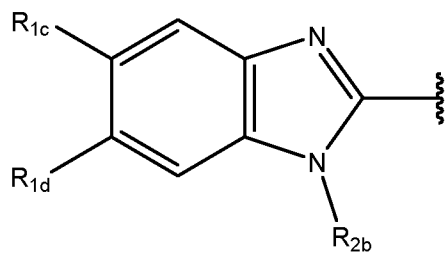
(where z is 1, 2 or 3), wherein R_p and R_q are each independently selected from

hydrogen or C_{1-4} alkyl;

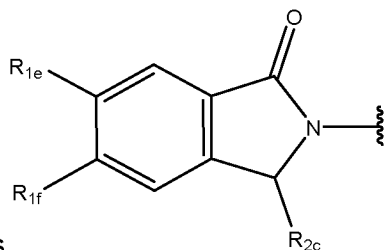
(19) R_{2a} , R_{2b} and R_{2c} are hydrogen;



(20) X is , wherein R_{1a} , R_{1b} , $R_{1a'}$ and R_{2a} are as herein defined;

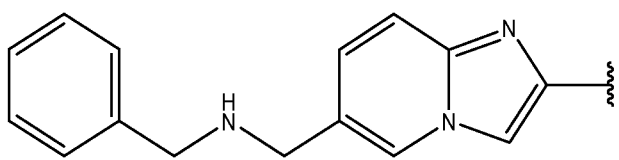


(21) X is , wherein R_{1c} , R_{1d} and R_{2b} are as herein defined;

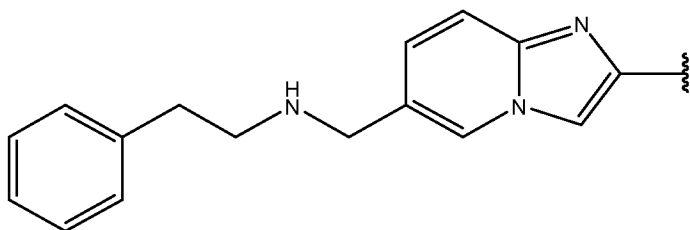


(22) X is , wherein R_{1e} , R_{1f} and R_{2c} are as herein defined;

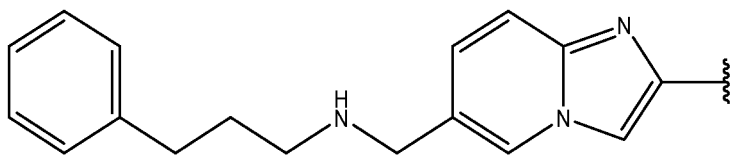
(23) X is selected from



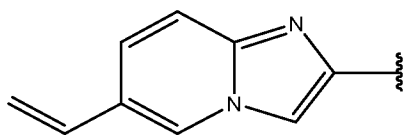
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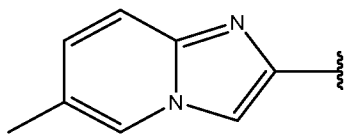
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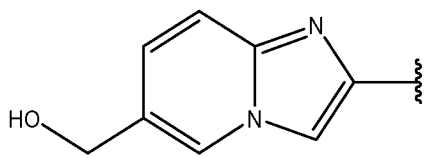
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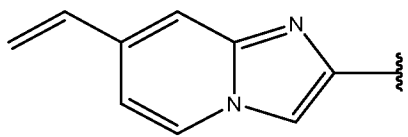
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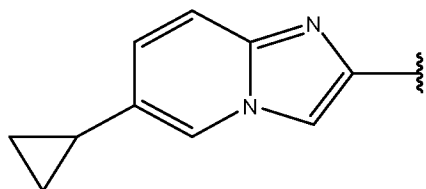
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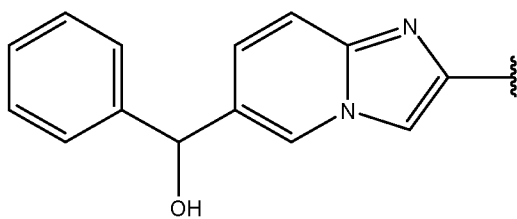
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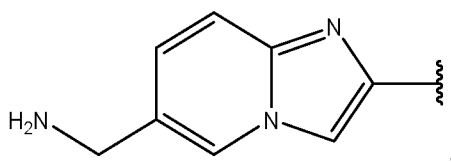
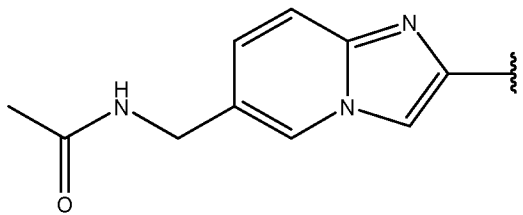
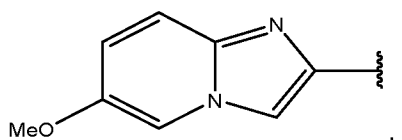
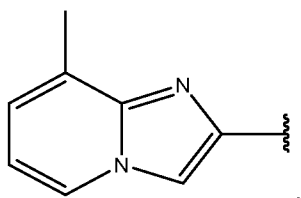
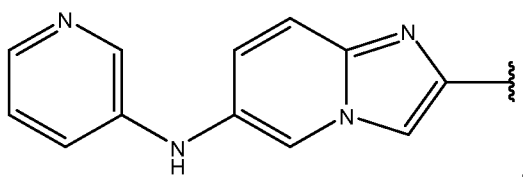
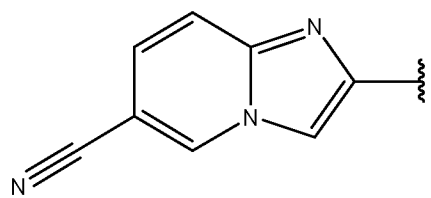
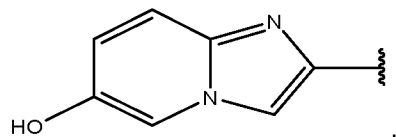
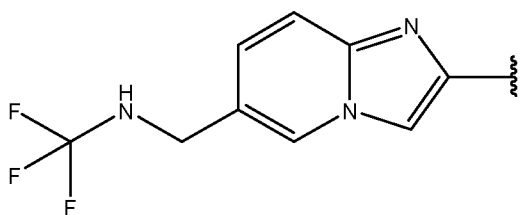
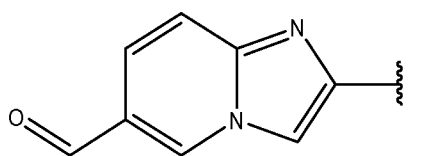
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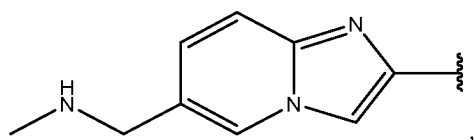
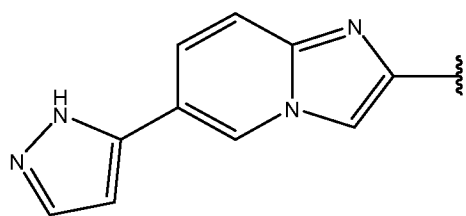
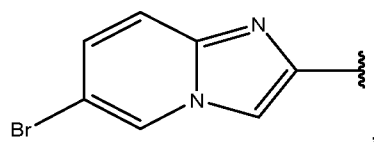
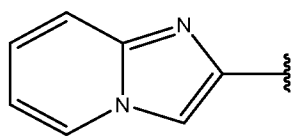
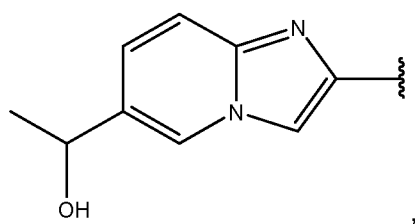
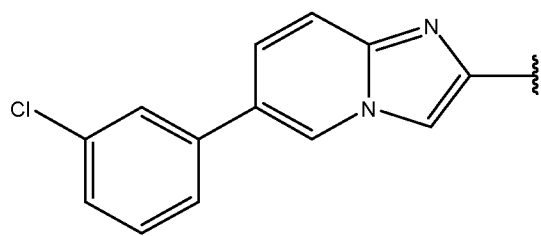
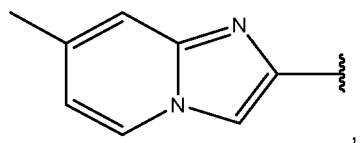
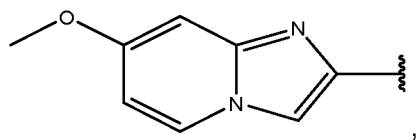
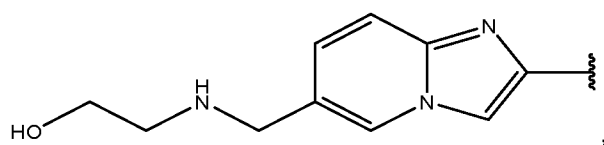
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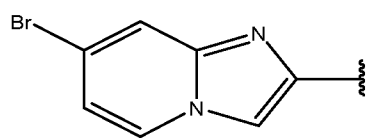
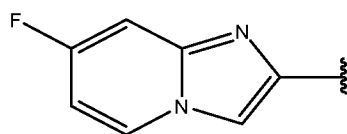
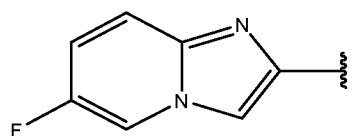
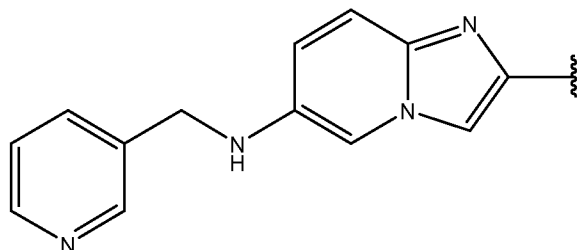
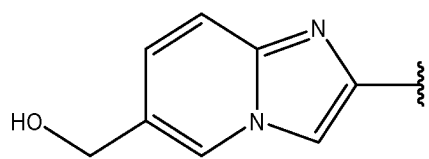
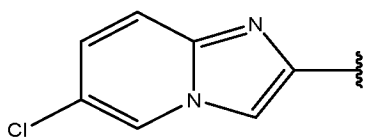
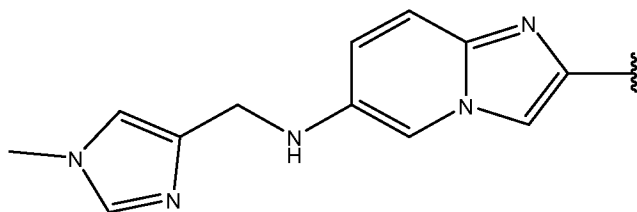
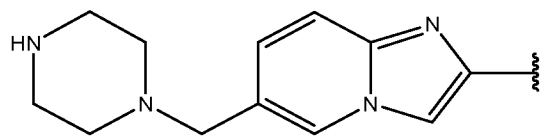
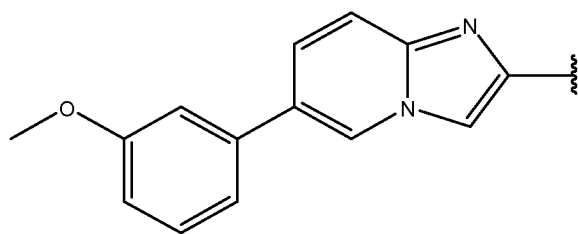
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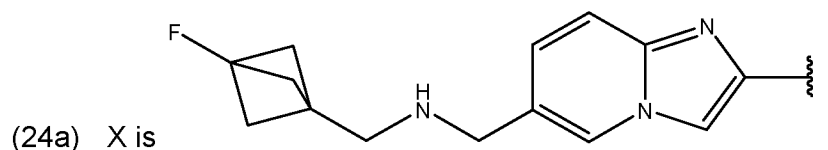
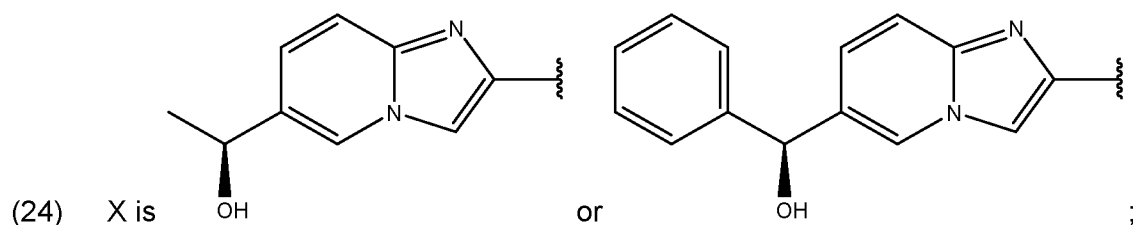


5





and



(25) R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} and R_{3o1} are independently selected from hydrogen, C_{1-6} alkyl, C_{3-4} cycloalkyl, hydroxy, and halo; and wherein C_{1-6} alkyl, or C_{3-4} cycloalkyl is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy; and R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} and R_{3o2} are hydrogen;

(25a) R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} and R_{3q1} are independently selected from hydrogen, C_{1-6} alkyl, C_{3-4} cycloalkyl, hydroxy, and halo; and wherein C_{1-6} alkyl, or C_{3-4} cycloalkyl is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy; and R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} , R_{3o2} , R_{3p2} and R_{3q2} are hydrogen;

(25b) R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} , R_{3q1} , R_{3r1} and R_{3s1} are independently selected from hydrogen, C_{1-6} alkyl, C_{3-4} cycloalkyl, hydroxy, and halo; and wherein C_{1-6} alkyl, or C_{3-4} cycloalkyl is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy; and R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} , R_{3o2} , R_{3p2} , R_{3q2} , R_{3r2} and R_{3s2} are hydrogen;

(26) R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} and R_{3o1} are independently selected from hydrogen and C_{1-6} alkyl; and wherein C_{1-6} alkyl is optionally substituted with one or more hydroxy substituents;

(26a) R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} and R_{3q1} are independently selected from hydrogen and C_{1-6} alkyl; and wherein C_{1-6} alkyl is optionally substituted with one or more hydroxy substituents;

- (26b) R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} , R_{3q1} , R_{3r1} and R_{3s1} are independently selected from hydrogen and C_{1-6} alkyl; and wherein C_{1-6} alkyl is optionally substituted with one or more hydroxy substituents;
- 5 (27) R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} and R_{3o1} are independently selected from hydrogen and methyl; and wherein methyl is optionally substituted with one or more hydroxy substituents;
- (27a) R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} and R_{3q1} are independently selected from hydrogen and methyl; and wherein methyl is optionally substituted with one or more hydroxy substituents;
- 10 (27b) R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} and R_{3q1} are independently selected from hydrogen and methyl; and wherein methyl is optionally substituted with one or more hydroxy substituents;
- (28) R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} and R_{3o1} are independently selected from hydrogen and methyl; and wherein methyl is substituted with a hydroxy substituent;
- 15 (28a) R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} and R_{3q1} are independently selected from hydrogen and methyl; and wherein methyl is substituted with a hydroxy substituent;
- (28b) R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} , R_{3q1} , R_{3r1} and R_{3s1} are independently selected from hydrogen and methyl; and wherein methyl is substituted with a hydroxy substituent;
- 20 (29) R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} and R_{3o2} are hydrogen;
- 25 (29a) R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} , R_{3o2} , R_{3p2} and R_{3q2} are hydrogen;
- (29b) R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} , R_{3o2} , R_{3p2} , R_{3q2} , R_{3r2} and R_{3s2} are hydrogen;
- 30 (30) R_{3a1} and R_{3a2} , R_{3b1} and R_{3b2} , R_{3c1} and R_{3c2} , R_{3d1} and R_{3d2} , R_{3e1} and R_{3e2} , R_{3f1} and R_{3f2} , R_{3g1} and R_{3g2} , R_{3h1} and R_{3h2} , R_{3i1} and R_{3i2} , R_{3j1} and R_{3j2} , R_{3k1} and R_{3k2} , R_{3l1} and R_{3l2} , R_{3m1} and R_{3m2} , R_{3n1} and R_{3n2} , or R_{3o1} and R_{3o2} are hydrogen;
- (30a) R_{3a1} and R_{3a2} , R_{3b1} and R_{3b2} , R_{3c1} and R_{3c2} , R_{3d1} and R_{3d2} , R_{3e1} and R_{3e2} , R_{3f1} and R_{3f2} , R_{3g1} and R_{3g2} , R_{3h1} and R_{3h2} , R_{3i1} and R_{3i2} , R_{3j1} and R_{3j2} , R_{3k1} and R_{3k2} , R_{3l1} and R_{3l2} , R_{3m1} and R_{3m2} , R_{3n1} and R_{3n2} , R_{3o1} and R_{3o2} , R_{3p1} and R_{3p2} , R_{3q1} and R_{3q2} are hydrogen.
- 35

- (30b) R_{3a1} and R_{3a2} , R_{3b1} and R_{3b2} , R_{3c1} and R_{3c2} , R_{3d1} and R_{3d2} , R_{3e1} and R_{3e2} , R_{3f1} and R_{3f2} , R_{3g1} and R_{3g2} , R_{3h1} and R_{3h2} , R_{3i1} and R_{3i2} , R_{3j1} and R_{3j2} , R_{3k1} and R_{3k2} , R_{3l1} and R_{3l2} , R_{3m1} and R_{3m2} , R_{3n1} and R_{3n2} , R_{3o1} and R_{3o2} , R_{3p1} and R_{3p2} , R_{3q1} and R_{3q2} , R_{3r1} and R_{3r2} , and R_{3s1} and R_{3s2} are hydrogen.

5

- (31) R_{3a1} and R_{3a2} , R_{3b1} and R_{3b2} , R_{3c1} and R_{3c2} , R_{3d1} and R_{3d2} , R_{3e1} and R_{3e2} , R_{3f1} and R_{3f2} , R_{3g1} and R_{3g2} , R_{3h1} and R_{3h2} , R_{3i1} and R_{3i2} , R_{3j1} and R_{3j2} , R_{3k1} and R_{3k2} , R_{3l1} and R_{3l2} , R_{3m1} and R_{3m2} , R_{3n1} and R_{3n2} , R_{3o1} and R_{3o2} may be linked to form a spiro-fused C_{3-4} cycloalkyl which is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

10

- (31a) R_{3a1} and R_{3a2} , R_{3b1} and R_{3b2} , R_{3c1} and R_{3c2} , R_{3d1} and R_{3d2} , R_{3e1} and R_{3e2} , R_{3f1} and R_{3f2} , R_{3g1} and R_{3g2} , R_{3h1} and R_{3h2} , R_{3i1} and R_{3i2} , R_{3j1} and R_{3j2} , R_{3k1} and R_{3k2} , R_{3l1} and R_{3l2} , R_{3m1} and R_{3m2} , R_{3n1} and R_{3n2} , R_{3o1} and R_{3o2} , R_{3p1} and R_{3p2} , R_{3q1} and R_{3q2} may be linked to form a spiro-fused C_{3-4} cycloalkyl which is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

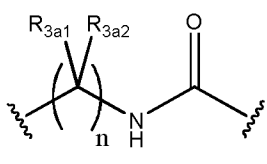
15

- (31b) R_{3a1} and R_{3a2} , R_{3b1} and R_{3b2} , R_{3c1} and R_{3c2} , R_{3d1} and R_{3d2} , R_{3e1} and R_{3e2} , R_{3f1} and R_{3f2} , R_{3g1} and R_{3g2} , R_{3h1} and R_{3h2} , R_{3i1} and R_{3i2} , R_{3j1} and R_{3j2} , R_{3k1} and R_{3k2} , R_{3l1} and R_{3l2} , R_{3m1} and R_{3m2} , R_{3n1} and R_{3n2} , R_{3o1} and R_{3o2} , R_{3p1} and R_{3p2} , and R_{3q1} and R_{3q2} , may be linked to form a spiro-fused C_{3-4} cycloalkyl which is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

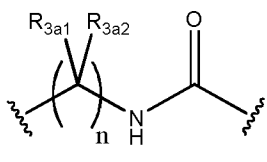
20

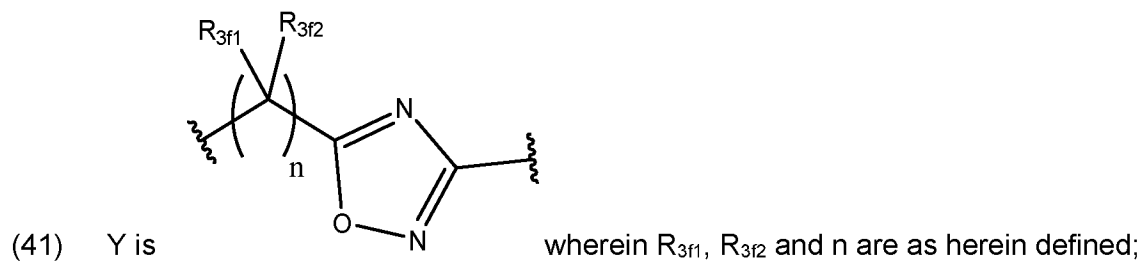
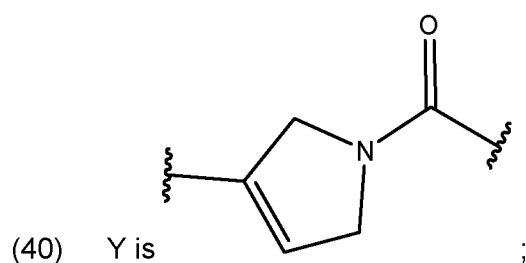
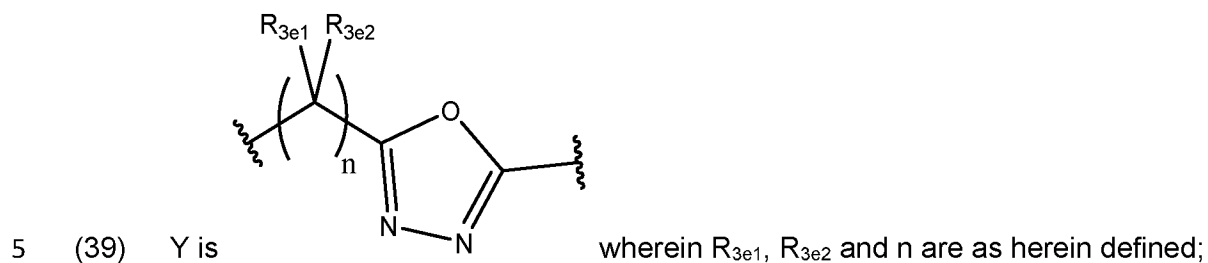
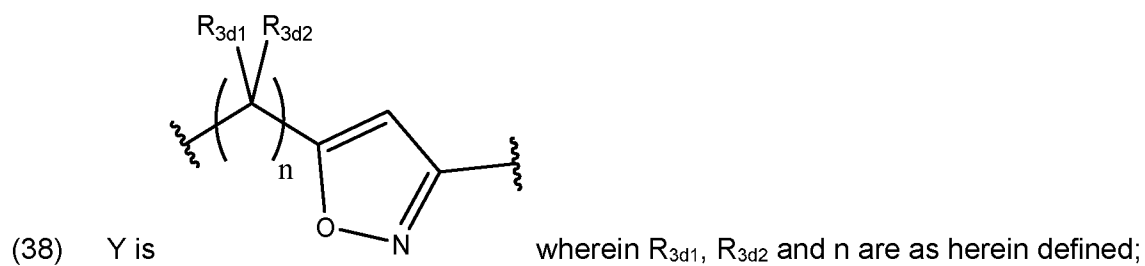
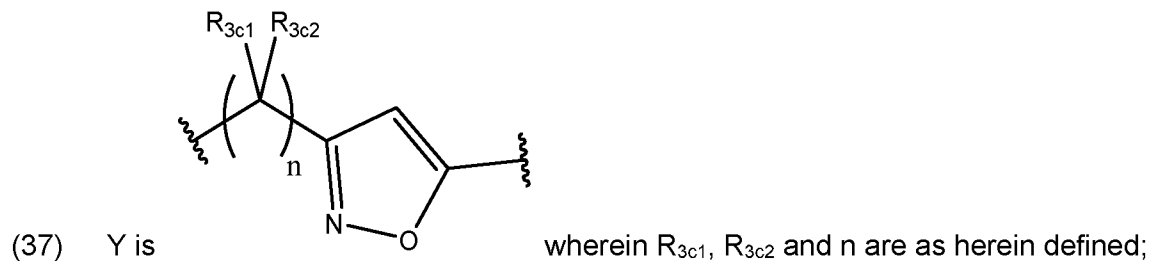
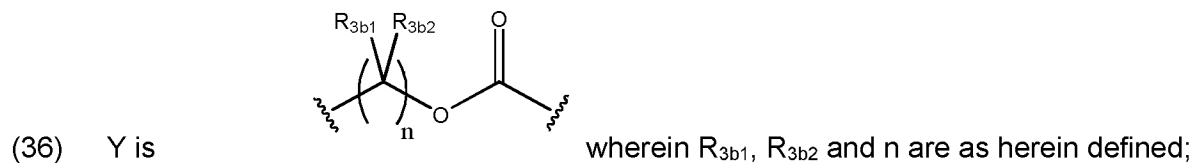
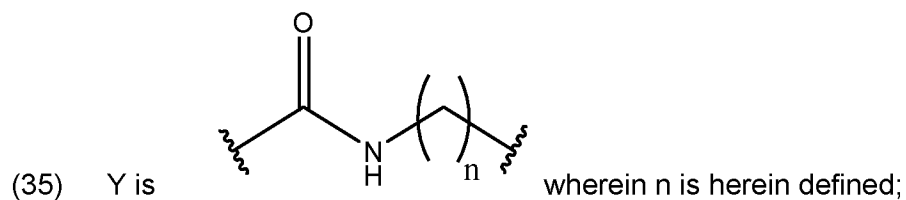
- (32) n is 0, 1 or 2;

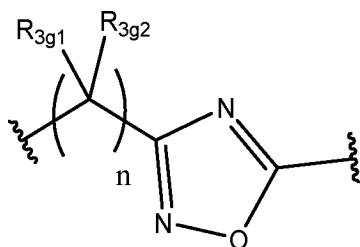
- (33) n is 1;

- (34) Y is  wherein R_{3a1} , R_{3a2} and n are as herein defined;

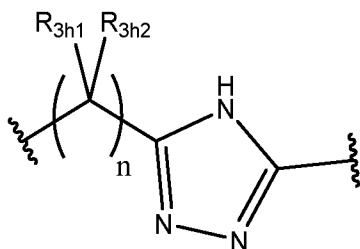
25

- (34a) Y is  wherein n is 1, and R_{3a1} , R_{3a2} are as herein defined;

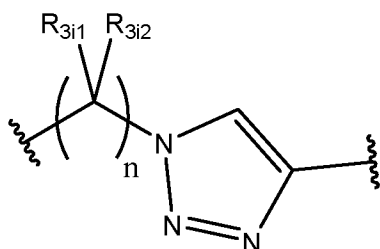




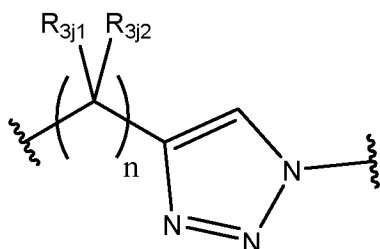
(42) Y is wherein R_{3g1} , R_{3g2} and n are as herein defined;



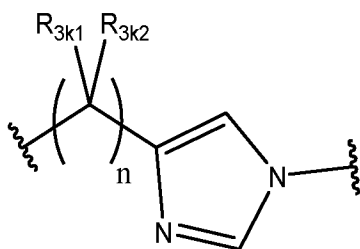
(43) Y is wherein R_{3h1} , R_{3h2} and n are as herein defined



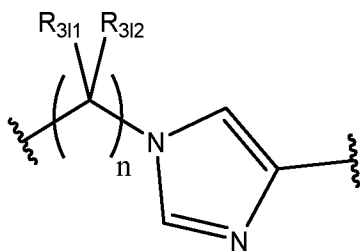
(44) Y is wherein R_{3i1} , R_{3i2} and n are as herein defined;



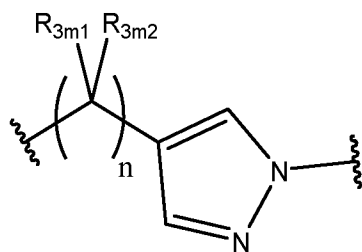
(45) Y is wherein R_{3j1} , R_{3j2} and n are as herein defined;



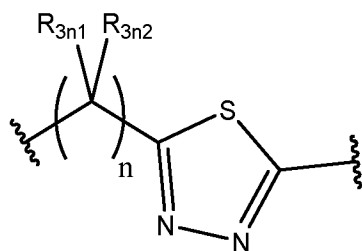
5 (46) Y is wherein R_{3k1} , R_{3k2} and n are as herein defined;



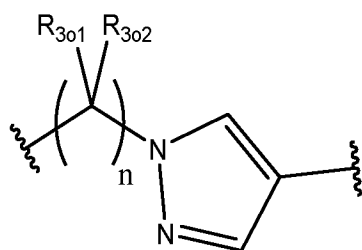
(47) Y is wherein R_{3l1} , R_{3l2} and n are as herein defined;



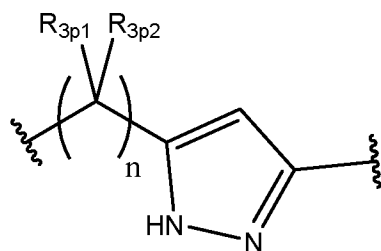
(48) Y is wherein R_{3m1} , R_{3m2} and n are as herein defined;



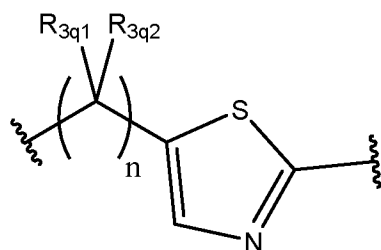
(49) Y is wherein R_{3n1} , R_{3n2} and n are as herein defined;



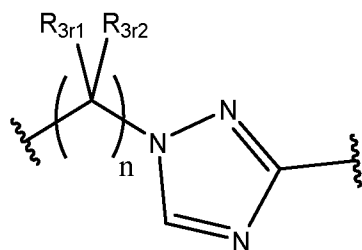
(50) Y is wherein R_{3o1} , R_{3o2} and n are as herein defined;



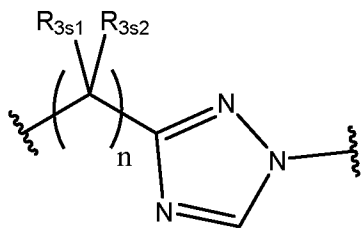
(50a) Y is wherein R_{3p1} , R_{3p2} and n are as herein defined;



5 (50b) Y is wherein R_{3q1} , R_{3q2} and n are as herein defined;



(50c) Y is wherein R_{3r1} , R_{3r2} and n are as herein defined;

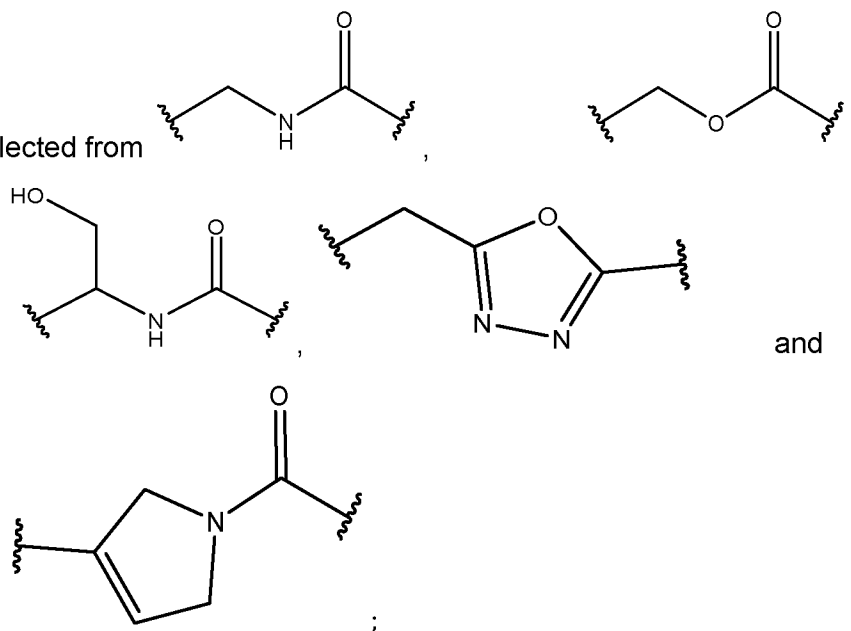


(50d) Y is

wherein R_{3s1} , R_{3s2} and n are as herein defined;

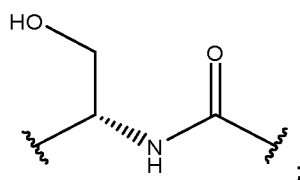
5

(51) Y is selected from

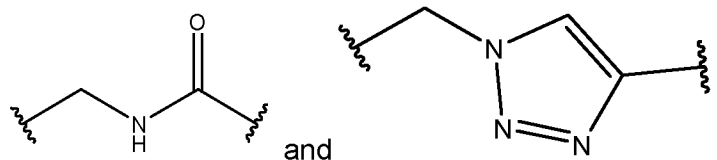


and

(52) Y is



10 (52a) Y is selected from



and

(53) R_4 is selected from hydrogen and methyl;(54) R_4 is hydrogen;15 (55) R_5 is selected from hydrogen and halo;(56) R_5 is hydrogen;

- (57) R_6 is selected from hydrogen, halo and methyl;
- (58) R_6 is hydrogen;
- (59) R_4 , R_5 and R_6 are hydrogen;
- (60) A_1 is selected from CR_{12} and N, wherein R_{12} is selected from hydrogen, halo, cyano
5 and C_{1-4} alkyl;
- (61) A_1 is CH;
- (62) A_2 is selected from CR_{13} and N, wherein R_{13} is selected from hydrogen, halo, cyano and methyl;
- (63) Suitably A_2 is CH;
- 10 (64) A_1 is CH and A_2 is CH;
- (65) R_7 is selected from hydrogen, halo and methyl;
- (65a) R_7 is selected from hydrogen and methyl;
- (66) R_7 is hydrogen;
- (67) R_8 is selected from hydrogen, halo and methyl;
- 15 (68) R_8 is hydrogen;
- (69) R_7 and R_8 are hydrogen;
- (70) A_3 is selected from CR_{14} and N, wherein R_{14} is selected from hydrogen, halo, cyano and C_{1-4} alkyl;
- (71) A_3 is CR_{14} , wherein R_{14} is selected from hydrogen and chloro;
- 20 (72) A_3 is CH;
- (73) A_4 is selected from CR_{15} and N, wherein R_{15} is selected from hydrogen, methoxy and methyl;
- (74) A_4 is CH;
- (75) A_3 is CH and A_4 is CH;
- 25 (76) A_5 is selected from CR_{16} and N, wherein R_{16} is selected from hydrogen, halo, cyano and C_{1-4} alkyl;
- (76a) A_5 is selected from CR_{16} and N, wherein R_{16} is selected from hydrogen, halo, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy and C_{3-4} cycloalkoxy;
- (76b) A_5 is selected from CR_{16} and N, wherein R_{16} is selected from hydrogen, halo, cyano,
30 C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl and C_{1-4} haloalkoxy;
- (76c) A_5 is selected from CR_{16} and N, wherein R_{16} is selected from hydrogen, halo, cyano and C_{1-4} alkoxy;
- (77) A_5 is CH;
- (78) A_6 is selected from CR_{17} and N, wherein R_{17} is selected from hydrogen, halo, cyano,
35 C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl and a 5- or 6-membered heteroaryl;
- (78a) A_6 is selected from CR_{17} and N, wherein R_{17} is selected from hydrogen, halo, cyano, C_{1-5} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{2-4} alkenyl, C_{2-4} alkynyl, phenyl,

a 5- or 6-membered or heteroaryl, C₃₋₆cycloalkyl, -O-C₃₋₆cycloalkyl, heterocyclyl, -O-heterocyclyl (carbon-linked), -(OCH₂CH₂)_m-OCH₃ wherein m is an integer from 1 to 6, NR_qR_r,

wherein R_q and R_r are each independently hydrogen, C₁₋₅ alkyl, C₃₋₆cycloalkyl, a 3- to 6- membered carbon-linked heterocyclyl, wherein C₁₋₅ alkyl, C₃₋₆cycloalkyl, a 3- to 6- membered carbon-linked heterocyclyl may be optionally substituted by one or more substituents selected from C₁₋₂alkyl, cyano, C₁₋₂haloalkyl, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, NR_{1ea}R_{1fa} or -S(O)₀₋₂R_{1ea}R_{1fa}, wherein R_{1ea} and R_{1fa} are H or C₁₋₂alkyl;

or R_q and R_r are linked together such that, together with the nitrogen atom to which they are attached, they form a 3- to 6-membered heterocyclic ring which may be optionally substituted by one or more substituents selected from C₁₋₂alkyl, cyano, C₁₋₂haloalkyl, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy;

wherein any C₁₋₅alkyl, C₁₋₄ alkoxy, C₂₋₄alkenyl, C₂₋₄alkynyl, phenyl, 5- or 6-membered or heteroaryl, C₃₋₆cycloalkyl, -O-C₃₋₆cycloalkyl, heterocyclyl or -O-heterocyclyl (carbon-linked) is optionally further substituted by one or more substituents selected from C₁₋₂alkyl, cyano, C₁₋₂haloalkyl, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, NR_{1ea}R_{1fa} or -S(O)₀₋₂R_{1ea}R_{1fa}, wherein R_{1ea} and R_{1fa} are H or C₁₋₂alkyl.

(78b) A₆ is selected from CR₁₇ and N, wherein R₁₇ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, C₂₋₄ alkenyl, C₂₋₄ alkynyl, phenyl a 5- or 6-membered or heteroaryl, C₃₋₆cycloalkyl, -O-C₃₋₆cycloalkyl, heterocyclyl, -O-heterocyclyl (carbon-linked), -(OCH₂CH₂)_m-OCH₃ wherein m is an integer from 1 to 6, NR_qR_r, wherein R_q and R_r are each independently hydrogen, C₁₋₂ alkyl or R_q and R_r are linked together such that, together with the nitrogen atom to which they are attached, they form a 3- to 6-membered heterocyclic ring;

wherein any C₁₋ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, phenyl, 5- or 6-membered or heteroaryl, C₃₋₆cycloalkyl, -O-C₃₋₆cycloalkyl, heterocyclyl or -O-heterocyclyl (carbon-linked) is optionally further substituted by one or more substituents selected from C₁₋₂alkyl, cyano, C₁₋₂haloalkyl, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, NR_{1ea}R_{1fa} or -S(O)₀₋₂R_{1ea}R_{1fa}, wherein R_{1ea} and R_{1fa} are H or C₁₋₂alkyl.

(78c) A₆ is selected from CR₁₇ and N, wherein R₁₇ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, C₂₋₄ alkenyl, C₂₋₄ alkynyl, phenyl, a 5- or 6-membered heteroaryl, C₃₋₆cycloalkyl, -O-C₃₋₆cycloalkyl, heterocyclyl, -O-heterocyclyl (carbon-linked), -(OCH₂CH₂)_m-OCH₃ wherein m is 1, 2 or 3, NR_qR_r, wherein R_q and R_r are each independently hydrogen, C₁₋₄ alkyl; or R_q and R_r are

linked together such that, together with the nitrogen atom to which they are attached, they form a 3- to 6-membered heterocyclic ring;

wherein any C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, phenyl, 5- or 6-membered or heteroaryl, C₃₋₆cycloalkyl, -O-C₃₋₆cycloalkyl, heterocyclyl or -O-heterocyclyl (carbon-linked) is
 5 optionally further substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo and C₁₋₂haloalkoxy.

(78d) A₆ is selected from CR₁₇ and N, wherein R₁₇ is selected from selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, C₂₋₄ alkenyl, C₂₋₄
 10 alkynyl, C₃₋₆cycloalkyl, -O-C₃₋₄cycloalkyl, heterocyclyl, -(OCH₂CH₂)_m-OCH₃ wherein m is 1, 2 or 3, NR_qR_r, wherein R_q and R_r are each independently hydrogen or C₁₋₂alkyl;

wherein any C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₃₋₆cycloalkyl, -O-C₃₋₄cycloalkyl, heterocyclyl, system is optionally further substituted by one or more substituents
 15 selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo and C₁₋₂haloalkoxy.

(79) A₆ is CR₁₇, wherein R₁₇ is selected from hydrogen, halo, C₂₋₄ alkynyl and 5- or 6-membered heteroaryl;

(79a) A₆ is CR₁₇, wherein R₁₇ is selected from hydrogen, halo, C₁₋₄alkyl, C₁₋₄ alkoxy, C₁₋₄
 20 haloalkoxy, C₂₋₄ alkynyl and 5- or 6-membered heteroaryl;

(79b) A₆ is CR₁₇, wherein R₁₇ is selected from hydrogen, halo, C₁₋₄ alkoxy or C₁₋₄ haloalkoxy;

(80) A₆ is CR₁₇, wherein R₁₇ is selected from hydrogen, bromo, ethynyl, and pyrazolyl;

25 (80a) A₆ is CR₁₇, wherein R₁₇ is selected from hydrogen, methoxy, bromo, ethynyl, and pyrazolyl;

(81) A₅ is CH and A₆ is CR₁₇, wherein R₁₇ is selected from hydrogen, halo, C₂₋₄ alkynyl and 5- or 6-membered heteroaryl;

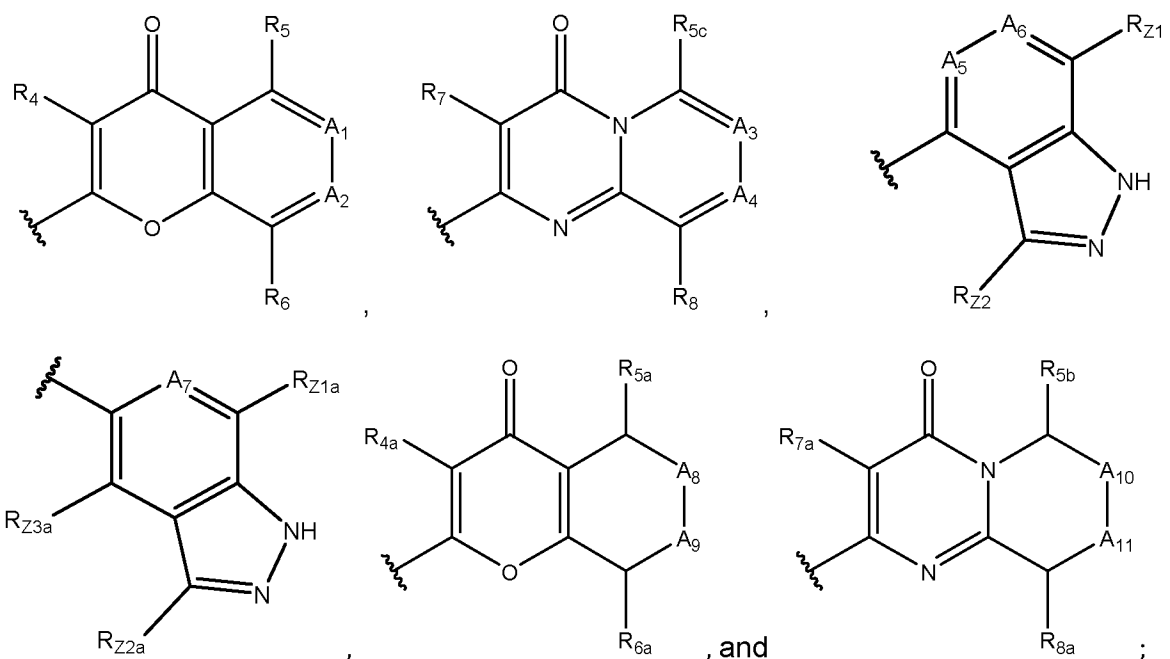
30 (82) R₉, R₁₀ and R₁₁ are independently selected from hydrogen, NH₂, halo, cyano, and C₁₋₆alkyl;

(82a) R₉, R_{9a}, R₁₀ and R₁₁ are independently selected from hydrogen, NH₂, halo, cyano, and C₁₋₆ alkyl

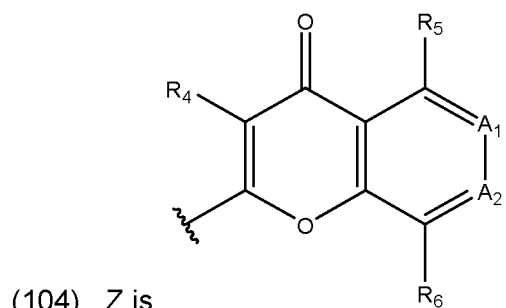
(82c) R₉, R₁₀ and R₁₁ are independently selected from hydrogen, NH₂, halo, cyano, and C₁₋₆
 35 alkyl; and R_{9a} is hydrogen;

- (83) R_9 and R_{10} may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system or R_{10} and R_{11} may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system;
- 5 (83a) R_9 and R_{10} may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system or R_{10} and R_{11} may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system; wherein either of the fused 5- or 6-membered saturated or unsaturated ring system may be optionally substituted by one or more substituents selected from C_{1-2} alkyl, cyano, C_{1-2} haloalkyl, hydroxy, C_{1-2} alkoxy, halo, C_{1-2} haloalkoxy, $NR_{1ia}R_{1ja}$ or $-S(O)_{0-2}R_{1ia}R_{1ja}$, wherein R_{1ia} and R_{1ja} are H or C_{1-2} alkyl;
- 10 (84) A_7 is selected from CR_{18} and N, wherein R_{18} is selected from hydrogen, halo, cyano, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl and a 5- or 6-membered heteroaryl;
- (85a) A_7 is selected from CR_{18} and N, wherein R_{18} is selected from hydrogen, halo, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy and C_{3-4} cycloalkoxy;
- 15 (85b) A_7 is selected from CR_{18} and N, wherein R_{18} is selected from hydrogen, halo, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl and C_{1-4} haloalkoxy;
- (85c) A_7 is selected from CR_{18} and N, wherein R_{18} is selected from hydrogen, halo, cyano and C_{1-4} alkoxy;
- 20 (85) A_7 is CH;
- (86) R_{4a} is selected from hydrogen, halo and methyl;
- (86a) R_{4a} is selected from hydrogen and methyl;
- (87) R_{4a} is hydrogen;
- 25 (88) R_{5a} is selected from hydrogen and halo;
- (89) R_{5a} is hydrogen;
- (90) R_{6a} is selected from hydrogen, halo and methyl;
- (91) R_{6a} is hydrogen;
- (92) R_{4a} , R_{5a} and R_{6a} are hydrogen;
- 30 (93) A_8 is selected from $CR_{19}R_{20}$ and NR_{21} , wherein R_{19} and R_{20} are selected from hydrogen, halo, cyano and C_{1-4} alkyl, and R_{21} is hydrogen;
- (94) A_9 is selected from $CR_{22}R_{23}$ and NR_{24} , wherein R_{22} and R_{23} are selected from hydrogen, halo, cyano and methyl, and R_{24} is hydrogen;
- (95) R_{5b} is selected from hydrogen and halo;
- 35 (96) R_{5b} is hydrogen;
- (96a) R_{5c} is selected from hydrogen and halo;

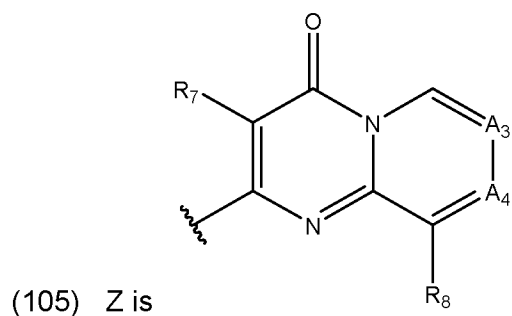
- (96b) R_{5c} is hydrogen;
- (97) R_{7a} is selected from hydrogen, halo and methyl;
- (97a) R_{7a} is selected from hydrogen and methyl;
- 5 (98) R_{7a} is hydrogen;
- (99) R_{8a} is selected from hydrogen, halo and methyl;
- (100) R_{8a} is hydrogen;
- (101) R_{5b}, R_{7a} and R_{8a} are hydrogen;
- (102) A₁₀ is selected from CR₂₅R₂₆ and NR₂₇, wherein R₂₅ and R₂₆ are selected from
 10 hydrogen, halo, cyano and C₁₋₄ alkyl, and R₂₇ is hydrogen;
- (103) A₁₁ is selected from CR₂₈R₂₉ and NR₃₀, wherein R₂₈ and R₂₉ are selected from
 hydrogen, methoxy and methyl, and R₃₀ is hydrogen;
- (104a) R_{Z1} and R_{Z1a} are selected from hydrogen, C₁₋₄alkyl, cyano, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, C₃₋₆cycloalkyl and -O-C₃₋₆cycloalkyl, wherein C₃₋₆cycloalkyl
 15 and -O-C₃₋₆cycloalkyl are optionally substituted by one or more of halo, methyl or methoxy;
- (104b) R_{Z1} and R_{Z1a} are selected from selected from hydrogen, C₁₋₂alkyl, cyano, halo, C₁₋₂haloalkyl, C₁₋₂haloalkoxy, C₁₋₂alkoxy;
- (104c) R_{Z1} and R_{Z1a} are selected from selected from hydrogen, C₁₋₂alkyl, cyano and halo;
- 20 (104d) R_{Z1} and R_{Z1a} are hydrogen;
- (104e) R_{Z2} and R_{Z2a} are selected from hydrogen, C₁₋₄alkyl, cyano, halo or C₁₋₄alkoxy;
- (104f) R_{Z2} and R_{Z2a} are selected from hydrogen, cyano or halo;
- 25 (104g) R_{Z2} and R_{Z2a} are hydrogen;
- (104h) R_{Z3a} is selected from hydrogen, C₁₋₄alkyl, cyano, halo or C₁₋₄alkoxy;
- (104i) R_{Z3a} is selected from from hydrogen, cyano or halo;
- (104j) R_{Z3a} is hydrogen;
- 30 (104k) Z is selected from:



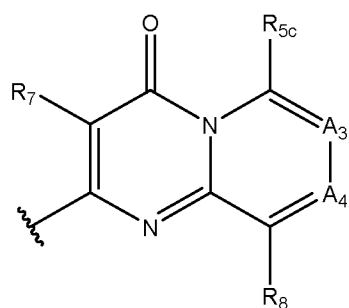
wherein R_4 , R_{4a} , R_5 , R_{5a} , R_{5b} , R_{5c} , R_6 , R_{6a} , R_7 , R_{7a} , R_8 , R_{8a} , R_{Z1} , R_{Z1a} , R_{Z2} , R_{Z2a} , R_{Z3a} , A_1 , A_2 , A_3 , A_4 , A_5 , A_6 , A_7 , A_8 , A_9 , A_{10} and A_{11} are as herein defined.



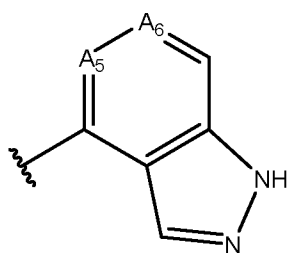
wherein R_4 , R_5 , R_6 , A_1 and A_2 are as herein defined;



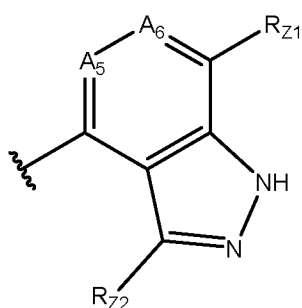
wherein R_7 , R_8 , A_3 and A_4 are as herein defined;



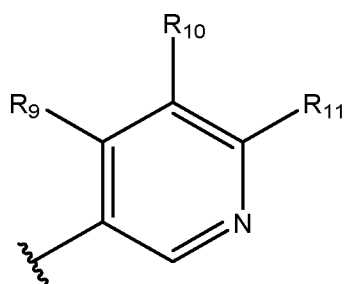
(105a) Z is

wherein R_{5c}, R₇, R₈, A₃ and A₄ are as herein defined

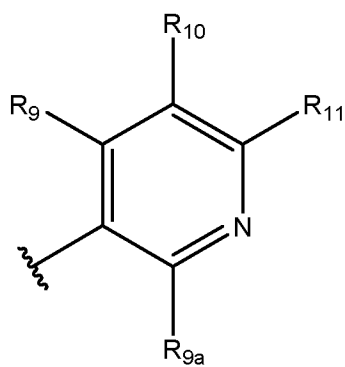
(106) Z is

wherein A₅ and A₆ are as herein defined;

(106a) Z is

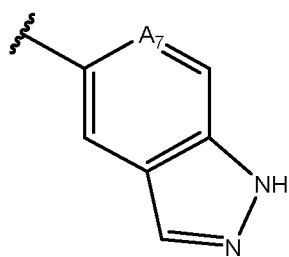
wherein R_{Z1}, R_{Z2}, A₅ and A₆ are as herein defined;

5 (107) Z is

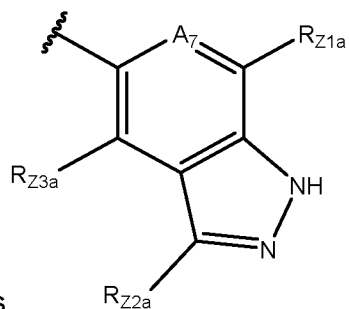
wherein R₉, R₁₀ and R₁₁ are as herein defined;

(107a) Z is

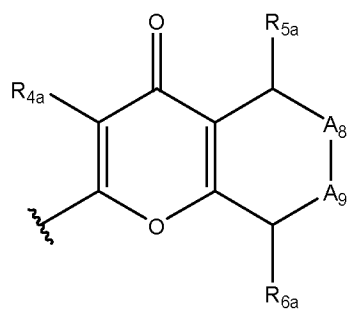
wherein R₉, R_{9a}, R₁₀ and R₁₁ are as herein defined;



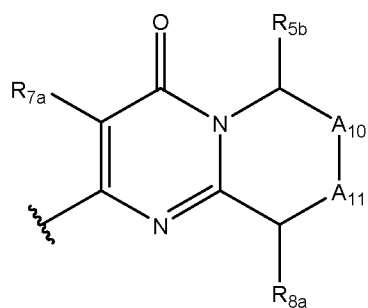
(108) Z is

wherein A₇ is as herein defined;

(108a) Z is

wherein R_{Z1a}, R_{Z2a}, R_{Z3a} and A₇ is as herein defined;

(109) Z is

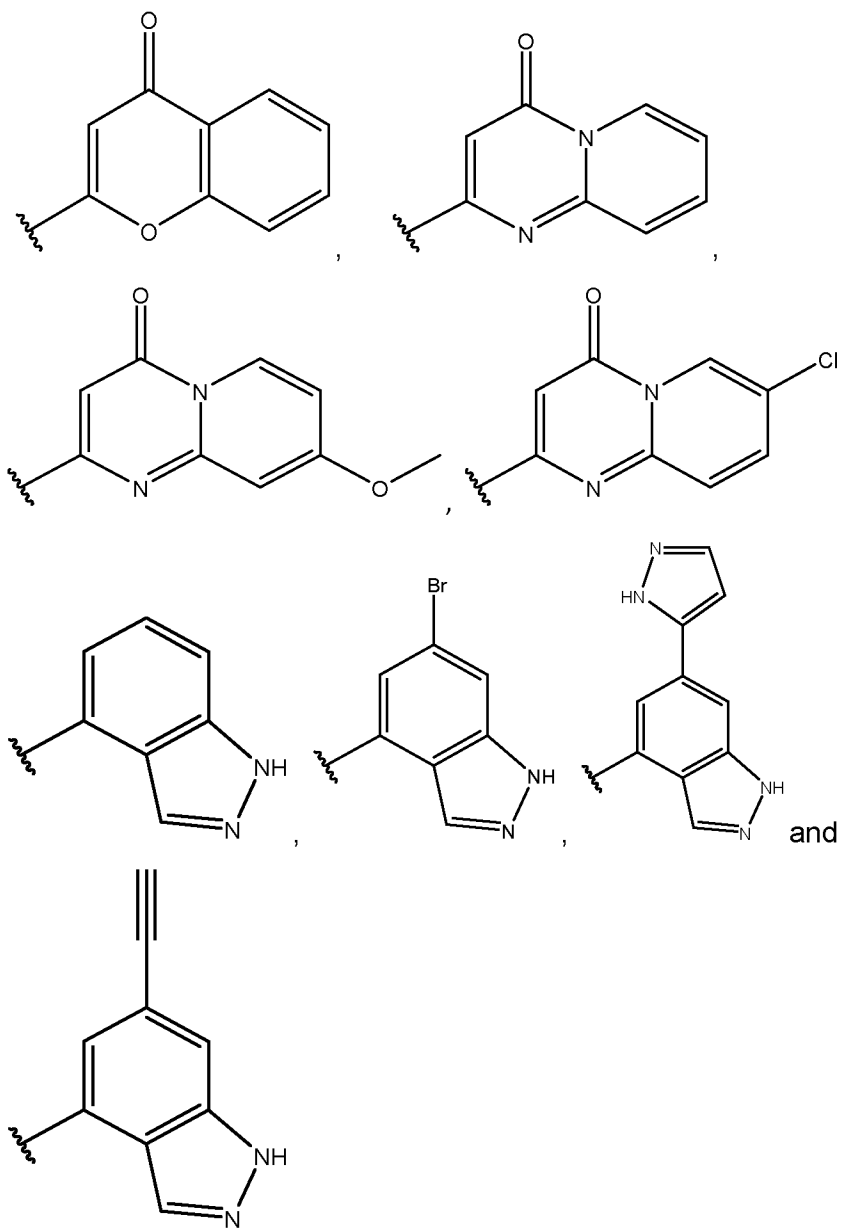
wherein R_{4a}, R_{5a}, R_{6a}, A₈ and A₉ are as herein defined;

5 (110) Z is

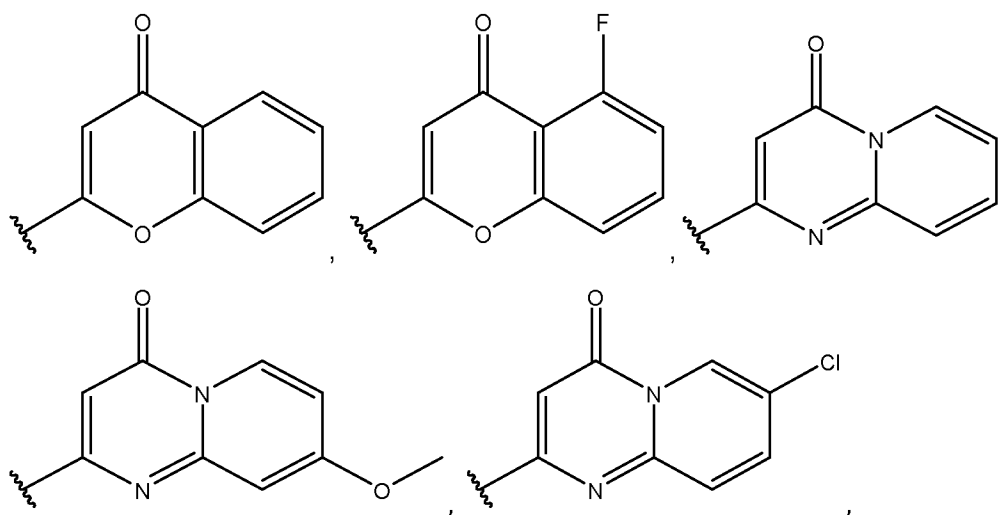
defined;

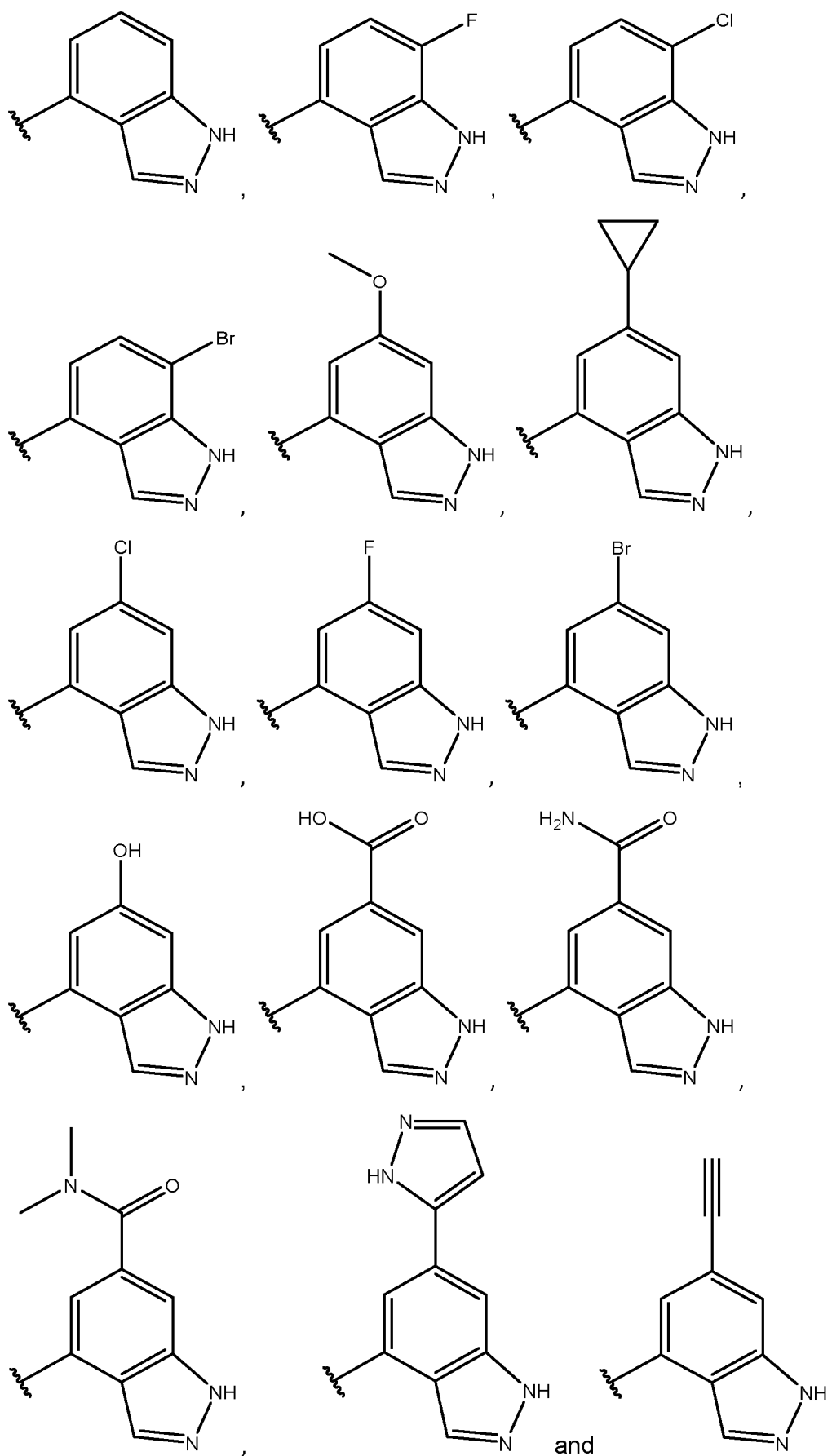
(111) Z is selected from:

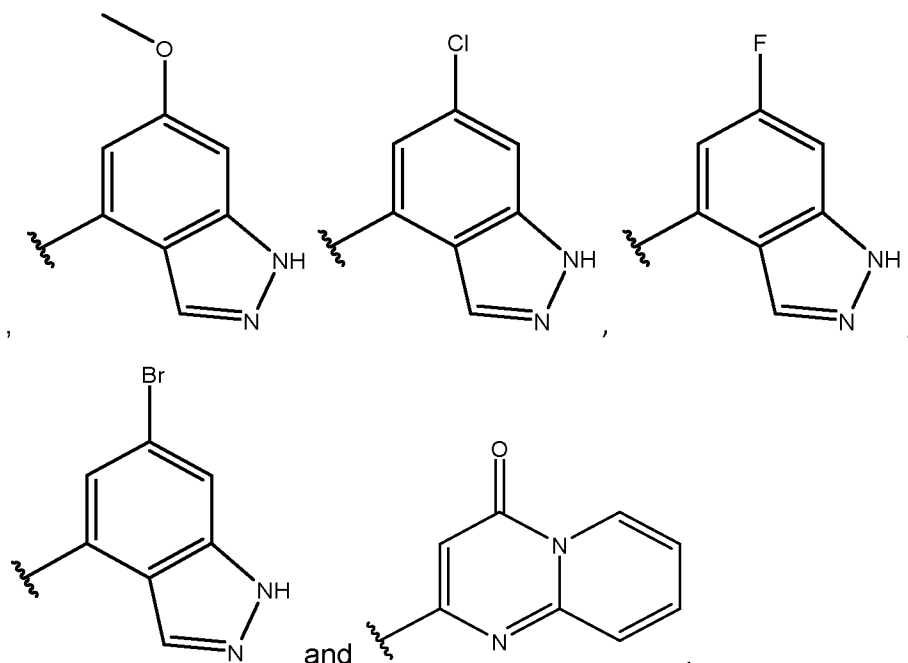
wherein R_{5b}, R_{7a}, R_{8a}, A₁₀ and A₁₁ are as herein



5 (111a) Z is selected from:







- 5 **[0093]** Suitably, a heteroaryl or heterocyclyl group as defined herein is a monocyclic heteroaryl or heterocyclyl group comprising one, two or three heteroatoms selected from N, O or S.
- [0094]** Suitably, a heteroaryl is a 5- or 6-membered heteroaryl ring comprising one, two or three heteroatoms selected from N, O or S.
- 10 **[0095]** Suitably, a heterocyclyl group is a 4-, 5- or 6-membered heterocyclyl ring comprising one, two or three heteroatoms selected from N, O or S. Most suitably, a heterocyclyl group is a 5- or 6-membered ring comprising one, two or three heteroatoms selected from N, O or S [e.g. morpholinyl (e.g. 4-morpholinyl), oxetane, methyloxetane (e.g. 3-methyloxetane), pyrrolidinone (e.g. pyrrolidin-2-one)].
- 15 **[0096]** Suitably, an aryl group is phenyl.
- [0097]** Suitably, X is as defined in any one of paragraphs (20) to (24) above. Most suitably, X is as defined in paragraph (20).
- [0098]** Suitably, X is as defined in any one of paragraphs (20) to (24a) above. Most suitably, X is as defined in paragraph (20) or (24a).
- 20 **[0099]** Suitably, R_{1a}, R_{1c} and R_{1e} are as defined in any one of paragraphs (1) to (6) above. Most suitably, R_{1a}, R_{1c} and R_{1e} are as defined in paragraph (6).
- [00100]** Suitably, R_{1b}, R_{1d} and R_{1f} are as defined in any one of paragraphs (1), (2), and from paragraphs (7) to (15) above. Most suitably, R_{1b}, R_{1d} and R_{1f} are as defined in paragraph (15).

[00101] Suitably, R_{1b} , R_{1d} and R_{1f} are as defined in any one of paragraphs (1), (2), and from paragraphs (6a) to (15a) above. Most suitably, R_{1b} , R_{1d} and R_{1f} are as defined in paragraph (15a).

[00102] Suitably, R_{1b} , R_{1d} and R_{1f} are as defined in any one of paragraphs (14a) to (15c) above. Suitably, R_{1b} , R_{1d} and R_{1f} are as defined in any one of paragraphs (14d) to (15c). Suitably, R_{1b} , R_{1d} and R_{1f} are as defined in paragraph (15c).

[00103] Suitably, R_{1b} , R_{1d} and R_{1f} are as defined in any one of paragraphs (14a) to (15g) above. Suitably, R_{1b} , R_{1d} and R_{1f} are as defined in any one of paragraphs (14a) to (14g). Suitably, R_{1b} , R_{1d} and R_{1f} are as defined in any one of paragraphs (15d) to (15g). Most suitably, R_{1b} , R_{1d} and R_{1f} are as defined in paragraph (15g).

[00104] Suitably, $R_{1a'}$ is as defined in paragraphs (16) and (17) above. Most suitably, $R_{1a'}$ is as defined in paragraph (17) above.

[00105] Suitably, R_{2a} , R_{2b} and R_{2c} are as defined in any one of paragraphs (18) and (19) above. Most suitably, R_{2a} , R_{2b} and R_{2c} are as defined in paragraph (19).

[00106] Suitably, Y is as defined in any one of paragraphs (34) to (52) above. Suitably, Y is as defined in paragraphs (34), (34a), (36), (39), (40), (43) and (50c). Suitably, Y is as defined in paragraphs (34a) or (43) above. Most suitably, Y is as defined in paragraph (52a).

[00107] Suitably, n is as defined in any one of paragraphs (32) and (33) above. Most suitably, n is as defined in paragraph (33).

[00108] Suitably, R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} and R_{3o1} are as defined in any one of paragraphs (25) to (28), and paragraphs (30) to (31) above. Most suitably, R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} and R_{3o1} are as defined in paragraph (28).

[00109] Suitably, R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} and R_{3o2} are as defined in any one of paragraphs (25), (29), (30) and (31) above. Most suitably, R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} and R_{3o2} are as defined in paragraph (29).

[00110] Suitably, R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} and R_{3q1} are as defined in any one of paragraphs (25) to (28a), and paragraphs (30) to (31a) above. Most suitably, R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} and R_{3q1} are as defined in paragraph (28a).

[00111] Suitably, R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} , R_{3o2} , R_{3p2} and R_{3q2} are as defined in any one of paragraphs (25), (25a), (29), (29a) (30), (30a), (31)

and (31a) above. Most suitably, R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} , R_{3o2} , R_{3p2} and R_{3q2} are as defined in paragraph (29a).

[00112] Suitably, R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} , R_{3q1} , R_{3r1} and R_{3s1} are as defined in any one of paragraphs (25) to (28b), and paragraphs (30a) to (31b) above. Most suitably, R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} , R_{3q1} , R_{3r1} and R_{3s1} are as defined in paragraph (28b).

[00113] Suitably, R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} , R_{3o2} , R_{3p2} , R_{3q2} , R_{3r2} and R_{3s2} are as defined in any one of paragraphs (25), (25a), (25b), (29), (29a), (29b), (30), (30a), (30b), (31), (31a) and (31b) above. Most suitably, R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} , R_{3o2} , R_{3p2} , R_{3q2} , R_{3r2} and R_{3s2} are as defined in paragraph (29b).

[00114] Suitably, Z is as defined in any one of paragraphs from (104k) and (104) to (111b) above. Suitably, Z is as defined in any one of paragraphs from (104) to (111a) above. Suitably, Z is as defined in any one of paragraphs from (104) to (111) above. Suitably, Z is as defined in any one of paragraphs (104) to (106a). Suitably, Z is as defined in paragraphs (104), (105a) and (106a). Most suitably, Z is as defined in any one of paragraphs (104) to (106). Most suitably, Z is as defined in paragraph (111b) above.

[00115] Suitably, R_4 is as defined in any one of paragraphs (53), (54) and (59) above. Most suitably, R_4 is as defined in paragraph (54).

[00116] Suitably, R_5 is as defined in any one of paragraphs (55), (56) and (59) above. Most suitably, R_5 is as defined in paragraph (56).

[00117] Suitably, R_6 is as defined in any one of paragraphs (57), (58) and (59) above. Most suitably, R_6 is as defined in paragraph (58).

[00118] Suitably, A_1 is as defined in any one of paragraphs (60), (61) and (64) above. Most suitably, A_1 is as defined in paragraph (61).

[00119] Suitably, A_2 is as defined in any one of paragraphs (62), (63) and (64) above. Most suitably, A_1 is as defined in paragraph (63).

[00120] Suitably, R_7 is as defined in any one of paragraphs (65), (66) and (69) above. Most suitably, R_7 is as defined in paragraph (66).

[00121] Suitably, R_8 is as defined in any one of paragraphs (67), (68) and (69) above. Most suitably, R_8 is as defined in paragraph (68).

[00122] Suitably, A_3 is as defined in any one of paragraphs (70), (71), (72) and (75) above. Most suitably, A_3 is as defined in paragraph (71).

[00123] Suitably, A_4 is as defined in any one of paragraphs (73), (74) and (75) above. Most suitably, A_4 is as defined in paragraph (74).

[00124] Suitably, A_5 is as defined in any one of paragraphs (76), (76a), (76b), (76c), (77) and (81) above. Suitably, A_5 is as defined in any one of paragraphs (76), (77) and (81) above.

5 Most suitably, A_5 is as defined in paragraph (77).

[00125] Suitably, A_6 is as defined in any one of paragraphs from (78) to (81) above. Suitably, A_6 is as defined in paragraph (79). Suitably, A_6 is as defined in paragraphs (78a), (78b), (78c), (79a) and (79b). Most suitably, A_6 is as defined in paragraph (79b).

[00126] Suitably, R_9 , R_{10} and R_{11} are as defined in any one of paragraphs (82) to (83a).

10 Suitably, R_9 , R_{10} and R_{11} are as defined in paragraphs (82) and (83).

[00127] Suitably, A_7 is as defined in any one of paragraphs (84) to (85c) above. Suitably, A_7 is as defined in any one of paragraphs (84) to (85) above.

[00128] Suitably R_{4a} is as defined in any one of paragraphs (86), (86a), (87) and (92) above. Most suitably, R_{4a} is as defined in paragraph (87).

15 **[00129]** Suitably R_{5a} is as defined in any one of paragraphs (88), (89) and (92) above. Most suitably, R_{5a} is as defined in paragraph (89).

[00130] Suitably R_{6a} is as defined in any one of paragraphs (90) to (92) above. Most suitably, R_{6a} is as defined in paragraph (91).

[00131] Suitably A_8 is as defined in any one of paragraphs (93) above.

20 **[00132]** Suitably A_9 is as defined in any one of paragraphs (94) above.

[00133] Suitably R_{5b} is as defined in any one of paragraphs (95) and (96) above. Most suitably, R_{5b} is as defined in paragraph (96).

[00134] Suitably R_{7a} is as defined in any one of paragraphs (97), (97a) and (98) above. Most suitably, R_{7a} is as defined in paragraph (98).

25 **[00135]** Suitably R_{8a} is as defined in any one of paragraphs (99) and (100) above. Most suitably, R_{8a} is as defined in paragraph (100).

[00136] Suitably A_{10} is as defined in any one of paragraphs (102) above.

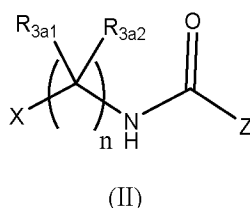
[00137] Suitably A_{11} is as defined in any one of paragraphs (103) above.

30 **[00138]** Suitably, R_{Z1} and R_{Z1a} are as defined in any one of paragraphs (104a) to (104d) above. Most suitably, R_{Z1} and R_{Z1a} are as defined in paragraph (104d).

[00139] Suitably, R_{Z2} and R_{Z2a} are as defined in any one of paragraphs (104e) to (104g) above. Most suitably, R_{Z2} and R_{Z2a} are as defined in paragraph (104g).

[00140] Suitably, R_{Z3a} is as defined in any one of paragraphs (104h) to (104j) above. Most suitably, R_{Z3a} is as defined in paragraph (104j).

[00141] In a particular group of compounds of the invention, Y is as defined in paragraph (34), i.e. the compounds have the structural formula (II) (a sub-definition of formula (1)) shown below:



wherein X, R_{3a1} , R_{3a2} , n and Z each having any one of the meanings defined herein; or a pharmaceutically acceptable salt thereof.

[00142] In an embodiment of the compounds of formula (II):

10 X is as defined in any one of paragraphs (20) to (24) above, suitably X is as defined in paragraph (24a);

R_{3a1} is as defined in any one of paragraphs from (25) to (28), and paragraphs (30) and (31) above;

R_{3a2} is as defined in any one of paragraphs (25), (29), (30) and (31) above;

15 n is as defined in any one of paragraphs (32) and (33) above; and

Z is as defined in any one of paragraphs (104) to (111b) above. Suitably, Z is as defined in any one of paragraphs (104) to (111) above.

[00143] In an embodiment of the compounds of formula (II):

X is as defined in paragraph (20) above;

20 R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above; and

Z is as defined in any one of paragraphs (104) to (106) above.

[00144] In a particular group of the compounds of formula (II):

25 X is as defined in paragraph (20), (21) or (22) above and R_{1b} , R_{1d} and R_{1f} are each as defined in any one of paragraphs (8a) to (8e) above;

R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above; and

Z is as defined in any one of paragraphs (104) to (106) above.

[00145] In a particular group of the compounds of formula (II):

- 5 X is as defined in paragraph (20) above and R_{1b} is as defined in any one of paragraphs (14a) to (14g) above; suitably R_{1b} is as defined in any one of paragraphs (14a) to (15g) above. Suitably, R_{1b}, is as defined in any one of paragraphs (15d) to (15g). Most suitably, R_{1b} is as defined in paragraph (15g);

R_{3a1} is as defined in paragraph (28) above;

- 10 R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above; and

Z is as defined in any one of paragraphs (104) to (106) above.

[00146] In a particular group of the compounds of formula (II):

- 15 X is as defined in paragraph (20) above and R_{1b} is as defined in any one of paragraphs (8a) to (8e) above;

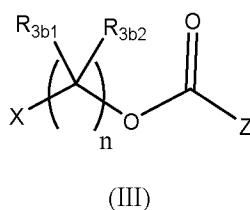
R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above; and

Z is as defined in any one of paragraphs (104) to (106) above.

- 20 **[00147]** In a particular group of compounds of the invention, Y is as defined in paragraph (36), i.e. the compounds have the structural formula (III) (a sub-definition of formula (1)) shown below:



- 25 wherein X, R_{3b1}, R_{3b2}, n and Z each having any one of the meanings defined herein; or a pharmaceutically acceptable salt thereof.

[00148] In an embodiment of the compounds of formula (III):

X is as defined in any one of paragraphs (20) to (24) above;

R_{3b1} is as defined in any one of paragraphs from (25) to (28), and paragraphs (30) and (31) above;

R_{3b2} is as defined in any one of paragraphs (25), (29), (30) and (31) above;

n is as defined in any one of paragraphs (32) and (33) above; and

5 Z is as defined in any one of paragraphs (104) to (111) above.

[00149] In an embodiment of the compounds of formula (III):

X is as defined in paragraph (20) above;

R_{3b1} is as defined in paragraph (28) above;

R_{3b2} is as defined in paragraph (29) above;

10 n is as defined in paragraph (33) above; and

Z is as defined in any one of paragraphs (104) to (106) above.

[00150] In a particular group of the compounds of formula (III):

X is as defined in paragraph (20), (21) or (22) above and R_{1b}, R_{1d} and R_{1f} are each as defined in any one of paragraphs (8a) to (8e) above;

15 R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above; and

Z is as defined in any one of paragraphs (104) to (106) above.

[00151] In a particular group of the compounds of formula (III):

20 X is as defined in paragraph (20) above and R_{1b} is as defined in any one of paragraphs (8a) to (8e) above;

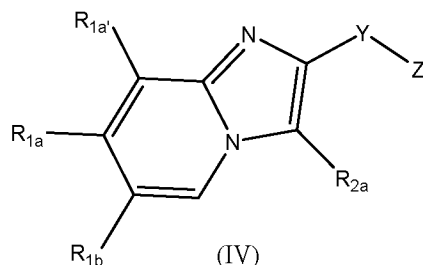
R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above; and

25 Z is as defined in any one of paragraphs (104) to (106) above.

[00152] In a particular group of compounds of the invention, X is as defined in paragraph (20), i.e. the compounds have the structural formula (IV) (a sub-definition of formula (I)) shown below:



wherein R_{1a} , R_{1b} , $R_{1a'}$, R_{2a} , Y and Z each having any one of the meanings defined herein; or a pharmaceutically acceptable salt thereof.

[00153] In an embodiment of the compounds of formula (IV):

- 5 R_{1a} is as defined in any one of paragraphs (1) to (6) above;
 R_{1b} is as defined in any one of paragraphs (1), (2), from paragraphs (7) to (15a) above;
 $R_{1a'}$ is as defined in paragraphs (16) and (17) above;
 R_{2a} is as defined in any one of paragraphs (18) to (19) above;
Y is as defined in any one of paragraphs (34) to (52); and
10 Z is as defined in any one of paragraphs (104) to (111) above.

[00154] In an embodiment of the compounds of formula (IV):

- R_{1a} is as defined in any one of paragraphs (1) to (6) above;
 R_{1b} is as defined in any one of paragraphs (14a) to (14g) above;
 $R_{1a'}$ is as defined in paragraphs (16) and (17) above;
15 R_{2a} is as defined in any one of paragraphs (18) to (19) above;
Y is as defined in any one of paragraphs (34) to (52); and
Z is as defined in any one of paragraphs (104) to (111) above.

[00155] In an embodiment of the compounds of formula (IV):

- 20 R_{1a} is as defined in paragraph (6) above;
 R_{1b} is as defined in paragraph (15) or (15a) above;
 $R_{1a'}$ is as defined in paragraph (17) above;
 R_{2a} is as defined in paragraph (19) above;
Y is as defined in paragraphs (34), (36), (39) and (40) above; and
25 Z is as defined in any one of paragraphs (104) to (106) above.

[00156] In a particular group of the compounds of formula (IV):

R_{1a} is as defined in any one of paragraphs (1) to (6) above;

R_{1b} is as defined in any one of paragraphs (8a) to (8e) or (15a) above;

R_{1a'} is as defined in paragraphs (16) and (17) above;

5 R_{2a} is as defined in any one of paragraphs (18) to (19) above;

Y is as defined in any one of paragraphs (34) to (52); and

Z is as defined in any one of paragraphs (104) to (111) above.

[00157] In a particular group of the compounds of formula (IV):

R_{1a} is as defined in paragraph (6) above;

10 R_{1b} is as defined in paragraph (8e) or (15a) above;

R_{1a'} is as defined in paragraph (17) above;

R_{2a} is as defined in paragraph (19) above;

Y is as defined in paragraphs (34), (36), (39) and (40) above; and

Z is as defined in any one of paragraphs (104) to (111b) above.

15 **[00158]** In an embodiment of the compounds of formula (IV):

R_{1a} is as defined in paragraph (6) above;

R_{1b} is as defined in any one of paragraphs (14a) to (14g) above; more suitably R_{1b} is as defined in paragraphs (15a) to (15g) above;

R_{1a'} is as defined in paragraph (17) above;

20 R_{2a} is as defined in paragraph (19) above;

Y is as defined in any one of paragraphs (34) to (52a); and

Z is as defined in any one of paragraphs (104) to (111b) above.

[00159] In a particular group of the compounds of formula (IV):

R_{1a} is as defined in any one of paragraphs (1) to (6) above;

25 R_{1b} is as defined in any one of paragraphs (15d), (15e), (15f) or (15g) above;

R_{1a'} is as defined in paragraphs (16) and (17) above;

R_{2a} is as defined in any one of paragraphs (18) to (19) above;

Y is as defined in any one of paragraphs (34), (34a), (36), (39) and (40) above; and

Z is as defined in any one of paragraphs (104) to (111b) above.

[00160] In a particular group of the compounds of formula (IV):

R_{1a} is as defined in paragraph (6) above;

R_{1b} is as defined in paragraph (15g) above;

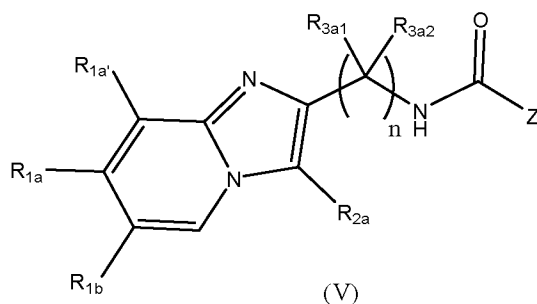
5 R_{1a'} is as defined in paragraph (17) above;

R_{2a} is as defined in paragraph (19) above;

Y is as defined in any one of paragraphs (34), (36), (39) and (40) above; more suitably Y is as defined in paragraph (52a) above; and

10 Z is as defined in any one of paragraphs (111) to (111b) above; more suitably Z is as defined in paragraph (111b) above.

[00161] In a particular group of compounds of the invention, X is as defined in paragraph (20) and Y is as defined in paragraph (34), i.e. the compounds have the structural formula (V) (a sub-definition of formula (I)) shown below:



15 wherein R_{1a}, R_{1b}, R_{1a'}, R_{2a}, R_{3a1}, R_{3a2}, n and Z each having any one of the meanings defined herein; or a pharmaceutically acceptable salt thereof.

[00162] In an embodiment of the compounds of formula (V):

R_{1a} is as defined in any one of paragraphs (1) to (6) above;

20 R_{1b} is as defined in any one of paragraphs (1), (2), and from paragraphs (7) to (15g) above;

R_{1a'} is as defined in paragraphs (16) and (17) above;

R_{2a} is as defined in any one of paragraphs (18) to (19) above;

R_{3a1} is as defined in any one of paragraphs from (25) to (28), and paragraphs (30) and (31) above;

25 R_{3a2} is as defined in any one of paragraphs (25), (29), (30) and (31) above;

n is as defined in any one of paragraphs (32) and (33) above; and

Z is as defined in any one of paragraphs (104) to (111) above.

[00163] In an embodiment of the compounds of formula (V):

R_{1a} is as defined in paragraph (6) above;

5 R_{1b} is as defined in paragraph (15) or (15a) above;

R_{1a'} is as defined in paragraph (17) above;

R_{2a} is as defined in paragraph (19) above;

R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

10 n is as defined in paragraph (33) above; and

Z is as defined in any one of paragraphs (104) to (106) above.

[00164] In a particular group of the compounds of formula (V):

R_{1a} is as defined in any one of paragraphs (1) to (6) above;

R_{1b} is as defined in any one of paragraphs (8a) to (8e) or (15a) above;

15 R_{1a'} is as defined in paragraphs (16) and (17) above;

R_{2a} is as defined in any one of paragraphs (18) to (19) above;

R_{3a1} is as defined in any one of paragraphs from (25) to (28), and paragraphs (30) and (31) above;

R_{3a2} is as defined in any one of paragraphs (25), (29), (30) and (31) above;

20 n is as defined in any one of paragraphs (32) and (33) above; and

Z is as defined in any one of paragraphs (104) to (111) above.

[00165] In a particular group of the compounds of formula (V):

R_{1a} is as defined in paragraph (6) above;

R_{1b} is as defined in paragraph (8e) or (15a) above;

25 R_{1a'} is as defined in paragraph (17) above;

R_{2a} is as defined in paragraph (19) above;

R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above; and

Z is as defined in any one of paragraphs (104) to (106) above.

[00166] In an embodiment of the compounds of formula (V):

R_{1a} is as defined in paragraph (6) above;

5 R_{1b} is as defined in paragraph (15g) above;

R_{1a'} is as defined in paragraph (17) above;

R_{2a} is as defined in paragraph (19) above;

R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

10 n is as defined in paragraph (33) above; and

Z is as defined in any one of paragraphs (104k) and (104) to (106) above.

[00167] In a particular group of the compounds of formula (V):

R_{1a} is as defined in any one of paragraphs (1) to (6) above;

R_{1b} is as defined in any one of paragraphs (15g) above;

15 R_{1a'} is as defined in paragraphs (16) and (17) above;

R_{2a} is as defined in any one of paragraphs (18) to (19) above;

R_{3a1} is as defined in any one of paragraphs from (25) to (28), and paragraphs (30) and (31) above;

R_{3a2} is as defined in any one of paragraphs (25), (29), (30) and (31) above;

20 n is as defined in any one of paragraphs (32) and (33) above; and

Z is as defined in any one of paragraphs (104k) and (104) to (111) above.

[00168] In a particular group of the compounds of formula (V):

R_{1a} is as defined in paragraph (6) above;

R_{1b} is as defined in paragraph (15g) above;

25 R_{1a'} is as defined in paragraph (17) above;

R_{2a} is as defined in paragraph (19) above;

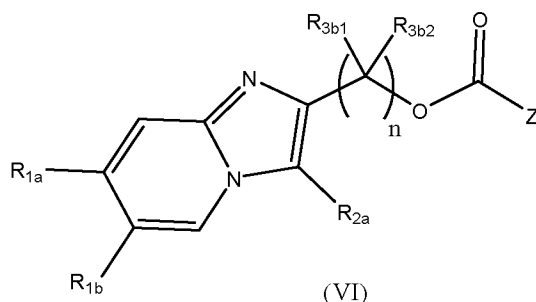
R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above; and

Z is as defined in paragraph (111b) above.

[00169] In a particular group of compounds of the invention, X is as defined in paragraph (20), R_{1a}' is as defined in paragraph (17) and Y is as defined in paragraph (36), i.e. the compounds have the structural formula (VI) (a sub-definition of formula (I)) shown below:



wherein R_{1a}, R_{1b}, R_{2a}, R_{3b1}, R_{3b2}, n and Z each having any one of the meanings defined herein; or a pharmaceutically acceptable salt thereof.

[00170] In an embodiment of the compounds of formula (VI):

R_{1a} is as defined in any one of paragraphs (1) to (6) above;

R_{1b} is as defined in any one of paragraphs (1), (2), and paragraphs (7) to (15g) above;

R_{2a} is as defined in any one of paragraphs (18) to (19) above;

R_{3b1} is as defined in any one of paragraphs from (25) to (28) and paragraphs (30) to (31) above;

R_{3b2} is as defined in any one of paragraphs (25), (29), (30) and (31) above;

n is as defined in any one of paragraphs (32) and (33) above; and

Z is as defined in any one of paragraphs (104k) or (104) to (111) above.

[00171] In an embodiment of the compounds of formula (VI):

R_{1a} is as defined in paragraph (6) above;

R_{1b} is as defined in paragraph (15) or (15a) above;

R_{2a} is as defined in paragraph (19) above;

R_{3b1} is as defined in paragraph (28) above;

R_{3b2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above; and

Z is as defined in any one of paragraphs (104) to (106) above.

[00172] In a particular group of the compounds of formula (VI):

R_{1a} is as defined in any one of paragraphs (1) to (6) above;

R_{1b} is as defined in any one of paragraphs (8a) to (8e) or (15a) above;

5 R_{2a} is as defined in any one of paragraphs (18) to (19) above;

R_{3b1} is as defined in any one of paragraphs from (25) to (28) and paragraphs (30) to (31) above;

R_{3b2} is as defined in any one of paragraphs (25), (29), (30) and (31) above;

n is as defined in any one of paragraphs (32) and (33) above; and

10 Z is as defined in any one of paragraphs (104) to (111b) above.

[00173] In a particular group of the compounds of formula (VI):

R_{1a} is as defined in paragraph (6) above;

R_{1b} is as defined in paragraph (8e) or (15a) above;

R_{2a} is as defined in paragraph (19) above;

15 R_{3b1} is as defined in paragraph (28) above;

R_{3b2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above; and

Z is as defined in any one of paragraphs (104) to (106) above.

[00174] In an embodiment of the compounds of formula (VI):

20 R_{1a} is as defined in paragraph (6) above;

R_{1b} is as defined in paragraph (15) to (15g) above;

R_{2a} is as defined in paragraph (19) above;

R_{3b1} is as defined in paragraph (28) above;

R_{3b2} is as defined in paragraph (29) above;

25 n is as defined in paragraph (33) above; and

Z is as defined in any one of paragraphs (104k), (104) to (106a) and (111) to (111b) above.

[00175] In a particular group of the compounds of formula (VI):

R_{1a} is as defined in any one of paragraphs (1) to (6) above;

R_{1b} is as defined in any one of paragraphs (15) to (15g) above;

R_{2a} is as defined in any one of paragraphs (18) to (19) above;

R_{3b1} is as defined in any one of paragraphs from (25) to (28) and paragraphs (30) to (31) above;

5 R_{3b2} is as defined in any one of paragraphs (25), (29), (30) and (31) above;

n is as defined in any one of paragraphs (32) and (33) above; and

Z is as defined in any one of paragraphs (105) to (106a) and (111b) above.

[00176] In a particular group of the compounds of formula (VI):

R_{1a} is as defined in paragraph (6) above;

10 R_{1b} is as defined in paragraph (15g) above;

R_{2a} is as defined in paragraph (19) above;

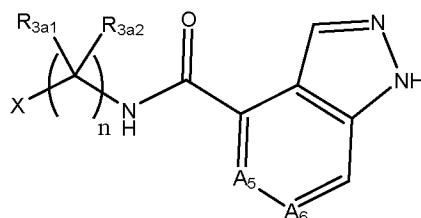
R_{3b1} is as defined in paragraph (28) above;

R_{3b2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above; and

15 Z is as defined in paragraph (111b) above.

[00177] In a particular group of compounds of the invention, Y is as defined in paragraph (34) and Z is defined as paragraph (106), i.e. the compounds have the structural formula (VII) (a sub-definition of formula (I)) shown below:



(VII)

20 wherein X, R_{3a1}, R_{3a2}, n, A₅ and A₆ each having any one of the meanings defined herein; or a pharmaceutically acceptable salt thereof.

[00178] In an embodiment of the compounds of formula (VII):

X is as defined in any one of paragraphs (20) to (24) above;

R_{3a1} is as defined in any one of paragraphs from (25) to (28), and paragraphs (30) to (31) above;

25

R_{3a2} is as defined in any one of paragraphs (25), (29), (30) and (31) above;

n is as defined in any one of paragraphs (32) and (33) above;

A₅ is as defined in any one of paragraphs (76), (77) and (81) above; and

A₆ is as defined in any one of paragraphs from (78) to (81) above.

5 **[00179]** In an embodiment of the compounds of formula (VII):

X is as defined in paragraph (20) above;

R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above;

10 A₅ is as defined in paragraph (77) above;

A₆ is as defined in paragraph (79) above or A₆ is as defined in paragraph (79a) above.

[00180] In a particular group of the compounds of formula (VII):

X is as defined in any one of paragraphs (20) to (22) above and R_{1b}, R_{1d} and R_{1f} are each as defined in any one of paragraphs (8a) to (8e) above;

15 R_{3a1} is as defined in any one of paragraphs from (25) to (28), and paragraphs (30) to (31) above;

R_{3a2} is as defined in any one of paragraphs (25), (29), (30) and (31) above;

n is as defined in any one of paragraphs (32) and (33) above;

A₅ is as defined in any one of paragraphs (76), (77) and (81) above; and

20 A₆ is as defined in any one of paragraphs from (78) to (81) above.

[00181] In a particular group of the compounds of formula (VII):

X is as defined in paragraph (20) above and R_{1b} is as defined in any one of paragraphs (8a) to (8e) above;

R_{3a1} is as defined in paragraph (28) above;

25 R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above;

A₅ is as defined in paragraph (77) above;

A₆ is as defined in paragraph (79) above.

[00182] In a particular group of the compounds of formula (VII):

X is as defined in paragraph (20) above, R_{1a}, R_{1b}, R_{1a'} and R_{2a} are hydrogen, and R_{1b} is as defined in any one of paragraphs (15e) to (15g) above, suitably R_{1b} is as defined in paragraph (15g);

R_{3a1} is as defined in paragraph (28) above;

5 R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above;

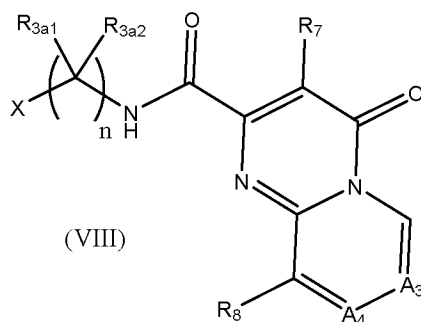
A₃ is as defined in paragraph (71) above;

A₄ is as defined in paragraph (74) above;

R₇ is as defined in paragraph (66) above; and

10 R₈ is as defined in paragraph (68) above.

[00183] In a particular group of compounds of the invention, Y is as defined in paragraph (34) and Z is defined as paragraph (105), i.e. the compounds have the structural formula (VIII) (a sub-definition of formula (I)) shown below:



15

wherein X, R_{3a1}, R_{3a2}, n, A₃, A₄, R₇ and R₈ each having any one of the meanings defined herein; or a pharmaceutically acceptable salt thereof.

[00184] In an embodiment of the compounds of formula (VIII):

X is as defined in any one of paragraphs (20) to (24) and (24a) above;

20 R_{3a1} is as defined in any one of paragraphs from (25) to (28), and paragraphs (30) to (31) above;

R_{3a2} is as defined in any one of paragraphs (25), (29), (30) and (31) above;

n is as defined in any one of paragraphs (32) and (33) above;

A₃ is as defined in any one of paragraphs (70), (71), (72) and (75) above;

25 A₄ is as defined in any one of paragraphs from (73) to (75) above;

R₇ is as defined in any one of paragraphs (65), (66) and (69) above; and

R₈ is as defined in any one of paragraphs (67), (68) and (69) above.

[00185] In an embodiment of the compounds of formula (VIII):

X is as defined in paragraph (20) above;

5 R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above;

A₃ is as defined in paragraph (71) above;

A₄ is as defined in paragraph (74) above;

10 R₇ is as defined in paragraph (66) above; and

R₈ is as defined in paragraph (68) above.

[00186] In a particular group of the compounds of formula (VIII):

X is as defined in any one of paragraphs (20) to (22) above and R_{1b}, R_{1d} and R_{1f} are each as defined in any one of paragraphs (8a) to (8e) above;

15 R_{3a1} is as defined in any one of paragraphs from (25) to (28), and paragraphs (30) to (31) above;

R_{3a2} is as defined in any one of paragraphs (25), (29), (30) and (31) above;

n is as defined in any one of paragraphs (32) and (33) above;

A₃ is as defined in any one of paragraphs (70), (71), (72) and (75) above;

20 A₄ is as defined in any one of paragraphs from (73) to (75) above;

R₇ is as defined in any one of paragraphs (65), (66) and (69) above; and

R₈ is as defined in any one of paragraphs (67), (68) and (69) above.

[00187] In a particular group of the compounds of formula (VIII):

25 X is as defined in paragraph (20) above and R_{1b} is as defined in any one of paragraphs (8a) to (8e) above;

R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

n is as defined in paragraph (33) above;

A₃ is as defined in paragraph (71) above;

A₄ is as defined in paragraph (74) above;

R₇ is as defined in paragraph (66) above; and

R₈ is as defined in paragraph (68) above.

[00188] In a particular group of the compounds of formula (VIII):

- 5 X is as defined in paragraph (20) above, R_{1a}, R_{1b}, R_{1a'} and R_{2a} are hydrogen, and R_{1b} is as defined in any one of paragraphs (15e) to (15g) above, suitably R_{1b} is as defined in paragraph (15g);

R_{3a1} is as defined in paragraph (28) above;

R_{3a2} is as defined in paragraph (29) above;

- 10 n is as defined in paragraph (33) above;

A₃ is as defined in paragraph (71) above;

A₄ is as defined in paragraph (74) above;

R₇ is as defined in paragraph (66) above; and

R₈ is as defined in paragraph (68) above.

15

[00189] Particular compounds of the present invention include any of the compounds exemplified in the present application, or a pharmaceutically acceptable salt thereof, and, in particular, any of the following:

N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

- 20 N-({7-bromoimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-bromoimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-chloroimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({7-fluoroimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-fluoroimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

- 25 N-({7-methoxyimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-6-(1H-pyrazol-5-yl)-1H-indazole-4-carboxamide;

N-({7-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

6-bromo-N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

- 30 6-bromo-N-({7-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-chromene-2-carboxamide;

N-({imidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-chromene-2-carboxamide;

- 6-ethynyl-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-chromene-2-carboxamide;
 5 N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-cyanoimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 8-methoxy-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-
 10 2-carboxamide;
 N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-5-carboxamide;
 7-chloro-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-fluoroimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
 15 carboxamide;
 N-({6-bromoimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-methoxyimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 20 N-({7-methoxyimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({8-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 25 N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-pyrazolo[4,3-c]pyridine-4-carboxamide;
 N-({7-bromoimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-(2-hydroxy-1-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 4-(3-({imidazo[1,2-a]pyridin-2-yl}-2,5-dihydro-1H-pyrrole-1-carbonyl)-1H-indazole;
 30 N-[(6-[(pyridin-3-yl)methyl]amino)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 N-[(6-[(1-methyl-1H-imidazol-4-yl)methyl]amino)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 N-[(6-(3-methoxyphenyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 35 N-[(6-(1H-pyrazol-5-yl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 N-[(6-(3-chlorophenyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;

- N-({6-[(pyridin-3-yl)amino]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 N-({6-[(piperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 N-({6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 N-({6-(acetamidomethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 5 {6-methylimidazo[1,2-a]pyridin-2-yl)methyl 1H-indazole-4-carboxylate;
 {6-methylimidazo[1,2-a]pyridin-2-yl)methyl 1H-indazole-4-carboxylate hydrochloride;
 N-({6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 N-({6-hydroxyimidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 N-({6-[(methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 10 N-({6-[(methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide
 dihydrochloride;
 N-[(6-[(2-hydroxyethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-
 carboxamide;
 N-[(6-[(2,2,2-trifluoroethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-
 15 carboxamide;
 N-({6-(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 N-({6-[hydroxy(phenyl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 N-({6-formylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
 carboxamide;
 20 N-({6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
 carboxamide;
 4-oxo-N-[(6-[(2,2,2-trifluoroethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-
 pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[(6-[(2-hydroxyethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-
 25 a]pyrimidine-2-carboxamide;
 4-oxo-N-[(6-[(2-phenylethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-
 a]pyrimidine-2-carboxamide;
 N-({6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-
 a]pyrimidine-2-carboxamide;
 30 4-oxo-N-[(6-[(3-phenylpropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-
 a]pyrimidine-2-carboxamide;
 N-({6-[hydroxy(phenyl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-
 a]pyrimidine-2-carboxamide;
 N-({6-(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
 35 carboxamide;

N-({6-ethenylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-({6-cyclopropylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

5 N-({7-ethenylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-({6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; and

2-(1H-indazol-4-yl)-5-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]-1,3,4-oxadiazole.

10 **[00190]** Particular compounds of the present invention include any of the compounds exemplified in the present application, or a pharmaceutically acceptable salt thereof, and, in particular, any of the following:

N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({7-bromoimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

15 N-({6-bromoimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-chloroimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({7-fluoroimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-fluoroimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({7-methoxyimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

20 N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-6-(1H-pyrazol-5-yl)-1H-indazole-4-carboxamide;

N-({7-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

6-bromo-N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

6-bromo-N-({7-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

25 N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-chromene-2-carboxamide;

N-({imidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-chromene-2-carboxamide;

6-ethynyl-N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

30 N-({7-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-chromene-2-carboxamide;

N-({7-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-({6-cyanoimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

35 8-methoxy-N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-5-carboxamide;
 7-chloro-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-fluoroimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 5 N-({6-bromoimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-methoxyimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 10 N-({7-methoxyimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({8-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 15 N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-pyrazolo[4,3-c]pyridine-4-carboxamide;
 N-({7-bromoimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-(2-hydroxy-1-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 4-(3-({imidazo[1,2-a]pyridin-2-yl}-2,5-dihydro-1H-pyrrole-1-carbonyl)-1H-indazole;
 20 N-[(6-[(pyridin-3-yl)methyl]amino)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 N-[(6-[(1-methyl-1H-imidazol-4-yl)methyl]amino)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 N-[(6-(3-methoxyphenyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 25 N-[(6-(1H-pyrazol-5-yl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 N-[(6-(3-chlorophenyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 N-[(6-[(pyridin-3-yl)amino]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 N-[(6-[(piperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 N-[(6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 30 N-[(6-(acetamidomethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 {6-methylimidazo[1,2-a]pyridin-2-yl)methyl 1H-indazole-4-carboxylate;
 {6-methylimidazo[1,2-a]pyridin-2-yl)methyl 1H-indazole-4-carboxylate hydrochloride;
 N-[(6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 N-[(6-hydroxyimidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 35 N-[(6-[(methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;

- N-({6-[(methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide dihydrochloride;
- N-({6-[(2-hydroxyethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;
- 5 N-({6-[(2,2,2-trifluoroethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;
- N-({6-(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- N-({6-[hydroxy(phenyl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;
- N-({6-formylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
- 10 carboxamide;
- N-({6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-[(2,2,2-trifluoroethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-({6-[(2-hydroxyethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-[(2-phenylethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-
- 20 a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-[(3-phenylpropyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[hydroxy(phenyl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-
- a]pyrimidine-2-carboxamide;
- 25 N-({6-(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-ethenylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-cyclopropylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
- 30 carboxamide;
- N-({7-ethenylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
- carboxamide;
- 35 2-(1H-indazol-4-yl)-5-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]-1,3,4-oxadiazole;

- N-{{6-(2-aminoethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H,6H,7H,8H,9H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-{{6-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- tert-butyl N-(2-{2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridin-6-yl}ethyl)carbamate;
- N-benzyl-2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridine-
- 10 6-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 7-chloro-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 15 6-chloro-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H,6H,7H,8H,9H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 6-amino-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]pyridine-
- 20 3-carboxamide;
- N-{{6-[(benzyloxy)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-7-fluoro-4-oxo-4H-
- 25 chromene-2-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-7-methyl-4-oxo-4H-chromene-2-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 30 8-chloro-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 6-bromo-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]quinoline-3-
- 35 carboxamide;

- N-[(6-{1-[(cyclohexylmethyl)amino]ethyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 6-chloro-N-[(6-{[(cyclohexylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 5 4-[5-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1,3,4-thiadiazol-2-yl]-1H-indazole;
 4-[1-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole;
 N-[(6-{[(3-chlorophenyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-{[(1-cyclohexyl-2-hydroxyethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 4-oxo-N-{[6-({[(pyridin-3-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{[6-({[(4-methoxyphenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-[(6-{[(cyclohexylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{[6-({[(4-chlorophenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-[(6-{[benzyl(methyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{[6-({[(1R)-1-phenylethyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{[6-({[(1S)-1-phenylethyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-{[6-({[(2-fluorophenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-{[(2-phenylpropan-2-yl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-{[6-({[(3-fluorophenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{[6-({[(4-fluorophenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-{[(4,4,4-trifluorobutyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35

- N-[[6-({[(oxan-4-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(3,3-difluorocyclobutyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-[[6-({[(cyclopropylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[[6-({[(3,3,3-trifluoropropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(cyclohexylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-
- 10 a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-({[(3-(trifluoromethyl)bicyclo[1.1.1]pentan-1-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(oxan-2-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 4-oxo-N-[[6-({[(3-phenyloxetan-3-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(oxan-3-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(1-fluorocyclohexyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-
- 20 4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(3-cyclopropylphenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(3,3-dimethylbutyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 4-oxo-N-{{6-({[(2-(trifluoromethoxy)ethyl)amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-({[(oxolan-2-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(2-methanesulfonyl)ethyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-
- 30 pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-[(3-phenylpyrrolidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(1-cyclohexylcyclopropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 4-oxo-N-{{6-({[(1,3-thiazol-5-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- tert-butyl 3-[[{2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amino)methyl]piperidine-1-carboxylate;
 N-[[6-[[{(4,4-difluorocyclohexyl)methyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 tert-butyl 2-[[{2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amino)methyl]piperidine-1-carboxylate;
 N-[[6-[[{(2-cyclopropylethyl)amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-[(6-[(piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-
- 10 a]pyrimidine-2-carboxamide;
 4-oxo-N-[(6-[[{(1-(2,2,2-trifluoroethyl)-1H-pyrazol-3-yl)methyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-[[{(1-methylcyclohexyl)methyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 4-oxo-N-[(6-[(2-(pyridin-3-yl)ethyl)amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-[[{(1,4-dioxan-2-yl)methyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[(6-[(cyclopropylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-
- 20 a]pyrimidine-2-carboxamide;
 N-[(6-[[{(3,3-difluorocyclobutyl)amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-[[{(oxetan-3-yl)methyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 4-oxo-N-[(6-[[{(1R,2R)-2-(trifluoromethyl)cyclopropyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[(6-[[{(2,2-dimethylpropyl)amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[(6-[[{(cyclohexylmethyl)(methyl)amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-
- 30 pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[(6-[[{(4,4-difluorocyclohexyl)amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[(6-[[{(bicyclo[1.1.1]pentan-1-yl)amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 4-oxo-N-[(6-[[{(2S)-oxolan-2-yl)methyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- 4-oxo-N-({6-([[(2R)-oxolan-2-yl]methyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(2,2-difluoroethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-({6-([[(oxolan-3-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(1-methylcyclopropyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 4-oxo-N-({6-([[(oxolan-3-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 methyl 3-methyl-2-[(2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl)amino]butanoate;
 N-({6-([[(oxan-3-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 4-oxo-N-({6-([[(2S)-3,3,3-trifluoro-2-hydroxypropyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(cyclobutyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-({6-([[(tert-butylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(2-fluoroethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(4,4-difluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-
- 25 pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(4-phenylpiperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(1,2,3,4-tetrahydroisoquinolin-2-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-({6-([[(diethylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(pyrrolidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(3-(pyridin-2-yl)azetidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-
- 35 pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(dicyclopropylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-[(6-[(cyclopropylmethyl)(methyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(4-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-[(6-[(4-(trifluoromethyl)piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(3-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-[(spiro[2.2]pentan-1-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-
- 10 4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(3,3-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-[(3-(trifluoromethyl)piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-[(6-[(5,5-dimethyloxolan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(4-fluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(3-methoxypropyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-
- 20 pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(1-methylcyclohexyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(4,4-dimethyloxolan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-[(6-[(1-methylcyclopentyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-[(propylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(3,3-dimethyloxolan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-
- 30 oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(2-methylpropyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(2-(tert-butoxy)ethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-[(6-[(4-chlorophenyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-{{6-({[2-(oxan-2-yl)ethyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(4-benzylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-{{6-[(4-phenoxy-piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2,2-difluorocyclopropyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2,2-dimethylcyclopropyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-{{6-({[(2-methyloxolan-2-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(4-tert-butylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-{{6-({[(4-tert-butylcyclohexyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2-cyclopentylethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(4-(2,2-dimethylpropanoyl)piperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-{{6-[(4-acetylpiperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[7-azabicyclo[2.2.1]heptan-7-yl)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-{{6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(2,2-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-({[(2,3,3-trimethylbutan-2-yl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-{{6-({[(5-fluoropyridin-2-yl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[1,1'-bi(cyclopropane)]-1-yl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-{{6-({[(1-fluorocyclopentyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-({6-[(2,6-dimethylmorpholin-4-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
methyl 1-({2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl)piperidine-3-carboxylate;
- 5 N-({6-[(2-fluoro-2-methylpropyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-({6-[(1-cyclohexylethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-({6-[(2-cyclopropylethyl)(methyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-({6-[(2,2-dimethylpropyl)(methyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-({6-[(1-fluorocyclobutyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-({6-[(4-fluoro-4-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-({6-[(3,3-difluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-({6-[(1-hydroxycyclohexyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-({6-[(cyclopentylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-({6-[(3,3-difluorocyclopentyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-({6-[(cyclobutylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-({6-[(2-(3,3-difluorocyclobutyl)ethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-({6-[(2-fluorocyclobutyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-({6-[(2S)-3,3-dimethylbutan-2-yl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-({6-({6-azaspiro[2.5]octan-6-yl)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 4-oxo-N-({6-[(1R,3R)-3-fluorocyclobutyl]methyl}amino)methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- 4-oxo-N-({6-[(2-phenylethyl)amino]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-[2-(benzylamino)ethyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-({6-[2-(cyclohexylamino)ethyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-[(phenylformamido)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-[(cyclohexylformamido)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-
- 10 a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(piperidin-3-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(piperidin-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-({6-([[(azetidin-3-yl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-[(cyclohexylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
 N-({6-[(2-cyclopropylethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-
- 20 chromene-2-carboxamide;
 4-oxo-N-({6-[(piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-chromene-2-carboxamide;
 N-({6-([[(4-chlorophenyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
- 25 N-({6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
 N-({6-([[(1-methylcyclohexyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
 N-({6-([[(2,2-dimethylpropyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-
- 30 chromene-2-carboxamide;
 4-oxo-N-({7-[(2-phenylethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({7-[(cyclohexylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-({7-([[(cyclopropylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-[(6-{1-[(cyclohexylmethyl)amino]cyclopropyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-(2-amino-3-phenylpropyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 (cyclohexylmethyl)[(2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methyl]amine;
- N-(cyclohexylmethyl)-2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridine-6-carboxamide;
- (2,2-dimethylpropyl)[(2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methyl]amine;
- 10 4-[1-({6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole;
- [(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methyl][(3,3-difluorocyclobutyl)methyl]amine;
- 15 [(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methyl](2,2-dimethylpropyl)amine;
- [(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methyl](cyclohexylmethyl)amine;
- 6-bromo-4-[1-({6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole;
- 20 (2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methanol;
- (2,2-dimethylpropyl)[(2-{[4-(1H-indazol-5-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methyl]amine;
- 25 ((cyclohexylmethyl)[1-(2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)ethyl]amine;
- (2,2-dimethylpropyl)({2-[(4-{1H-pyrazolo[3,4-c]pyridin-4-yl}-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl}amine;
- {2-[(4-{1H-pyrazolo[3,4-c]pyridin-4-yl}-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methanol;
- 30 N-({6-[(3R,5S)-5-tert-butylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(3S,5R)-5-tert-butylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;

5 N-({6-[4-(2,2-dimethylpropyl)morpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-({6-[(3S,5R)-5-methylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; and

10 N-({6-(9-methoxy-2,3,4,5-tetrahydro-1,4-benzoxazepin-3-yl)imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide.

[00191] Particular compounds of the present invention include any of the compounds exemplified in the present application, or a pharmaceutically acceptable salt thereof, and, in particular, any of the following:

N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

15 N-({7-bromoimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

N-({6-bromoimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

N-({6-chloroimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

N-({7-fluoroimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

N-({6-fluoroimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

20 N-({7-methoxyimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-6-(1H-pyrazol-5-yl)-1H-indazole-4-carboxamide;

N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

6-bromo-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

25 6-bromo-N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;

N-({imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;

6-ethynyl-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-

30 carboxamide;

N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;

N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-({6-cyanoimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-

35 carboxamide;

- 8-methoxy-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-5-carboxamide;
- 7-chloro-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
- 5 carboxamide;
- N-({6-fluoroimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-bromoimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-({6-methoxyimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({7-methoxyimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-({8-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-pyrazolo[4,3-c]pyridine-4-carboxamide;
- N-({7-bromoimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-(2-hydroxy-1-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;
- 4-(3-({imidazo[1,2-a]pyridin-2-yl)-2,5-dihydro-1H-pyrrole-1-carbonyl)-1H-indazole;
- N-[(6-({(pyridin-3-yl)methyl}amino)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-({(1-methyl-1H-imidazol-4-yl)methyl}amino)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-
- 25 indazole-4-carboxamide;
- N-[(6-(3-methoxyphenyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-(1H-pyrazol-5-yl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-(3-chlorophenyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-[(pyridin-3-yl)amino]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 30 N-[(6-[(piperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-(acetamidomethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- {6-methylimidazo[1,2-a]pyridin-2-yl)methyl 1H-indazole-4-carboxylate;
- {6-methylimidazo[1,2-a]pyridin-2-yl)methyl 1H-indazole-4-carboxylate hydrochloride;
- 35 N-[(6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-({6-hydroxyimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

- N-({6-[(methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 N-({6-[(methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide
 dihydrochloride;
 N-[(6-[(2-hydroxyethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-
 5 carboxamide;
 N-[(6-[(2,2,2-trifluoroethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-
 carboxamide;
 N-[(6-(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
 N-({6-[hydroxy(phenyl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
 10 N-({6-formylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
 carboxamide;
 N-[(6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
 carboxamide;
 4-oxo-N-[(6-[(2,2,2-trifluoroethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-
 15 pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[(6-[(2-hydroxyethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-
 a]pyrimidine-2-carboxamide;
 4-oxo-N-[(6-[(2-phenylethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-
 a]pyrimidine-2-carboxamide;
 20 N-({6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-
 a]pyrimidine-2-carboxamide;
 4-oxo-N-[(6-[(3-phenylpropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-
 a]pyrimidine-2-carboxamide;
 N-({6-[hydroxy(phenyl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-
 25 a]pyrimidine-2-carboxamide;
 N-[(6-(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
 carboxamide;
 N-({6-ethenylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
 carboxamide;
 30 N-({6-cyclopropylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
 carboxamide;
 N-({7-ethenylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
 carboxamide;
 N-[(6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
 35 carboxamide;
 2-(1H-indazol-4-yl)-5-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]-1,3,4-oxadiazole;

- N-{{6-(2-aminoethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H,6H,7H,8H,9H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-{{6-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- tert-butyl N-(2-{2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridin-6-yl}ethyl)carbamate;
- N-benzyl-2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridine-
- 10 6-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 7-chloro-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 15 6-chloro-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H,6H,7H,8H,9H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 6-amino-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]pyridine-
- 20 3-carboxamide;
- N-{{6-[(benzyloxy)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-7-fluoro-4-oxo-4H-
- 25 chromene-2-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-7-methyl-4-oxo-4H-chromene-2-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 30 8-chloro-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 6-bromo-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]quinoline-3-
- 35 carboxamide;

- N-[(6-{1-[(cyclohexylmethyl)amino]ethyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 6-chloro-N-[(6-{[(cyclohexylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 5 4-[5-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1,3,4-thiadiazol-2-yl]-1H-indazole;
 4-[1-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole;
 N-[(6-{[(3-chlorophenyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-{[(1-cyclohexyl-2-hydroxyethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 4-oxo-N-{[6-({[(pyridin-3-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{[6-({[(4-methoxyphenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-[(6-{[(cyclohexylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{[6-({[(4-chlorophenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-[(6-{[benzyl(methyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{[6-({[(1R)-1-phenylethyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{[6-({[(1S)-1-phenylethyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-{[6-({[(2-fluorophenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-{[(2-phenylpropan-2-yl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-{[6-({[(3-fluorophenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{[6-({[(4-fluorophenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-{[(4,4,4-trifluorobutyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35

- N-[[6-({[(oxan-4-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(3,3-difluorocyclobutyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-[[6-({[(cyclopropylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[[6-({[(3,3,3-trifluoropropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(cyclohexylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-
- 10 a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-({[(3-(trifluoromethyl)bicyclo[1.1.1]pentan-1-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(oxan-2-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 4-oxo-N-[[6-({[(3-phenyloxetan-3-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(oxan-3-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(1-fluorocyclohexyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-
- 20 4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(3-cyclopropylphenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(3,3-dimethylbutyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 4-oxo-N-{{6-({[(2-(trifluoromethoxy)ethyl)amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-({[(oxolan-2-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(2-methanesulfonyl)ethyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-
- 30 pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-[(3-phenylpyrrolidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(1-cyclohexylcyclopropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 4-oxo-N-{{6-({[(1,3-thiazol-5-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- tert-butyl 3-[[{2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amino)methyl]piperidine-1-carboxylate;
 N-[[6-[[{4,4-difluorocyclohexyl)methyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 tert-butyl 2-[[{2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amino)methyl]piperidine-1-carboxylate;
 N-[[6-[(2-cyclopropylethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 4-oxo-N-[(6-[(piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-[(6-[[{1-(2,2,2-trifluoroethyl)-1H-pyrazol-3-yl]methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-[[{1-methylcyclohexyl)methyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 4-oxo-N-[[6-[(2-(pyridin-3-yl)ethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-[[{1,4-dioxan-2-yl)methyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(cyclopropylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-[(6-[(3,3-difluorocyclobutyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-[[{(oxetan-3-yl)methyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 4-oxo-N-[[6-[[{(1R,2R)-2-(trifluoromethyl)cyclopropyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[(6-[(2,2-dimethylpropyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[[{(cyclohexylmethyl)(methyl)amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-[(6-[(4,4-difluorocyclohexyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[[{bicyclo[1.1.1]pentan-1-yl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 4-oxo-N-[(6-[[{(2S)-oxolan-2-yl]methyl]amino}methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- 4-oxo-N-({6-([[(2R)-oxolan-2-yl]methyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(2,2-difluoroethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-({6-([[(oxolan-3-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(1-methylcyclopropyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 4-oxo-N-({6-([[(oxolan-3-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 methyl 3-methyl-2-[(2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl)amino]butanoate;
 N-({6-([[(oxan-3-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 4-oxo-N-({6-([[(2S)-3,3,3-trifluoro-2-hydroxypropyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(cyclobutyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-({6-([[(tert-butylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(2-fluoroethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(4,4-difluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-
- 25 pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(4-phenylpiperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(1,2,3,4-tetrahydroisoquinolin-2-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-({6-([[(diethylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(pyrrolidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(3-(pyridin-2-yl)azetidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-
- 35 pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(dicyclopropylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-[(6-[(cyclopropylmethyl)(methyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(4-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-[(6-[(4-(trifluoromethyl)piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(3-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-[(spiro[2.2]pentan-1-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-
- 10 4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(3,3-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-[(3-(trifluoromethyl)piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-[(6-[(5,5-dimethyloxolan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(4-fluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(3-methoxypropyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-
- 20 pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(1-methylcyclohexyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(4,4-dimethyloxolan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-[(6-[(1-methylcyclopentyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-[(propylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(3,3-dimethyloxolan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-
- 30 oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(2-methylpropyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(2-(tert-butoxy)ethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-[(6-[(4-chlorophenyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-{{6-({[2-(oxan-2-yl)ethyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(4-benzylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-{{6-[(4-phenoxy-piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2,2-difluorocyclopropyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2,2-dimethylcyclopropyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-{{6-({[(2-methyloxolan-2-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(4-tert-butylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-{{6-[(4-tert-butylcyclohexyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2-cyclopentylethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(4-(2,2-dimethylpropanoyl)piperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-{{6-[(4-acetylpiperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[7-azabicyclo[2.2.1]heptan-7-yl)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-{{6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(2,2-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-({[(2,3,3-trimethylbutan-2-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-{{6-({[(5-fluoropyridin-2-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[1,1'-bi(cyclopropane)]-1-yl)amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-{{6-({[(1-fluorocyclopentyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-({6-[(2,6-dimethylmorpholin-4-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
methyl 1-({2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl)piperidine-3-carboxylate;
- 5 N-[(6-[(2-fluoro-2-methylpropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(1-cyclohexylethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(2-cyclopropylethyl)(methyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-[(6-[(2,2-dimethylpropyl)(methyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(1-fluorocyclobutyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-({6-[(4-fluoro-4-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-({6-[(3,3-difluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(1-hydroxycyclohexyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-[(6-[(cyclopentylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(3,3-difluorocyclopentyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-[(6-[(cyclobutylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(2-(3,3-difluorocyclobutyl)ethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(2-fluorocyclobutyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-[(6-[(2S)-3,3-dimethylbutan-2-yl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-({6-azaspiro[2.5]octan-6-yl)methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 4-oxo-N-({6-[(1R,3R)-3-fluorocyclobutyl]methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- 4-oxo-N-({6-[(2-phenylethyl)amino]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-[2-(benzylamino)ethyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-({6-[2-(cyclohexylamino)ethyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-[(phenylformamido)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-[(cyclohexylformamido)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-
- 10 a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(piperidin-3-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(piperidin-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-({6-([[(azetidin-3-yl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-[(cyclohexylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
 N-({6-[(2-cyclopropylethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-
- 20 chromene-2-carboxamide;
 4-oxo-N-({6-[(piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-chromene-2-carboxamide;
 N-({6-([[(4-chlorophenyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
- 25 N-({6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
 N-({6-([[(1-methylcyclohexyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
 N-({6-([[(2,2-dimethylpropyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-
- 30 chromene-2-carboxamide;
 4-oxo-N-({7-[(2-phenylethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({7-[(cyclohexylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-({7-([[(cyclopropylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-[(6-{1-[(cyclohexylmethyl)amino]cyclopropyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-{[6-(2-amino-3-phenylpropyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

5 (cyclohexylmethyl)[(2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amine;

N-(cyclohexylmethyl)-2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridine-6-carboxamide;

10 (2,2-dimethylpropyl)[(2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amine;

4-[1-({6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole;

[(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl][(3,3-difluorocyclobutyl)methyl]amine;

15 [(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl](2,2-dimethylpropyl)amine;

[(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl](cyclohexylmethyl)amine;

20 6-bromo-4-[1-({6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole;

(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methanol;

(2,2-dimethylpropyl)[(2-{[4-(1H-indazol-5-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amine;

25 ((cyclohexylmethyl)[1-(2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)ethyl]amine;

(2,2-dimethylpropyl)({2-[(4-{1H-pyrazolo[3,4-c]pyridin-4-yl}-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl)amine;

30 {2-[(4-{1H-pyrazolo[3,4-c]pyridin-4-yl}-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methanol;

N-({6-[(3R,5S)-5-tert-butylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-({6-[(3S,5R)-5-tert-butylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

35 N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;
- N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
- 5 N-({6-[4-(2,2-dimethylpropyl)morpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(3S,5R)-5-methylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-[[6-(9-methoxy-2,3,4,5-tetrahydro-1,4-benzoxazepin-3-yl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]triazol-4-yl]-1H-indazol-6-ol
- 4-[1-[[6-[(1-hydroxycyclobutyl)methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]triazol-4-yl]-1H-indazol-6-ol
- 15 1-[[[2-[[4-(5-methoxy-1H-indazol-4-yl)triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methylamino)methyl]cyclobutanol
- 1-[[[2-[[4-(6-methoxy-1H-indazol-4-yl)triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methylamino)methyl]cyclobutanol
- N-(cyclobutylmethyl)-1-[2-[[4-(6-methoxy-1H-indazol-4-yl)triazol-1-yl)methyl]imidazo[1,2-
- 20 a]pyridin-6-yl]methanamine
- N-(cyclobutylmethyl)-1-[2-[[4-(5-methoxy-1H-indazol-4-yl)triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl]methanamine
- 4-[1-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]triazol-4-yl]-1H-indazol-3-amine
- N-[[6-[(1-methoxycyclobutyl)methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-
- 25 pyrido[1,2-a]pyrimidine-2-carboxamide
- N-[[6-(1,4-oxazepan-3-yl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- N-[[6-[(2-cyano-2-methyl-propyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- 30 N-[[6-[(3-fluoro-1-bicyclo[1.1.1]pentanyl)methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- 4-oxo-N-[[6-[(spiro[3.3]heptan-2-yl)methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]pyrido[1,2-a]pyrimidine-2-carboxamide
- 4-oxo-N-[[6-[(spiro[2.3]hexan-5-yl)methylamino)methyl]imidazo[1,2-a]pyridin-2-
- 35 yl)methyl]pyrido[1,2-a]pyrimidine-2-carboxamide
- N-[[6-[(1-bicyclo[1.1.1]pentanyl)methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide

- 4-oxo-N-[[6-[(spiro[2.3]hexan-2-ylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]pyrido[1,2-a]pyrimidine-2-carboxamide
- N-[[6-[[[(2-methoxy-2-methyl-propyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- 5 N-[[6-[[[(1-methylcyclobutyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- N-[[6-(butylaminomethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- N-[[6-[[[(1-hydroxycyclopentyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- 10 N-[[6-[(2-methylbutylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- N-[[6-[(2-cyclobutylethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- 15 N-[[6-[[[(2-hydroxy-2-methyl-propyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- N-[[6-[[[(1-hydroxycyclobutyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- N-[[6-[(2-hydroxybutylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-
- 20 a]pyrimidine-2-carboxamide
- N-[[6-[[[(3-methylcyclobutyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- N-[[6-[[[(3,3-dimethylcyclobutyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- 25 N-[[6-[(2,2-dimethylbutylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- N-[[6-[[[(2S)-2-methylbutyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- 1-[[[2-[[4-(6-bromo-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-
- 30 yl]methylamino]methyl]cyclohexanol
- 1-[[[2-[[4-(6-bromo-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol
- 1-[2-[[4-(6-bromo-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]-N-(cyclobutylmethyl)methanamine
- 35 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazole-6-carboxylic acid

- 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazole-6-carboxamide
- 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-N,N-dimethyl-1H-indazole-6-carboxamide
- 5 [4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazol-6-yl]-morpholino-methanone
- 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-N-(2-hydroxyethyl)-1H-indazole-6-carboxamide
- 1-[2-[[4-(6-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]-N-
- 10 (cyclobutylmethyl)methanamine
- 1-[[[2-[[4-(6-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol
- N-[[2-[[4-(6-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methyl]-2,2-dimethyl-propan-1-amine
- 15 N-(cyclobutylmethyl)-1-[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine
- 1-[[[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclohexanol
- N-(cyclohexylmethyl)-1-[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-
- 20 a]pyridin-6-yl]methanamine
- 1-[[[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol
- 1-[[[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclopentanamine
- 25 N-[[6-[(4,4-dimethyl-1-piperidyl)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-5-fluoro-4-oxo-chromene-2-carboxamide
- N-(cyclobutylmethyl)-1-[2-[[4-(6-morpholino-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine
- 6-[2-(2-aminoethoxy)ethoxy]-N-[[6-[(4,4-dimethyl-1-piperidyl)methyl]imidazo[1,2-a]pyridin-2-
- 30 yl]methyl]-1H-indazole-4-carboxamide
- N-[[6-[1-(cyclobutylmethylamino)-2-phenyl-ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- N-[[6-[1-[bis(cyclobutylmethyl)amino]-2-phenyl-ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
- 35 1-[2-[[4-(7-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]-N-(cyclobutylmethyl)methanamine

- 1-[[[2-[[4-(7-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol
 [2-[[4-(6-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanol
 N-(cyclobutylmethyl)-1-[2-[[4-(6-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-
 5 a]pyridin-6-yl]methanamine
 1-[[[2-[[4-(6-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol
 N-(cyclohexylmethyl)-1-[2-[[4-(6-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-
 a]pyridin-6-yl]methanamine
 10 N-[[2-[[4-(6-cyclopropyl-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methyl]-
 2,2-dimethyl-propan-1-amine
 N-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-1H-indazole-4-
 carboxamide
 N-(cyclobutylmethyl)-1-[2-[[4-(1H-pyrazolo[4,3-c]pyridin-4-yl)triazol-1-yl]methyl]imidazo[1,2-
 15 a]pyridin-6-yl]methanamine
 N-(cyclohexylmethyl)-1-[2-[[4-(1H-pyrazolo[4,3-c]pyridin-4-yl)triazol-1-yl]methyl]imidazo[1,2-
 a]pyridin-6-yl]methanamine
 1-[[[2-[[4-(1H-pyrazolo[4,3-c]pyridin-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol
 20 N-(cyclobutylmethyl)-1-[2-[[4-(1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine
 1-[[[2-[[4-(1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclohexanol
 2-[[4-(1H-indazol-4-yl)imidazol-1-yl]methyl]-6-methyl-imidazo[1,2-a]pyridine
 25 N-[[6-[2-cyano-1-(cyclobutylmethylamino)ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-
 pyrido[1,2-a]pyrimidine-2-carboxamide
 N-[[6-(6-methylmorpholin-3-yl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-
 a]pyrimidine-2-carboxamide
 N-[[6-(7-bromo-9-methoxy-2,3,4,5-tetrahydro-1,4-benzoxazepin-3-yl)imidazo[1,2-a]pyridin-2-
 30 yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide
 4-oxo-N-[(6-piperazin-2-ylimidazo[1,2-a]pyridin-2-yl)methyl]pyrido[1,2-a]pyrimidine-2-
 carboxamide
 N-[[6-(6-cyclohexyl-4-oxo-2-piperidyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-
 a]pyrimidine-2-carboxamide
 35 1-[2-(1H-indazol-4-yl)thiazol-5-yl]-1-(6-methylimidazo[1,2-a]pyridin-2-yl)ethanol
 2-[[1-(1H-indazol-4-yl)triazol-4-yl]methyl]imidazo[1,2-a]pyridine

N-[(3,3-difluorocyclobutyl)methyl]-1-[2-[[1-(1H-indazol-4-yl)triazol-4-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine

4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazole-6-carbonitrile

- 5 N-(cyclobutylmethyl)-1-[2-[[4-(1H-indazol-4-yl)imidazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine

N-[[6-[[acetyl(cyclobutylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide

- 10 N-(cyclobutylmethyl)-1-[2-[[3-(1H-indazol-4-yl)-1,2,4-triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine

2-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]pyrido[1,2-a]pyrimidin-4-one

N-[[6-[(2-bicyclo[2.2.1]hept-5-enylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide

- 15 N-[[6-[[[(1R,2R,4S)-norbornan-2-yl]methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide

N-[[6-[[[(1R,2S,4S)-norbornan-2-yl]methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide

- 20 N-[[6-(2-oxa-5-azabicyclo[2.2.1]heptan-5-ylmethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide

N-[[6-(2-azabicyclo[2.2.1]heptan-2-ylmethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide

N-[[6-(2-azabicyclo[2.2.2]octan-2-ylmethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide

- 25 N-[[6-[[[(2,2-difluorospiro[3.3]heptan-6-yl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide

4-oxo-N-[[6-[[[rac-(1S,2S,4S)-7-oxabicyclo[2.2.1]hept-5-en-2-yl]methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]pyrido[1,2-a]pyrimidine-2-carboxamide

- 30 4-oxo-N-[[6-[[[rac-(1S,2R,4S)-7-oxabicyclo[2.2.1]hept-5-en-2-yl]methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]pyrido[1,2-a]pyrimidine-2-carboxamide; and

N-[(1-methoxycyclobutyl)methyl]-1-[2-[[4-(6-methoxy-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine.

- 35 **[00192]** The various functional groups and substituents making up the compounds of the formula (I) are typically chosen such that the molecular weight of the compound of the formula

(l) does not exceed 1000. More usually, the molecular weight of the compound will be less than 900, for example less than 800, or less than 750, or less than 700, or less than 650. More preferably, the molecular weight is less than 600 and, for example, is 550 or less.

[00193] A suitable pharmaceutically acceptable salt of a compound of the invention is, for example, an acid-addition salt of a compound of the invention which is sufficiently basic, for example, an acid-addition salt with, for example, an inorganic or organic acid, for example hydrochloric, hydrobromic, sulfuric, phosphoric, trifluoroacetic, formic, citric methane sulfonate or maleic acid. In addition, a suitable pharmaceutically acceptable salt of a compound of the invention which is sufficiently acidic is an alkali metal salt, for example a sodium or potassium salt, an alkaline earth metal salt, for example a calcium or magnesium salt, an ammonium salt or a salt with an organic base which affords a pharmaceutically acceptable cation, for example a salt with methylamine, dimethylamine, trimethylamine, piperidine, morpholine or tris-(2-hydroxyethyl)amine.

[00194] Compounds that have the same molecular formula but differ in the nature or sequence of bonding of their atoms or the arrangement of their atoms in space are termed "isomers". Isomers that differ in the arrangement of their atoms in space are termed "stereoisomers". Stereoisomers that are not mirror images of one another are termed "diastereomers" and those that are non-superimposable mirror images of each other are termed "enantiomers". When a compound has an asymmetric center, for example, it is bonded to four different groups, a pair of enantiomers is possible. An enantiomer can be characterized by the absolute configuration of its asymmetric center and is described by the R- and S-sequencing rules of Cahn and Prelog, or by the manner in which the molecule rotates the plane of polarized light and designated as dextrorotatory or levorotatory (i.e., as (+) or (-)-isomers respectively). A chiral compound can exist as either individual enantiomer or as a mixture thereof. A mixture containing equal proportions of the enantiomers is called a "racemic mixture".

[00195] The compounds of this invention may possess one or more asymmetric centers; such compounds can therefore be produced as individual (R)- or (S)-stereoisomers or as mixtures thereof. Unless indicated otherwise, the description or naming of a particular compound in the specification and claims is intended to include both individual enantiomers and mixtures, racemic or otherwise, thereof. The methods for the determination of stereochemistry and the separation of stereoisomers are well-known in the art (see discussion in Chapter 4 of "Advanced Organic Chemistry", 4th edition J. March, John Wiley and Sons, New York, 2001), for example by synthesis from optically active starting materials or by resolution of a racemic form. Some of the compounds of the invention may have geometric isomeric centres (E- and Z- isomers). It is to be understood that the present invention encompasses all optical,

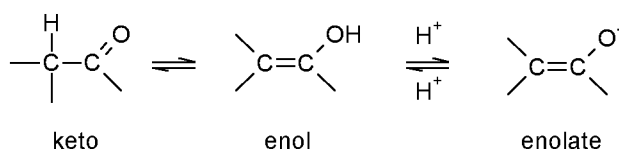
diastereoisomers and geometric isomers and mixtures thereof that possess antiproliferative activity.

[00196] The present invention also encompasses compounds of the invention as defined herein which comprise one or more isotopic substitutions. For example, H may be in any isotopic form, including ^1H , $^2\text{H}(\text{D})$, and $^3\text{H}(\text{T})$; C may be in any isotopic form, including ^{12}C , ^{13}C , and ^{14}C ; and O may be in any isotopic form, including ^{16}O and ^{18}O ; and the like.

[00197] It is also to be understood that certain compounds of the formula (I) (and compounds of formula (II), (III) and (IV)) may exist in solvated as well as unsolvated forms such as, for example, hydrated forms. It is to be understood that the invention encompasses all such solvated forms that possess antiproliferative activity.

[00198] It is also to be understood that certain compounds of the formula (I) (and compounds of formula (II), (III) and (IV)) may exhibit polymorphism, and that the invention encompasses all such forms that possess antiproliferative activity.

[00199] Compounds of the formula (I) (and compounds of formula (II), (III) and (IV)) may exist in a number of different tautomeric forms and references to compounds of the formula (I) include all such forms. For the avoidance of doubt, where a compound can exist in one of several tautomeric forms, and only one is specifically described or shown, all others are nevertheless embraced by formula (I). Examples of tautomeric forms include keto-, enol-, and enolate-forms, as in, for example, the following tautomeric pairs: keto/enol (illustrated below), imine/enamine, amide/imino alcohol, amidine/amidine, nitroso/oxime, thioketone/enethiol, and nitro/aci-nitro.



[00200] Compounds of the formula (I) containing an amine function may also form N-oxides. A reference herein to a compound of the formula (I) that contains an amine function also includes the N-oxide. Where a compound contains several amine functions, one or more than one nitrogen atom may be oxidised to form an N-oxide. Particular examples of N-oxides are the N-oxides of a tertiary amine or a nitrogen atom of a nitrogen-containing heterocycle. N-Oxides can be formed by treatment of the corresponding amine with an oxidizing agent such as hydrogen peroxide or a per-acid (e.g. a peroxycarboxylic acid), see for example *Advanced Organic Chemistry*, by Jerry March, 4th Edition, Wiley Interscience, pages. More particularly, N-oxides can be made by the procedure of L. W. Deady (*Syn. Comm.* 1977, 7, 509-514) in

which the amine compound is reacted with *m*-chloroperoxybenzoic acid (*m*CPBA), for example, in an inert solvent such as dichloromethane.

[00201] The compounds of formula (I) may be administered in the form of a pro-drug which is broken down in the human or animal body to release a compound of the invention. A pro-drug may be used to alter the physical properties and/or the pharmacokinetic properties of a compound of the invention. A pro-drug can be formed when the compound of the invention contains a suitable group or substituent to which a property-modifying group can be attached. Examples of pro-drugs include *in vivo* cleavable ester derivatives that may be formed at a carboxy group or a hydroxy group in a compound of the formula (I) and *in-vivo* cleavable amide derivatives that may be formed at a carboxy group or an amino group in a compound of the formula (I).

[00202] Accordingly, the present invention includes those compounds of the formula I as defined hereinbefore when made available by organic synthesis and when made available within the human or animal body by way of cleavage of a pro-drug thereof. Accordingly, the present invention includes those compounds of the formula (I) that are produced by organic synthetic means and also such compounds that are produced in the human or animal body by way of metabolism of a precursor compound, that is a compound of the formula (I) may be a synthetically-produced compound or a metabolically-produced compound.

[00203] A suitable pharmaceutically acceptable pro-drug of a compound of the formula (I) is one that is based on reasonable medical judgement as being suitable for administration to the human or animal body without undesirable pharmacological activities and without undue toxicity.

[00204] Various forms of pro-drug have been described, for example in the following documents :-

- a) Methods in Enzymology, Vol. 42, p. 309-396, edited by K. Widder, *et al.* (Academic Press, 1985);
- b) Design of Pro-drugs, edited by H. Bundgaard, (Elsevier, 1985);
- c) A Textbook of Drug Design and Development, edited by Krogsgaard-Larsen and H. Bundgaard, Chapter 5 "Design and Application of Pro-drugs", by H. Bundgaard p. 113-191 (1991);
- d) H. Bundgaard, Advanced Drug Delivery Reviews, 8, 1-38 (1992);
- e) H. Bundgaard, *et al.*, Journal of Pharmaceutical Sciences, 77, 285 (1988);
- f) N. Kakeya, *et al.*, Chem. Pharm. Bull., 32, 692 (1984);

g) T. Higuchi and V. Stella, "Pro-Drugs as Novel Delivery Systems", A.C.S. Symposium Series, Volume 14; and

h) E. Roche (editor), "Bioreversible Carriers in Drug Design", Pergamon Press, 1987.

[00205] A suitable pharmaceutically acceptable pro-drug of a compound of the formula

(I) that possesses a carboxy group is, for example, an *in vivo* cleavable ester thereof. An *in vivo* cleavable ester of a compound of the formula (I) containing a carboxy group is, for example, a pharmaceutically acceptable ester which is cleaved in the human or animal body to produce the parent acid. Suitable pharmaceutically acceptable esters for carboxy include C₁₋₆alkyl esters such as methyl, ethyl and *tert*-butyl, C₁₋₆alkoxymethyl esters such as methoxymethyl esters, C₁₋₆alkanoyloxymethyl esters such as pivaloyloxymethyl esters, 3-phthalidyl esters, C₃₋₈cycloalkylcarbonyloxy- C₁₋₆alkyl esters such as cyclopentylcarbonyloxymethyl and 1-cyclohexylcarbonyloxyethyl esters, 2-oxo-1,3-dioxolenylmethyl esters such as 5-methyl-2-oxo-1,3-dioxolen-4-ylmethyl esters and C₁₋₆alkoxycarbonyloxy- C₁₋₆alkyl esters such as methoxycarbonyloxymethyl and 1-methoxycarbonyloxyethyl esters.

[00206] A suitable pharmaceutically acceptable pro-drug of a compound of the formula

(I) that possesses a hydroxy group is, for example, an *in vivo* cleavable ester or ether thereof. An *in vivo* cleavable ester or ether of a compound of the formula (I) containing a hydroxy group is, for example, a pharmaceutically acceptable ester or ether which is cleaved in the human or animal body to produce the parent hydroxy compound. Suitable pharmaceutically acceptable ester forming groups for a hydroxy group include inorganic esters such as phosphate esters (including phosphoramidic cyclic esters). Further suitable pharmaceutically acceptable ester forming groups for a hydroxy group include C₁₋₁₀alkanoyl groups such as acetyl, benzoyl, phenylacetyl and substituted benzoyl and phenylacetyl groups, C₁₋₁₀alkoxycarbonyl groups such as ethoxycarbonyl, *N,N*-(C₁₋₆)₂carbamoyl, 2-dialkylaminoacetyl and 2-carboxyacetyl groups. Examples of ring substituents on the phenylacetyl and benzoyl groups include aminomethyl, *N*-alkylaminomethyl, *N,N*-dialkylaminomethyl, morpholinomethyl, piperazin-1-ylmethyl and 4-(C₁₋₄alkyl)piperazin-1-ylmethyl. Suitable pharmaceutically acceptable ether forming groups for a hydroxy group include α -acyloxyalkyl groups such as acetoxymethyl and pivaloyloxymethyl groups.

[00207] A suitable pharmaceutically acceptable pro-drug of a compound of the formula

(I) that possesses a carboxy group is, for example, an *in vivo* cleavable amide thereof, for example an amide formed with an amine such as ammonia, a C₁₋₄alkylamine such as methylamine, a (C₁₋₄alkyl)₂amine such as dimethylamine, *N*-ethyl-*N*-methylamine or diethylamine, a C₁₋₄alkoxy- C₂₋₄alkylamine such as 2-methoxyethylamine, a phenyl-C₁₋

4alkylamine such as benzylamine and amino acids such as glycine or an ester thereof.

[00208] A suitable pharmaceutically acceptable pro-drug of a compound of the formula (I) that possesses an amino group is, for example, an *in vivo* cleavable amide derivative thereof. Suitable pharmaceutically acceptable amides from an amino group include, for
5 example an amide formed with C₁₋₁₀alkanoyl groups such as an acetyl, benzoyl, phenylacetyl and substituted benzoyl and phenylacetyl groups. Examples of ring substituents on the phenylacetyl and benzoyl groups include aminomethyl, *N*-alkylaminomethyl, *N,N*-dialkylaminomethyl, morpholinomethyl, piperazin-1-ylmethyl and 4-(C₁₋₄alkyl)piperazin-1-ylmethyl.

10 [00209] The *in vivo* effects of a compound of the formula (I) may be exerted in part by one or more metabolites that are formed within the human or animal body after administration of a compound of the formula (I). As stated hereinbefore, the *in vivo* effects of a compound of the formula (I) may also be exerted by way of metabolism of a precursor compound (a pro-drug).

15 [00210] Though the present invention may relate to any compound or particular group of compounds defined herein by way of optional, preferred or suitable features or otherwise in terms of particular embodiments, the present invention may also relate to any compound or particular group of compounds that specifically excludes said optional, preferred or suitable features or particular embodiments.

20 [00211] Suitably, the present invention excludes any individual compounds not possessing the biological activity defined herein.

Synthesis

[00212] The compounds of the present invention can be prepared by any suitable technique known in the art. Particular processes for the preparation of these compounds are
25 described further in the accompanying examples.

[00213] In the description of the synthetic methods described herein and in any referenced synthetic methods that are used to prepare the starting materials, it is to be understood that all proposed reaction conditions, including choice of solvent, reaction atmosphere, reaction temperature, duration of the experiment and workup procedures, can
30 be selected by a person skilled in the art.

[00214] It is understood by one skilled in the art of organic synthesis that the functionality present on various portions of the molecule must be compatible with the reagents and reaction conditions utilised.

[00215] It will be appreciated that during the synthesis of the compounds of the invention in the processes defined herein, or during the synthesis of certain starting materials, it may be desirable to protect certain substituent groups to prevent their undesired reaction. The skilled chemist will appreciate when such protection is required, and how such protecting groups may be put in place, and later removed.

[00216] For examples of protecting groups see one of the many general texts on the subject, for example, 'Protective Groups in Organic Synthesis' by Theodora Green (publisher: John Wiley & Sons). Protecting groups may be removed by any convenient method described in the literature or known to the skilled chemist as appropriate for the removal of the protecting group in question, such methods being chosen so as to effect removal of the protecting group with the minimum disturbance of groups elsewhere in the molecule.

[00217] Thus, if reactants include, for example, groups such as amino, carboxy or hydroxy it may be desirable to protect the group in some of the reactions mentioned herein.

[00218] By way of example, a suitable protecting group for an amino or alkylamino group is, for example, an acyl group, for example an alkanoyl group such as acetyl, an alkoxycarbonyl group, for example a methoxycarbonyl, ethoxycarbonyl or *t*-butoxycarbonyl group, an arylmethoxycarbonyl group, for example benzyloxycarbonyl, or an aroyl group, for example benzoyl. The deprotection conditions for the above protecting groups necessarily vary with the choice of protecting group. Thus, for example, an acyl group such as an alkanoyl or alkoxycarbonyl group or an aroyl group may be removed by, for example, hydrolysis with a suitable base such as an alkali metal hydroxide, for example lithium or sodium hydroxide. Alternatively an acyl group such as a *tert*-butoxycarbonyl group may be removed, for example, by treatment with a suitable acid as hydrochloric, sulfuric or phosphoric acid or trifluoroacetic acid and an arylmethoxycarbonyl group such as a benzyloxycarbonyl group may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon, or by treatment with a Lewis acid for example boron tris(trifluoroacetate). A suitable alternative protecting group for a primary amino group is, for example, a phthaloyl group which may be removed by treatment with an alkylamine, for example dimethylaminopropylamine, or with hydrazine.

[00219] A suitable protecting group for a hydroxy group is, for example, an acyl group, for example an alkanoyl group such as acetyl, an aroyl group, for example benzoyl, or an arylmethyl group, for example benzyl. The deprotection conditions for the above protecting groups will necessarily vary with the choice of protecting group. Thus, for example, an acyl group such as an alkanoyl or an aroyl group may be removed, for example, by hydrolysis with a suitable base such as an alkali metal hydroxide, for example lithium, sodium hydroxide or

ammonia. Alternatively an arylmethyl group such as a benzyl group may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon.

[00220] A suitable protecting group for a carboxy group is, for example, an esterifying group, for example a methyl or an ethyl group which may be removed, for example, by hydrolysis with a base such as sodium hydroxide, or for example a *t*-butyl group which may be removed, for example, by treatment with an acid, for example an organic acid such as trifluoroacetic acid, or for example a benzyl group which may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon.

[00221] Resins may also be used as a protecting group.

[00222] The methodology employed to synthesise a compound of formula I will vary depending on the nature of the variable groups. Suitable processes for their preparation are described further in the accompanying Examples.

[00223] Once a compound of formula I has been synthesised by any one of the processes defined herein, the processes may then further comprise the additional steps of:

- (i) removing any protecting groups present;
- (ii) converting the compound formula I into another compound of formula I;
- (iii) forming a pharmaceutically acceptable salt, hydrate or solvate thereof; and/or
- (iv) forming a prodrug thereof.

[00224] The resultant compounds of formula I can be isolated and purified using techniques well known in the art.

Biological Activity

[00225] The METTL3 enzyme and cell assays described in accompanying Example section may be used to measure the pharmacological effects of the compounds of the present invention.

[00226] Although the pharmacological properties of the compounds of formula I vary with structural change, as expected, the compounds of the invention were found to be active in these METTL3 assays.

[00227] In general, the compounds of the invention demonstrate an IC_{50} of 10 μM or less in the METTL3 enzyme assay described herein, with preferred compounds of the invention demonstrating an IC_{50} of 5 μM or less and the most preferred compounds of the invention demonstrating an IC_{50} of 2 μM or less.

[00228] In the METTL3 cell assay described in the Example section, the compounds of formula (I) suitably possess an activity of less than 10 μ M, with preferred compounds of the invention demonstrating an IC₅₀ of 5 μ M or less and the most preferred compounds demonstrating an activity of 2 μ M or less.

5 Pharmaceutical Compositions

[00229] According to a further aspect of the invention there is provided a pharmaceutical composition which comprises a compound of the invention as defined hereinbefore, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable excipients.

10 [00230] The compositions of the invention may be in a form suitable for oral use (for example as tablets, lozenges, hard or soft capsules, aqueous or oily suspensions, emulsions, dispersible powders or granules, syrups or elixirs), for topical use (for example as creams, ointments, gels, or aqueous or oily solutions or suspensions), for administration by inhalation (for example as a finely divided powder or a liquid aerosol), for administration by insufflation
15 (for example as a finely divided powder) or for parenteral administration (for example as a sterile aqueous or oily solution for intravenous, subcutaneous, intramuscular, intraperitoneal or intramuscular dosing or as a suppository for rectal dosing).

[00231] The compositions of the invention may be obtained by conventional procedures using conventional pharmaceutical excipients, well known in the art. Thus, compositions
20 intended for oral use may contain, for example, one or more colouring, sweetening, flavouring and/or preservative agents.

[00232] An effective amount of a compound of the present invention for use in therapy is an amount sufficient to treat or prevent a proliferative condition and/or treat or prevent an autoimmune disease referred to herein, slow its progression and/or reduce the symptoms
25 associated with the condition and/or disease.

[00233] The amount of active ingredient that is combined with one or more excipients to produce a single dosage form will necessarily vary depending upon the individual treated and the particular route of administration. For example, a formulation intended for oral administration to humans will generally contain, for example, from 0.5 mg to 0.5 g of active
30 agent (more suitably from 0.5 to 100 mg, for example from 1 to 30 mg) compounded with an appropriate and convenient amount of excipients which may vary from about 5 to about 98 percent by weight of the total composition.

[00234] The size of the dose for therapeutic or prophylactic purposes of a compound of the formula (I) will naturally vary according to the nature and severity of the conditions, the

age and sex of the animal or patient and the route of administration, according to well known principles of medicine.

[00235] In using a compound of the invention for therapeutic or prophylactic purposes it will generally be administered so that a daily dose in the range, for example, 0.1 mg/kg to 75 mg/kg body weight is received, given if required in divided doses. In general lower doses will be administered when a parenteral route is employed. Thus, for example, for intravenous or intraperitoneal administration, a dose in the range, for example, 0.1 mg/kg to 30 mg/kg body weight will generally be used. Similarly, for administration by inhalation, a dose in the range, for example, 0.05 mg/kg to 25 mg/kg body weight will be used. Oral administration may also be suitable, particularly in tablet form. Typically, unit dosage forms will contain about 0.5 mg to 0.5 g of a compound of this invention.

Therapeutic Uses and Applications

[00236] The present invention provides compounds that function as inhibitors of METTL3 activity.

[00237] The present invention therefore provides a method of inhibiting METTL3 activity *in vitro* or *in vivo*, said method comprising contacting a cell with an effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00238] The present invention also provides a method of treating a disease or disorder in which METTL3 activity is implicated in a patient in need of such treatment, said method comprising administering to said patient a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein. Suitably, the disease or disorder in which METTL3 activity is implicated is cancer, such as lung cancer, renal cancer, solid organ cancer, pancreatic cancer or leukaemia, type 2 diabetes, a neuropsychiatric behavioural disorder or a depressive disorder.

[00239] The present invention provides a method of inhibiting cell proliferation, *in vitro* or *in vivo*, said method comprising contacting a cell with an effective amount of a compound, or a pharmaceutically acceptable salt thereof, as defined herein.

[00240] The present invention provides a method of treating a proliferative disorder, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00241] The present invention provides a method of treating cancer, said method comprising administering to a subject in need thereof a therapeutically effective amount of a

compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein. Suitably the cancer is lung cancer, renal cancer, solid organ cancer, pancreatic cancer or leukaemia suitably AML leukaemia or chronic myeloid leukaemia.

[00242] The present invention provides a method of treating leukaemia, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00243] The present invention provides a method of treating AML leukaemia, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00244] The present invention provides a method of treating an autoimmune disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein. Suitably the autoimmune disease is colitis, multiple sclerosis, rheumatoid arthritis, lupus, cirrhosis, or dermatitis.

[00245] The present invention provides a method of treating a neurological disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00246] The present invention provides a method of treating an infectious disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00247] The present invention provides a method of treating an inflammatory disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein.

[00248] The present invention provides a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein for use in therapy.

[00249] The present invention provides a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein for use in the treatment of a proliferative condition.

[00250] The present invention provides a compound, or a pharmaceutically acceptable

salt thereof, or a pharmaceutical composition as defined herein for use in the treatment of cancer. In a particular embodiment, the cancer is human cancer. Suitably the cancer is lung cancer, renal cancer, solid organ cancer, pancreatic cancer or leukaemia suitably AML leukaemia or chronic myeloid leukaemia.

5 **[00251]** The present invention provides a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein for use in the treatment of leukaemia.

10 **[00252]** The present invention provides a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein for use in the treatment of AML leukaemia.

[00253] The present invention provides a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein for use in the inhibition of METTL3 activity.

15 **[00254]** The present invention provides a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein for use in the treatment of an autoimmune disease. Suitably the autoimmune disease is colitis, multiple sclerosis, rheumatoid arthritis, lupus, cirrhosis, or dermatitis.

20 **[00255]** The present invention provides a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein for use in the treatment of an neurological disease.

[00256] The present invention provides a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein for use in the treatment of an infectious disease.

25 **[00257]** The present invention provides a compound, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as defined herein for use in the treatment of an inflammatory disease.

30 **[00258]** The present invention provides a compound, or a pharmaceutically acceptable salt thereof, as defined herein for use in the treatment of a disease or disorder in which METTL3 activity is implicated. Suitably, the disease or disorder in which METTL3 activity is implicated is cancer, such as lung cancer, renal cancer, solid organ cancer, pancreatic cancer or leukaemia, type 2 diabetes, a neuropsychiatric behavioural disorder or a depressive disorder.

[00259] The present invention provides a use of a compound, or a pharmaceutically acceptable salt thereof, as defined herein in the manufacture of a medicament for the

treatment of a proliferative condition.

[00260] The present invention provides a use of a compound, or a pharmaceutically acceptable salt thereof, as defined herein in the manufacture of a medicament for the treatment of cancer. Suitably, the medicament is for use in the treatment of human cancers.

5 Suitably the cancer is lung cancer, renal cancer, solid organ cancer, pancreatic cancer or leukaemia suitably AML leukaemia or chronic myeloid leukaemia.

[00261] The present invention provides a use of a compound, or a pharmaceutically acceptable salt thereof, as defined herein in the manufacture of a medicament for the treatment of leukaemia.

10 **[00262]** The present invention provides a use of a compound, or a pharmaceutically acceptable salt thereof, as defined herein in the manufacture of a medicament for the treatment of AML leukaemia.

[00263] The present invention provides a use of a compound, or a pharmaceutically acceptable salt thereof, as defined herein in the manufacture of a medicament for the
15 treatment of an autoimmune disease. Suitably the autoimmune disease is colitis, multiple sclerosis, rheumatoid arthritis, lupus, cirrhosis, or dermatitis.

[00264] The present invention provides a use of a compound, or a pharmaceutically acceptable salt thereof, as defined herein in the manufacture of a medicament for the treatment of a neurological disease.

20 **[00265]** The present invention provides a use of a compound, or a pharmaceutically acceptable salt thereof, as defined herein in the manufacture of a medicament for the treatment of an inflammatory disease.

[00266] The present invention provides a use of a compound, or a pharmaceutically acceptable salt thereof, as defined herein in the manufacture of a medicament for the
25 treatment of an infectious disease.

[00267] The present invention provides a use of a compound, or a pharmaceutically acceptable salt thereof, as defined herein in the manufacture of a medicament for the inhibition of METTL3 activity.

[00268] The present invention provides a use of a compound, or a pharmaceutically
30 acceptable salt thereof, as defined herein in the manufacture of a medicament for the treatment of a disease or disorder in which METTL3 activity is implicated. Suitably, the disease or disorder in which METTL3 activity is implicated is cancer, such as lung cancer, renal cancer, solid organ cancer, pancreatic cancer or leukaemia, type 2 diabetes, a neuropsychiatric behavioural disorder or a depressive disorder.

[00269] The term "proliferative disorder" are used interchangeably herein and pertain to an unwanted or uncontrolled cellular proliferation of excessive or abnormal cells which is undesired, such as, neoplastic or hyperplastic growth, whether *in vitro* or *in vivo*. Examples of proliferative conditions include, but are not limited to, pre-malignant and malignant cellular proliferation, including but not limited to, malignant neoplasms and tumours, cancers, leukemias, psoriasis, bone diseases, fibroproliferative disorders (e.g., of connective tissues), and atherosclerosis. Any type of cell may be treated, including but not limited to, lung, colon, breast, ovarian, prostate, liver, pancreas, brain and skin.

[00270] The anti-proliferative effects of the compounds of the present invention have particular application in the treatment of human cancers (by virtue of their inhibition of METTL3 activity).

[00271] The anti-cancer effect may arise through one or more mechanisms, including but not limited to, the regulation of cell proliferation, the inhibition of angiogenesis (the formation of new blood vessels), the inhibition of metastasis (the spread of a tumour from its origin), the inhibition of invasion (the spread of tumour cells into neighbouring normal structures), or the promotion of apoptosis (programmed cell death).

[00272] In a particular embodiment of the invention, the proliferative condition to be treated is cancer.

Routes of Administration

[00273] The compounds of the invention or pharmaceutical compositions comprising these compounds may be administered to a subject by any convenient route of administration, whether systemically/ peripherally or topically (i.e., at the site of desired action).

[00274] Routes of administration include, but are not limited to, oral (e.g, by ingestion); buccal; sublingual; transdermal (including, e.g., by a patch, plaster, etc.); transmucosal (including, e.g., by a patch, plaster, etc.); intranasal (e.g., by nasal spray); ocular (e.g., by eye drops); pulmonary (e.g., by inhalation or insufflation therapy using, e.g., via an aerosol, e.g., through the mouth or nose); rectal (e.g., by suppository or enema); vaginal (e.g., by pessary); parenteral, for example, by injection, including subcutaneous, intradermal, intramuscular, intravenous, intra-arterial, intracardiac, intrathecal, intraspinal, intracapsular, subcapsular, intraorbital, intraperitoneal, intratracheal, subcuticular, intraarticular, subarachnoid, and intrasternal; by implant of a depot or reservoir, for example, subcutaneously or intramuscularly.

Combination Therapies

[00275] The antiproliferative treatment defined hereinbefore may be applied as a sole therapy or may involve, in addition to the compound of the invention, conventional surgery or

radiotherapy or chemotherapy. Such chemotherapy may include one or more of the following categories of anti-tumour agents:-

- (i) other antiproliferative/antineoplastic drugs and combinations thereof, as used in medical oncology, such as alkylating agents (for example cis-platin, oxaliplatin, carboplatin, cyclophosphamide, nitrogen mustard, melphalan, chlorambucil, busulphan, temozolamide and nitrosoureas); antimetabolites (for example gemcitabine and antifolates such as fluoropyrimidines like 5-fluorouracil and tegafur, raltitrexed, methotrexate, cytosine arabinoside, and hydroxyurea); antitumour antibiotics (for example anthracyclines like adriamycin, bleomycin, doxorubicin, daunomycin, epirubicin, idarubicin, mitomycin-C, dactinomycin and mithramycin); antimitotic agents (for example vinca alkaloids like vincristine, vinblastine, vindesine and vinorelbine and taxoids like taxol and taxotere and polokinese inhibitors); and topoisomerase inhibitors (for example epipodophyllotoxins like etoposide and teniposide, amsacrine, topotecan and camptothecin);
- (ii) cytostatic agents such as antioestrogens (for example tamoxifen, fulvestrant, toremifene, raloxifene, droloxifene and idoxifene), antiandrogens (for example bicalutamide, flutamide, nilutamide and cyproterone acetate), LHRH antagonists or LHRH agonists (for example goserelin, leuprorelin and buserelin), progestogens (for example megestrol acetate), aromatase inhibitors (for example as anastrozole, letrozole, vorazole and exemestane) and inhibitors of 5 α -reductase such as finasteride;
- (iii) anti-invasion agents [for example c-Src kinase family inhibitors like 4-(6-chloro-2,3-methylenedioxyanilino)-7-[2-(4-methylpiperazin-1-yl)ethoxy]-5-tetrahydropyran-4-yloxyquinazoline (AZD0530; International Patent Application WO 01/94341), *N*-(2-chloro-6-methylphenyl)-2-{6-[4-(2-hydroxyethyl)piperazin-1-yl]-2-methylpyrimidin-4-ylamino}thiazole-5-carboxamide (dasatinib, BMS-354825; *J. Med. Chem.*, 2004, **47**, 6658-6661) and bosutinib (SKI-606), and metalloproteinase inhibitors like marimastat, inhibitors of urokinase plasminogen activator receptor function or antibodies to Heparanase];
- (iv) inhibitors of growth factor function: for example such inhibitors include growth factor antibodies and growth factor receptor antibodies (for example the anti-erbB2 antibody trastuzumab [HerceptinTM], the anti-EGFR antibody panitumumab, the anti-erbB1 antibody cetuximab [Erbix, C225] and any growth factor or growth factor receptor antibodies disclosed by Stern *et al.* (Critical reviews in oncology/haematology, 2005, Vol. 54, pp11-29); such inhibitors also include tyrosine kinase inhibitors, for example inhibitors of the epidermal growth factor family (for example EGFR family tyrosine kinase inhibitors such as *N*-(3-chloro-4-fluorophenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine (gefitinib, ZD1839), *N*-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine (erlotinib, OSI-774) and 6-

acrylamido-*N*-(3-chloro-4-fluorophenyl)-7-(3-morpholinopropoxy)-quinazolin-4-amine (CI 1033), erbB2 tyrosine kinase inhibitors such as lapatinib); inhibitors of the hepatocyte growth factor family; inhibitors of the insulin growth factor family; inhibitors of the platelet-derived growth factor family such as imatinib and/or nilotinib (AMN107); inhibitors of serine/threonine
 5 kinases (for example Ras/Raf signalling inhibitors such as farnesyl transferase inhibitors, for example sorafenib (BAY 43-9006), tipifarnib (R115777) and lonafarnib (SCH66336)), inhibitors of cell signalling through MEK and/or AKT kinases, c-kit inhibitors, abl kinase inhibitors, PI3 kinase inhibitors, Plt3 kinase inhibitors, CSF-1R kinase inhibitors, IGF receptor (insulin-like growth factor) kinase inhibitors; aurora kinase inhibitors (for example AZD1152,
 10 PH739358, VX-680, MLN8054, R763, MP235, MP529, VX-528 AND AX39459) and cyclin dependent kinase inhibitors such as CDK2 and/or CDK4 inhibitors;

(v) antiangiogenic agents such as those which inhibit the effects of vascular endothelial growth factor, [for example the anti-vascular endothelial cell growth factor antibody bevacizumab (Avastin™) and for example, a VEGF receptor tyrosine kinase inhibitor such as
 15 vandetanib (ZD6474), vatalanib (PTK787), sunitinib (SU11248), axitinib (AG-013736), pazopanib (GW 786034) and 4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-pyrrolidin-1-ylpropoxy)quinazoline (AZD2171; Example 240 within WO 00/47212), compounds such as those disclosed in International Patent Applications WO97/22596, WO 97/30035, WO 97/32856 and WO 98/13354 and compounds that work by other mechanisms (for example
 20 linomide, inhibitors of integrin $\alpha v \beta 3$ function and angiostatin)];

(vi) vascular damaging agents such as Combretastatin A4 and compounds disclosed in International Patent Applications WO 99/02166, WO 00/40529, WO 00/41669, WO 01/92224, WO 02/04434 and WO 02/08213;

(vii) an endothelin receptor antagonist, for example zibotentan (ZD4054) or atrasentan;

25 (viii) antisense therapies, for example those which are directed to the targets listed above, such as ISIS 2503, an anti-ras antisense;

(ix) gene therapy approaches, including for example approaches to replace aberrant genes such as aberrant p53 or aberrant BRCA1 or BRCA2, GDEPT (gene-directed enzyme pro-drug therapy) approaches such as those using cytosine deaminase, thymidine kinase or a bacterial
 30 nitroreductase enzyme and approaches to increase patient tolerance to chemotherapy or radiotherapy such as multi-drug resistance gene therapy;

(x) immunotherapy approaches, including for example *ex-vivo* and *in-vivo* approaches to increase the immunogenicity of patient tumour cells, such as transfection with cytokines such as interleukin 2, interleukin 4 or granulocyte-macrophage colony stimulating factor,
 35 approaches to decrease T-cell anergy, approaches using transfected immune cells such as

cytokine-transfected dendritic cells, approaches using cytokine-transfected tumour cell lines and approaches using anti-idiotypic antibodies; and

(xi) Agents used to treat AML leukaemia, including for example, cytarabine, FLT3 inhibitors, BCL2 inhibitors or IDH1/2 inhibitors.

5 **[00276]** In a particular embodiment, the antiproliferative treatment defined hereinbefore may involve, in addition to the compound of the invention, conventional surgery or radiotherapy or chemotherapy.

10 **[00277]** Such conjoint treatment may be achieved by way of the simultaneous, sequential or separate dosing of the individual components of the treatment. Such combination products employ the compounds of this invention within the dosage range described hereinbefore and the other pharmaceutically-active agent within its approved dosage range.

15 **[00278]** According to this aspect of the invention there is provided a combination for use in the treatment of a cancer (for example a cancer involving a solid tumour) comprising a compound of the invention as defined hereinbefore, or a pharmaceutically acceptable salt thereof, and another anti-tumour agent.

20 **[00279]** According to this aspect of the invention there is provided a combination for use in the treatment of a proliferative condition, such as cancer (for example a cancer involving a solid tumour), comprising a compound of the invention as defined hereinbefore, or a pharmaceutically acceptable salt thereof, and any one of the anti-tumour agents listed herein above.

[00280] In a further aspect of the invention there is provided a compound of the invention or a pharmaceutically acceptable salt thereof, for use in the treatment of cancer in combination with another anti-tumour agent, optionally selected from one listed herein above.

25 **[00281]** Herein, where the term “combination” is used it is to be understood that this refers to simultaneous, separate or sequential administration. In one aspect of the invention “combination” refers to simultaneous administration. In another aspect of the invention “combination” refers to separate administration. In a further aspect of the invention “combination” refers to sequential administration. Where the administration is sequential or
30 separate, the delay in administering the second component should not be such as to lose the beneficial effect of the combination.

[00282] According to a further aspect of the invention there is provided a pharmaceutical composition which comprises a compound of the invention, or a pharmaceutically acceptable salt thereof, in combination with an anti-tumour agent (optionally

selected from one listed herein above), in association with a pharmaceutically acceptable diluent or carrier.

[00283] In another embodiment, the invention relates to a therapeutic combination comprising a compound as defined herein and another agent used to treat AML leukaemia e.g., cytarabine, FLT3 inhibitors, BCL2 inhibitors or IDH1/2 inhibitors.

Examples

The following abbreviations have been used in the Examples:

[00284] HATU - [dimethylamino(triazolo[4,5-b]pyridin-3-yloxy)methylene]-dimethylammonium;hexafluorophosphate

10 **[00285]** DIPEA - N-ethyl-N-isopropyl-propan-2-amine

[00286] DEAD – Diethylazodicarboxylate

[00287] DMF – Dimethylformamide

[00288] RT – Retention Time

[00289] Phase sep cartridge – Telos phase separator 6 mL

15 **Example 1: Characterisation Methodology**

The following HPLC methodology was used:

Method 1:

Column	Phenomenex Gemini –NX C18 Part No. 00D-4453-B0 2.0 x100mm, 3µm column	
Column Temp	40°C	
Mobile Phase	A, 2mM amm. bicarbonate, buffered to pH10	
	B, Acetonitrile	
Gradient	Time (mins)	% organic
	0.00	5
	5.50	100
	5.90	100
	5.92	5
	7.00	5

Flow rate	0.5 ml/min
Injection Vol	3 µl
Detection	
Signal	UV 215
PDA Spectrum	Range: 210-420nm step: 1nm

Method 2:

Column	Phenomenex Gemini –NX C18 Part No. 00D-4453-B0 2.0 x100mm, 3µm column	
Column Temp	40°C	
Mobile Phase	A, 2mM amm. bicarbonate, buffered to pH10	
	B, Acetonitrile	
Gradient	Time (mins)	% organic
	0.00	5
	5.50	100
	5.90	100
	5.92	5
	7.00	5
Flow rate	0.6 ml/min	
Injection Vol	3 µl	
Detection		
Signal	UV 215	
PDA Spectrum	Range: 210-420nm step: 1nm	

MSD Signal settings	Scan Pos 150-850 or 130-850

Method 3:

Column	Phenomenex Kinetix-XB C18	
	Part No.00D-4498-AN	
	2.1 x 100mm, 1.7µm	
Column Temp	40°C	
Mobile Phase	A, Water + 0.1% Formic acid	
	B, Acetonitrile + 0.1% Formic acid	
Gradient	Time (mins)	% organic
	0.00	5
	5.30	100
	5.80	100
	5.82	5
	7.00	5
Flow rate	0.6 ml/min	
Injection Vol	1 µl	
Detection		
Signal	UV 215	
PDA Spectrum	Range: 200-400nm step: 1nm	
MSD Signal settings	Scan Pos: 150-850	

Method 4:

	Waters UPLC® CSH™ C18	
Column	Part No. 186005297 2.1 x 100mm, 1.7µm	
Column Temp	40°C	
Mobile Phase	A, 2mM amm. bicarbonate, buffered to pH10	
	B, Acetonitrile	
Gradient	Time (mins)	% organic
	0.00	5
	5.30	100
	5.80	100
	5.82	5
	7.00	5
Flow rate	0.6 ml/min	
Injection Vol	2 µl	
Detection		
Signal	UV 215	
PDA Spectrum	Range: 200-400nm step: 1nm	
MSD Signal settings	Scan Pos: 150-850	

The following LCMS methodologies were used:

- 5 **LCMS method A** refers to low pH analysis using a mobile phase consisting of 0.1% formic acid in a gradient of 5-100% MeCN in water over 1.2 min at a flow rate of 1.2 mL/min. The stationary phase consisted of a Kinetex Core-Shell C18, 2.1mmx50mm, 5 µm. The experiment was run at 40 °C.

LCMS Method B refers to high pH analysis using a mobile phase consisting of 2 mM ammonium bicarbonate, buffered to pH10 in a gradient of 5-100% MeCN in water over 2.1 min at a flow rate of 1.0 mL/min. The stationary phase consisted of a Phenomenex Gemini-NX C18, 2.0 x 50 mm, 3 µm. The experiment was run at 40 °C.

5

LCMS Method C refers to high pH analysis using a mobile phase consisting of 2 mM ammonium bicarbonate, buffered to pH10 in a gradient of 5-100% MeCN in water over 5.8 min at a flow rate of 0.6 mL/min. The stationary phase consisted of a Waters UPLC® BEH™ C18, 2.1 x 100 mm, 1.7 µm. The experiment was run at 40 °C.

10

LCMS Method D refers to high pH analysis using a mobile phase consisting of 2 mM ammonium bicarbonate, buffered to pH10 in a gradient of 5-100% MeCN in water over 5.9 min at a flow rate of 0.6 mL/min. The stationary phase consisted of a Phenomenex Gemini – NX C18, 2.0 x 100 mm, 3 µm. The experiment was run at 40 °C.

15

LCMS method E refers to low pH analysis using a mobile phase consisting of 0.1% formic acid in a gradient of 5-100% MeCN in water over 5.3 min at a flow rate of 0.6 mL/min. The stationary phase consisted of a Phenomenex Kinetix-XB C18, 2.1mm x 100 mm, 1.7 µm. The experiment was run at 40 °C.

20

LCMS method F refers to high pH analysis using a mobile phase consisting of 2 mM ammonium bicarbonate, buffered to pH10 in a gradient of 5-100% MeCN in water over 0.75 min at a flow rate of 1.0 mL/min. The stationary phase consisted of a Waters UPLC® BEH™ C18, 2.1 x 100 mm, 1.7 µm. The experiment was run at 40 °C.

25

Method G refers to low pH analysis using a mobile phase consisting of 0.1 % Formic acid in water (pH= 2.70) in a gradient of 3-100% of 0.1% formic acid in water: acetonitrile (10:90) over 3.00 min at a flow rate of 0.8 mL/min. The stationary phase consisted of C18, 50*2.1mm, 1.6 µm column. The experiment was run at 35 °C.

30

Method H refers to a high pH analysis using a mobile phase consisting of 5 mM ammonium bicarbonate, (pH 7.35) in a gradient of MeCN in water over 3.0 min at a flow rate of 0.5 mL/min. The stationary phase consisted of C18, 50*2.1mm, 2.5 µm. The experiment was run at 35 °C.

35

Method I refers to a high pH analysis using a mobile phase consisting of 5 mM ammonium bicarbonate, (pH 7.35) in a gradient of MeCN in water over 3.0 min at a flow rate of 0.5

mL/min. The stationary phase consisted of C18, 50*2.1mm, 2.5 µm. The experiment was run at 35 °C.

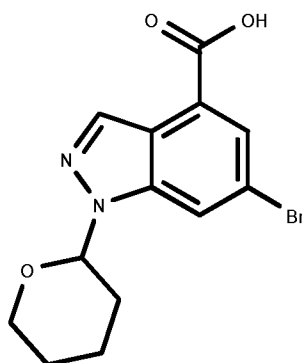
5 The following preparative HPLC methodologies were used:

Preparative Method A refers to low pH purification using a mobile phase consisting of 0.1% Formic acid in a gradient of 10-95% MeCN in water over 14.4 min at a flow rate of 40 mL/min. The stationary phase consisted of a Waters Sunfire C18, 30 x 100 mm, 10 µm.

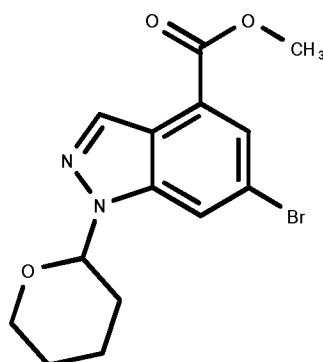
10 **Preparative Method B** refers to high pH purification using a mobile phase consisting of 0.2% ammonium hydroxide in a gradient of 30-95% MeCN in water over 10 min at a flow rate of 40 mL/min. The stationary phase consisted of a Waters XBridge™ C18 OBD™, 30 x 100 mm, 10 µm.

15 **Example 2: Chemical Synthesis and Characterisation**

[00290] Synthesis of Intermediate 1: 6-bromo-1-tetrahydropyran-2-yl-indazole-4-carboxylic acid



[00291] Step 1: methyl 6-bromo-1-tetrahydropyran-2-yl-indazole-4-carboxylate



20

Methyl 6-bromo-1H-indazole-4-carboxylate (1.0g, 3.92mmol) and TsOH.H₂O (75mg, 0.39mmol) were combined in DCM (40ml) and 3,4-dihydro-2H-pyran (1.07ml, 11.8mmol)

was added. The mixture was stirred at room temperature for 20 minutes during which time the mixture darkened. The mixture was quenched with aqueous sodium hydrogen carbonate (sat, 100ml) and the mixture was stirred vigorously for 5 minutes. The phases were separated, the aqueous phase was extracted with DCM (3 x 80ml) and the combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage 50 g eluting with 0-50% ethyl acetate/heptane) to afford the title compound (1.26g, 92%) as a white solid.

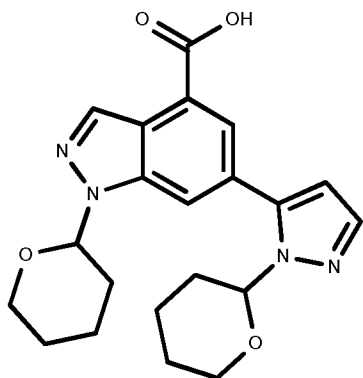
LCMS Method A (electrospray): m/z = 338.9/340.9 ($M+H$)⁺, RT = 1.34 min.

[00292] Step 2: 6-bromo-1-tetrahydropyran-2-yl-indazole-4-carboxylic acid

A solution of methyl 6-bromo-1-tetrahydropyran-2-yl-indazole-4-carboxylate (600mg, 1.77mmol) in THF (10ml) and Water (10ml) was treated with lithium hydroxide (132mg, 5.31mmol) and the mixture was heated at 60°C for 90 minutes. The reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was diluted with water (10ml) and acidified to ~pH1 using 1M HCl(aq). The mixture was then extracted with chloroform/isopropanol (3:1, 4 x 30ml) and the combined organic extracts were dried over sodium sulfate and evaporated under vacuum to afford the title compound (566mg, 97%) as a white solid.

LCMS Method A (electrospray): m/z = 324.9/326.9 ($M+H$)⁺, RT = 1.14 min.

[00293] Synthesis of Intermediate 2: 1-tetrahydropyran-2-yl-6-(2-tetrahydropyran-2-ylpyrazol-3-yl)indazole-4-carboxylic acid



[00294] Step 1: methyl 1-tetrahydropyran-2-yl-6-(2-tetrahydropyran-2-ylpyrazol-3-yl)indazole-4-carboxylate

[00295] Methyl 6-bromo-1-tetrahydropyran-2-yl-indazole-4-carboxylate Intermediate

1 Step 1 (300mg, 0.88mmol), 1-(tetrahydro-2H-pyran-2-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (295mg, 1.06mmol) and aqueous K₂CO₃ (1.2M, 2.21ml, 2.65mmol) were combined in 1,4-Dioxane (6ml) and the mixture was sparged with nitrogen for 5 mins. 1,1'-bis(di-tert-butylphosphanyl)ferrocene - dichloropalladium [Pd-118] (58mg, 0.09mmol) was added and the mixture sparged for a further 5 mins. The vessel was sealed

and the mixture heated at 100°C for 2 hours. The reaction mixture was cooled to RT, diluted with aqueous Sodium hydrogen carbonate (sat, 30ml) and extracted with ethyl acetate (2 x 50ml). The combined organic extracts were washed with brine (4 x 30ml), dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage 25 g, eluting with 0-50% ethyl acetate/heptane) to afford the title compound (291mg, 79%) as a yellow foam.

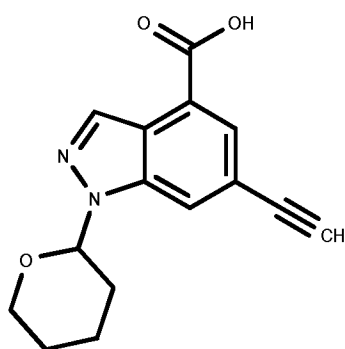
LCMS Method A (electrospray): m/z = 433.1 ($M+H$)⁺, RT = 1.29 min.

[00296] Step 2: The title compound was prepared using the procedure described in

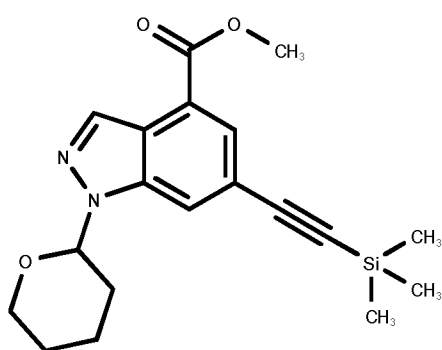
Intermediate 1 Step 2 giving (175mg, 62%) as an off-white solid.

LCMS Method A (electrospray): m/z = 395.15 ($M+H$)⁺, RT = 1.11 min.

[00297] Synthesis of Intermediate 3: 6-ethynyl-1-(oxan-2-yl)-1H-indazole-4-carboxylic acid



[00298] Step 1: Methyl 1-tetrahydropyran-2-yl-6-(2-trimethylsilylethynyl)indazole-4-carboxylate



[00299] Methyl 6-bromo-1-tetrahydropyran-2-yl-indazole-4-carboxylate (500mg, 1.47mmol), $PdCl_2(PPh_3)_2$ (104mg, 0.15mmol), CuI (28mg, 0.15mmol) and triethylamine (1.03ml, 7.37mmol) were combined in DMF (3ml) and the mixture sparged with nitrogen for 5mins. Ethynyl(trimethyl)silane (1.0ml, 7.37mmol) was added, the mixture sparged briefly and the vessel sealed. The mixture was heated at 100°C for 2.5h. The reaction mixture was cooled to RT, diluted with ethyl acetate (50ml) and washed with sat. aqueous Sodium

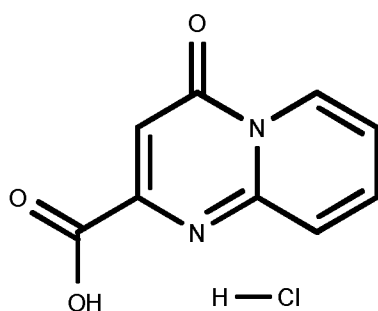
hydrogen carbonate (50ml) and brine (5 x 50ml). The organic layer was dried over sodium sulfate and evaporated under vacuum. The residue was purified by Chromatography on silica gel [Biotage 50 g, eluting with 0-30% ethyl acetate/heptane] to afford the title compound (553mg (99% yield) as a pale brown oil.

5 LCMS Method A (electrospray): m/z = 357.1 ($M+H$)⁺, RT = 1.54 min.

[00300] **Step 2:** The title compound was prepared from methyl 1-tetrahydropyran-2-yl-6-(2-trimethylsilylethynyl)indazole-4-carboxylate using the method described in **Intermediate 1 Step 2** giving (342mg, 75%) as a pale brown solid.

10 LCMS Method A (electrospray): m/z = 270.95 ($M+H$)⁺, RT = 1.10 min.

[00301] **Synthesis of Intermediate 4: 4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxylic acid hydrochloride**

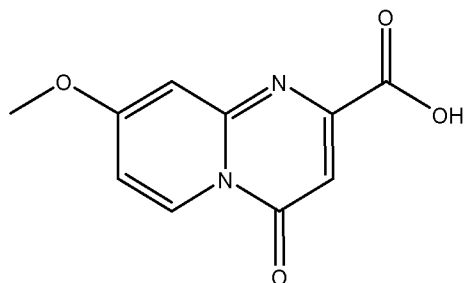


[00302] A suspension of methyl 4-oxopyrido[1,2-a]pyrimidine-2-carboxylate [Tetrahedron (2014), 70(17), 2761-2765] (5g, 24.5mmol) in THF (150ml) was treated with potassium trimethylsilanolate (6.28g, 49.0mmol) and the mixture was heated at reflux for an hour before HCl Solution (4M HCl in dioxane 15ml) was added and the heating was continued for 15 mins before cooling to room temperature. The solid was collected by filtration, washed with diethyl ether and dried under suction to afford the title compound (7.98g, 86%) as a pale yellow solid which contained ~40% residual KCl.

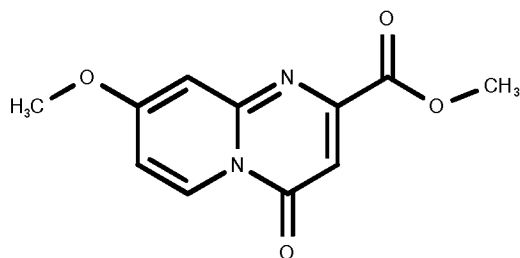
20

LCMS Method B (electrospray): m/z = 191.2 ($M+H$)⁺, RT = 0.23 min.

25 **[00303]** **Synthesis of Intermediate 5: 8-methoxy-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxylic acid**



[00304] Step 1: methyl 8-methoxy-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxylate



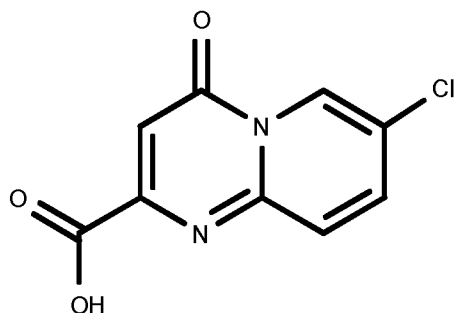
[00305] A suspension of 4-methoxypyridin-2-amine (2g, 16.1mmol) in Water (150ml) was stirred vigorously whilst dimethyl but-2-ynedioate (2.38ml, 19.3mmol) was added slowly and the mixture was stirred at room temperature for 3 hours. The reaction mixture was diluted with DCM (100ml) and allowed to stand at room temperature overnight. The phases were separated and the aqueous phase was extracted with DCM (2 x 80ml), the combined organic extracts were dried over sodium sulfate and evaporated under vacuum to a residue which was purified by chromatography on silica gel [Biotage 50 g eluting with 50-100% ethyl acetate/heptane] to afford a crude material which was triturated with ethyl acetate/heptane. The solids were collected by filtration and washed with heptane to afford the title compound (850mg (23%) as a beige solid.

LCMS Method B (electrospray): m/z = 235.2 ($M+H$)⁺, RT = 1.20 min.

[00306] Step 2: The title compound was prepared from methyl 8-methoxy-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxylate using the method described in **Intermediate 1 Step 2** giving (535 mg, 67%) as a white solid.

LCMS Method B (electrospray): m/z = 221.2 ($M+H$)⁺, RT = 0.31 min.

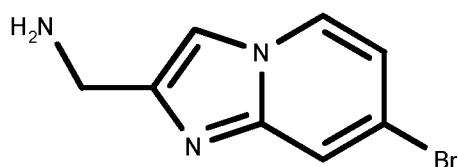
[00307] Synthesis of Intermediate 6: 7-chloro-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxylic acid



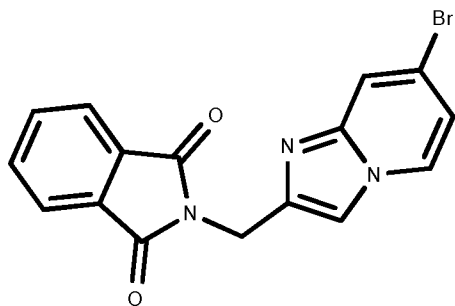
[00308] The title compound was prepared from methyl 7-chloro-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxylate [Tetrahedron (2014), 70(17), 2761-2765] using the method described in **Intermediate 1 Step 2** giving (195 mg, 51%) as a pale yellow solid.

5 LCMS Method B (electrospray): m/z = 225.1 ($M+H$)⁺, RT = 0.31 min.

[00309] **Synthesis of Intermediate 7: {7-bromoimidazo[1,2-a]pyridin-2-yl}methanamine**



10 **Step 1: 2-[(7-bromoimidazo[1,2-a]pyridin-2-yl)methyl]isoindoline-1,3-dione**



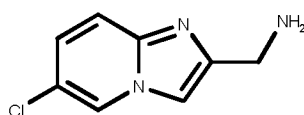
[00310] A suspension of 4-bromopyridin-2-amine (2g, 11.6mmol) and 2-(3-bromo-2-oxo-propyl)isoindoline-1,3-dione (3.26g, 11.6mmol) (US7105508, 2006) in Ethanol (40ml) was heated at reflux for 3 hours during which time the materials slowly dissolved followed by a slow precipitation. The mixture was cooled to room temperature and the solids were collected by filtration, washed with MeOH followed by diethyl ether and dried under vacuum to afford the title compound (3.09g, 51%) as a white solid.

LCMS Method B (electrospray): m/z = 356.1/358.1 ($M+H$)⁺, RT = 1.49 min.

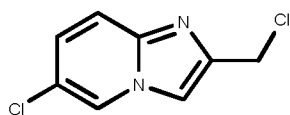
20 [00311] **Step 2: {7-bromoimidazo[1,2-a]pyridin-2-yl}methanamine**

2-[(7-bromoimidazo[1,2-a]pyridin-2-yl)methyl]isoindoline-1,3-dione (3.09g, 5.89mmol) and hydrazine hydrate (2.9ml, 59.0mmol) were combined in Ethanol (40ml) and the mixture was stirred at room temperature for 2 hours. The solids were collected by filtration and the filtrate was left standing overnight. Further solids were collected by filtration. The filtrates were
5 evaporated directly onto silica gel (kp-NH) and the solids were deposited onto a short plug of kp-NH silica and the system eluted with 10% MeOH/DCM. The eluent was evaporated to afford the title compound (1.09g 72% yield) as a pale yellow solid
LCMS Method B: LC-MS (electrospray): $m/z = 226.1/228.1$ ($M+H$)⁺, RT = 1.25 min.

10 **[00312] Synthesis of Intermediate 8: {6-chloroimidazo[1,2-a]pyridin-2-yl}methanamine**

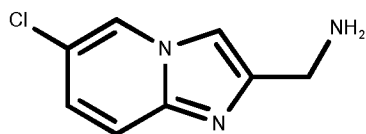


[00313] Step 1: 6-chloro-2-(chloromethyl)imidazo[1,2-a]pyridine



15 A suspension of 5-chloropyridin-2-amine (1.0 g, 7.78 mmol) and 1,3-dichloropropan-2-one (0.71 mL, 7.8 mmol) in ethanol (7.4 mL) was heated to 80 °C for 3 hours. The mixture was cooled to room temperature and evaporated to dryness under vacuum. The residue was diluted with Sodium hydrogen carbonate (sat, 20 mL) and extracted with DCM (3 x 15 mL). The combined organics were evaporated under vacuum and the residue was purified by
20 chromatography on silica gel (Biotage; 50 g KPNH eluting with 0-100% ethyl acetate/heptane) to afford the title compound (435 mg, 28 % Yield) as an orange solid.
Method A: LC-MS (electrospray): $m/z = 200.85$ ($M+H$)⁺, RT = 0.64 min.

[00314] Step 2: (6-chloroimidazo[1,2-a]pyridin-2-yl)methanamine



25 A solution of 6-chloro-2-(chloromethyl)imidazo[1,2-a]pyridine (750 mg, 3.73 mmol) in ammonia solution (7M in methanol, 5.3 mL, 37.3 mmol) was stirred at room temperature for 16 hours and at 60 °C for 3 hours. The mixture allowed to cool to room temperature and left standing for two days before it was evaporated under vacuum. The residue was purified by

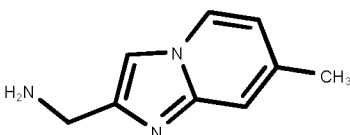
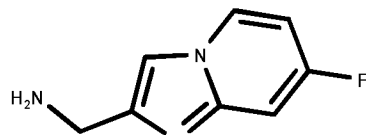
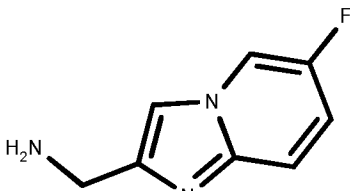
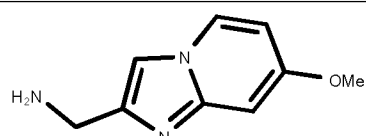
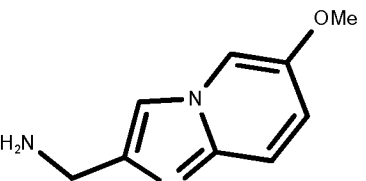
chromatography on silica gel [Biotage; KP-NH 28 g eluting with 0-10% MeOH in DCM] to give the title compound (83 mg, 9.2% Yield) as a yellow sticky solid.

Method A: LC-MS (electrospray): m/z = 181.9 ($M+H$)⁺, RT = 0.23 min.

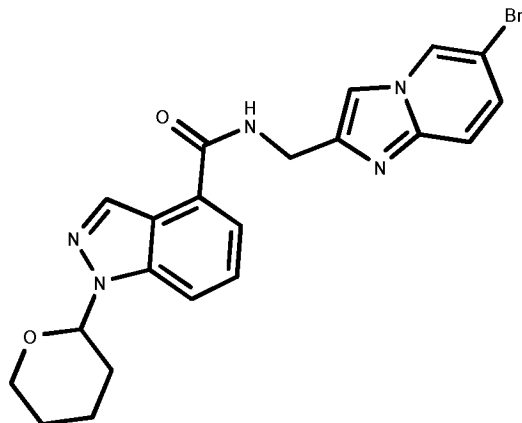
5 [00315] **Synthesis of Intermediates 9-13**

[00316] The intermediates listed in **table 1** were prepared in the same way as **Intermediate 8** using the appropriate aminopyridine.

Table 1

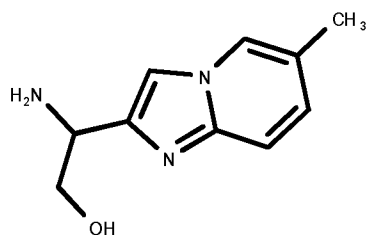
Intermediate	Name	Structure	LCMS method	LCMS Retention time	Mass ion
9	{7methylimidazo[1,2-a]pyridin-2-yl}methanamine		B	1.19	162.2
10	{7-fluoroimidazo[1,2-a]pyridin-2-yl}methanamine		B	1.09	166.2
11	{6-fluoroimidazo[1,2-a]pyridin-2-yl}methanamine		B	1.10	166.2
12	{7-methoxyimidazo[1,2-a]pyridin-2-yl}methanamine		B	1.26	178.3
13	{6-methoxyimidazo[1,2-a]pyridin-2-yl}methanamine		B	1.25	178.2

10 [00317] **Synthesis of Intermediate 14: N-[(6-bromoimidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide**

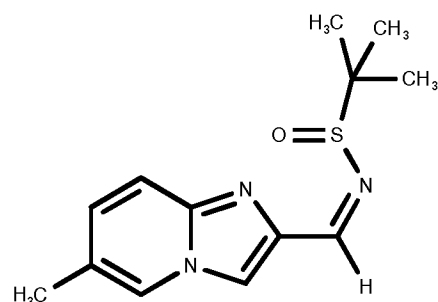


[00318] Prepared from 1-tetrahydropyran-2-ylindazole-4-carboxylic acid and (6-bromoimidazo[1,2-a]pyridin-2-yl)methanamine using the procedure described in **Compound 1** and purified by chromatography on silica gel [Biotage 50 g eluting with 0-10% MeOH/DCM] to give the title compound (950 mg, 83%) as an orange solid.
LCMS Method B (electrospray): m/z = 454./456. $(M+H)^+$, RT = 1.49 min.

[00319] **Synthesis of Intermediate 15: 2-amino-2-(6-methylimidazo[1,2-a]pyridin-2-yl)ethanol**



[00320] **Step 1:** 2-methyl-N-[(1Z)-{6-methylimidazo[1,2-a]pyridin-2-yl}methylidene]propane-2-sulfinamide



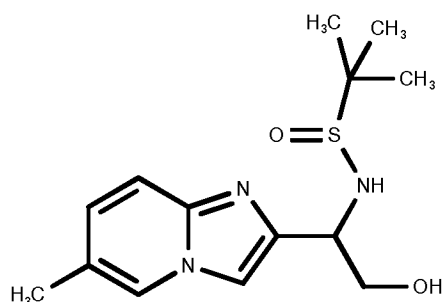
A solution of 6-methylimidazo[1,2-a]pyridine-2-carbaldehyde (550 mg, 3.43 mmol) (Eur. J. Org. Chem. 2015 (18), 3957) and 2-methylpropane-2-sulfinamide (378 mg, 3.12 mmol) in DCM (20 mL), under a nitrogen atmosphere, was treated with $\text{CuSO}_4 \cdot 5 \text{H}_2\text{O}$ (1.0g, 6.24 mmol) and the resultant blue solution was stirred at room temperature for 85 hours. The dark green suspension was filtered through Celite washing with DCM and the filtrate was

concentrated under vacuum and purified by chromatography on silica gel [Biotage 50 g eluting with 20-100% ethyl acetate/heptane] to give the title compound (553 mg, 67%) as an off white solid.

LCMS Method B (electrospray): m/z = 264.2 ($M+H$)⁺, RT = 1.37 min.

5

[00321] Step 2: N-[2-hydroxy-1-(6-methylimidazo[1,2-a]pyridin-2-yl)ethyl]-2-methyl-propane-2-sulfonamide



[00322] 2-methyl-N-[(1Z)-{6-methylimidazo[1,2-a]pyridin-2-yl}methylidene]propane-2-sulfonamide (430 mg, 1.63 mmol), and potassium;2-methylpropan-2-olate (550 mg, 4.90 mmol) were combined in a microwave vial, toluene (anhydrous, 2.9 mL) was added and the mixture was degassed via a stream of N₂ and the resultant suspension was heated at 50 °C for 16 hours. The mixture was cooled to room temperature, degassed via a stream of N₂, and heated at 100 °C for 3 hours. The purple mixture was quenched by the addition of NH₄Cl (sat) and extracted with DCM (phase sep cartridge) and the organic phase was evaporated under vacuum to a purple gum 332 mg. The gum was dissolved in THF/water (6:1) 3.5 mL and treated with NaBO₃·4H₂O (440 mg, 2.85 mmol) and the mixture was stirred at room temperature for an hour. The mixture was diluted with water and extracted with DCM. The organics were dried (magnesium sulfate) and evaporated under vacuum to a residue which was purified by chromatography on silica gel [Biotage KPNH 11g, eluting with 0-100% ethyl acetate/heptane] to give the title compound (mixture of diastereoisomers, 70 mg, 14%) as a dark gum.

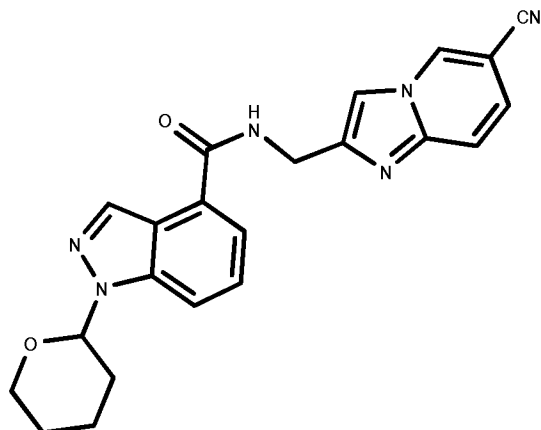
LCMS Method B (electrospray): m/z = 295.9 ($M+H$)⁺, RT = 0.70/0.75 min.

[00323] Step 3: The title compound was prepared from N-[2-hydroxy-1-(6-methylimidazo[1,2-a]pyridin-2-yl)ethyl]-2-methyl-propane-2-sulfonamide using the procedure described in **Compound 1** and purified by ion exchange [SCX-2] giving (50 mg 45%) as a dark gum.

LCMS Method B (electrospray): m/z = 192.3 ($M+H$)⁺, RT = 1.09 min.

30

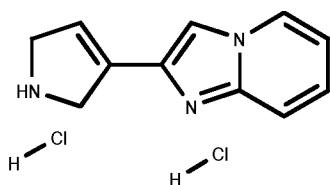
[00324] **Synthesis of Intermediate 16: N-[(6-cyanoimidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide**



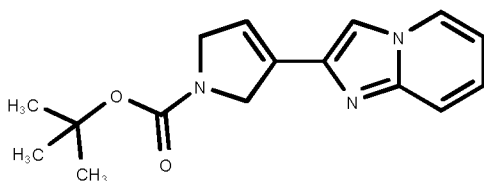
[00325] Prepared from 1-tetrahydropyran-2-ylindazole-4-carboxylic acid and (6-cyanoimidazo[1,2-a]pyridin-2-yl)methanamine (commercial) using the procedure described in **Compound 1** and purified by trituration with cold ethyl acetate to give the title compound (3.8 g, 98%) as a light brown solid.

LCMS Method A (electrospray): m/z = 401.1 ($M+H$)⁺, RT = 0.92 min.

[00326] **Synthesis of Intermediate 17: 3-{imidazo[1,2-a]pyridin-2-yl}-2,5-dihydro-1H-pyrrole dihydrochloride**



[00327] **Step 1: tert-butyl 3-imidazo[1,2-a]pyridin-2-yl-2,5-dihydropyrrole-1-carboxylate**



[00328] A mixture of 2-bromoimidazo[1,2-a]pyridine (520mg, 2.64mmol), tert-butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,5-dihydropyrrole-1-carboxylate (935mg, 3.17mmol) and K₂CO₃ (1.2M aqueous solution, 6.6ml, 7.92mmol) were combined in 1,4-Dioxane (12ml) and the mixture sparged with nitrogen for 5mins. Pd-118 (86mg, 0.13mmol) was added and the mixture sparged for a further 5mins. The vessel was sealed and the mixture heated at 100°C for 2.5h. The reaction mixture was cooled to room temperature

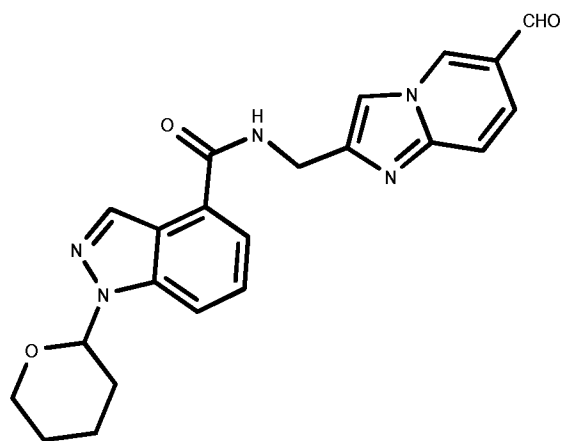
diluted with ethyl acetate (100ml), washed with aqueous sodium hydrogen carbonate (sat, 80ml) and brine (3 x 80ml). The organic layer was dried over sodium sulfate and evaporated under vacuum to a residue which was purified by chromatography on silica gel (Biotage 25 g, eluting with 50-100% ethyl acetate/heptane) to afford the title compound (669mg, 89%) as a pale yellow solid

Method A: LC-MS (electrospray): m/z = 286.5 ($M+H$)⁺, RT = 0.90 min.

[00329] Step 2: The title compound was prepared from tert-butyl 3-imidazo[1,2-a]pyridin-2-yl-2,5-dihydropyrrole-1-carboxylate using the procedure described in **Compound 1** and purified by trituration with ethyl acetate/heptane giving (606 mg, 100%) as a white solid.

LCMS Method A (electrospray): m/z = 186.0 ($M+H$)⁺, RT = 0.14 min.

[00330] Synthesis of Intermediate 18: N-({6-formylimidazo[1,2-a]pyridin-2-yl}methyl)-1-(oxan-2-yl)-1H-indazole-4-carboxamide

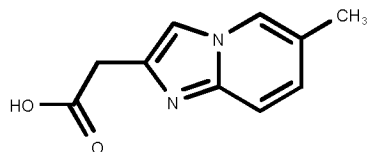


Isopropylmagnesium chloride lithium chloride complex (1.3M in THF, 4.1 mL, 5.35 mmol) was added dropwise to a solution of N-[(6-bromoimidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide (**Intermediate 14**) (750 mg, 1.34 mmol) in THF (10 mL) at -78 °C. Once the addition was complete the mixture was stirred at -78 °C for 10 minutes and allowed to warm to 5 °C over 3 hours. The mixture was then allowed to warm to room temperature and stirred for 30 minutes before it was cooled to -70 °C and treated with DMF (414 uL, 5.35 mmol) and allowed to slowly warm to room temperature overnight. The mixture was quenched by the addition of HCl (2M, 15 mL), basified with aqueous NaOH (2M) and extracted with ethyl acetate (2 x 15 mL). The combined organics were washed with brine, dried (magnesium sulfate) evaporated to dryness under reduced pressure to afford the title compound (460 mg, 42%, 1:1 mixture with N-({imidazo[1,2-a]pyridin-2-yl}methyl)-1-

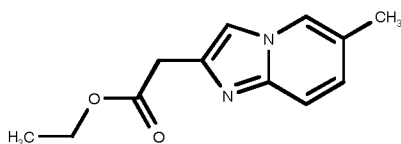
(oxan-2-yl)-1H-indazole-4-carboxamide) as a brown gum which was used without further purification.

LCMS Method A (electrospray): $m/z = 404.5$ ($M+H$)⁺, RT = 0.90 min.

5 **[00331] Synthesis of Intermediate 19: 2-{6-methylimidazo[1,2-a]pyridin-2-yl}acetic acid**



[00332] Step 1: ethyl 2-(6-methylimidazo[1,2-a]pyridin-2-yl)acetate



- 10 5-methylpyridin-2-amine (2g, 18.5mmol) and ethyl 4-chloro-3-oxo-butanoate (2.50ml, 18.5mmol) were combined in Ethanol (20ml) and the mixture was heated at reflux for 3 hours and then stirred at room temperature for 16 hours. The reaction mixture was concentrated under vacuum, the residue was basified with aqueous sodium hydrogen carbonate (sat, 300ml) and extracted with DCM (4 x 150ml). The extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (biotage 100 g, eluting with 0-100 % ethyl acetate/heptane) to afford a dark brown oil which was further purified by chromatography on silica gel (biotage 55 g kp-NH, eluting with 0-100 % ethyl acetate/heptane) to afford the title compound 3.3 g, 40% at 50% purity) of as a pale brown oil.
- 15
- 20 LCMS Method B (electrospray): $m/z = 219.3$ ($M+H$)⁺, RT = 1.34 min.

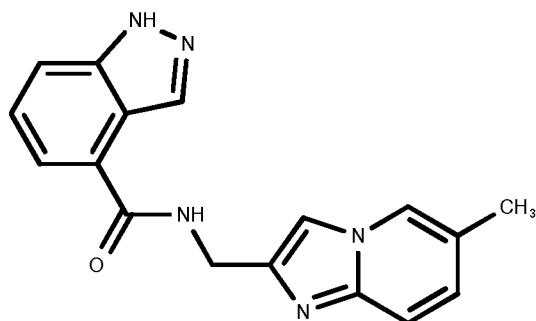
[00333] Step 2: 2-{6-methylimidazo[1,2-a]pyridin-2-yl}acetic acid

The title compound was prepared from ethyl 2-(6-methylimidazo[1,2-a]pyridin-2-yl)acetate using the method described in **Intermediate 1 Step 2** to give the title compound (1.35 g, 95% as a pale yellow solid.

LCMS Method A (electrospray): $m/z = 190.95$ ($M+H$)⁺, RT = 0.18 min.

[00334] Synthesis of Compound 1: N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide

30



A solution of 1-tetrahydropyran-2-ylindazole-4-carboxylic acid (75 mg, 0.3 mmol) and DIPEA (271 μ L, 1.52 mmol) in THF (10 mL) was treated with HATU (150mg, 0.4 mmol) and the mixture was stirred at room temperature for 20 minutes before {6-methylimidazo[1,2-a]pyridin-2-yl}methanamine dihydrochloride (85 mg, 0.37 mmol) (commercially available) was added and the solution was stirred at room temperature for 3 hours. The brown solution was diluted with water and extracted with DCM (via a phase sep cartridge) and the extracts were evaporated under vacuum to a brown gum. The gum was dissolved in Methanol (5 mL), treated with 4 M 1,4-dioxane hydrochloride (0.76 mL, 3.05 mmol) and stirred at room temperature for 16 hours. The solution was evaporated under vacuum and the residue was purified by chromatography on silica gel [Biotage 25 g eluting with 0-100% ethyl acetate/Heptane] to give the title compound (72mg, 93%) as a beige solid.

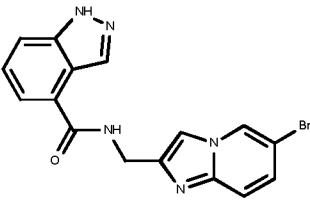
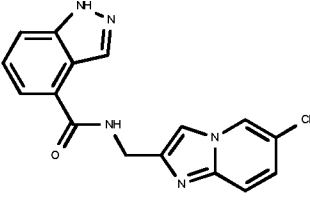
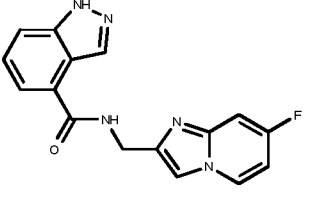
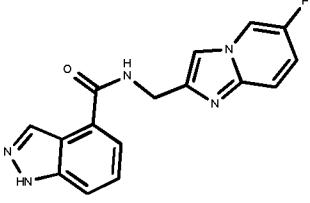
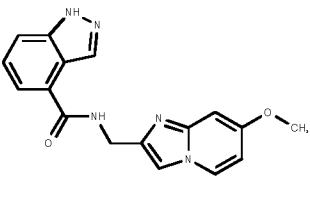
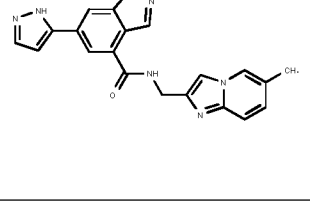
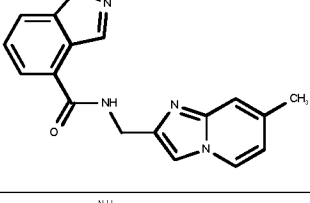
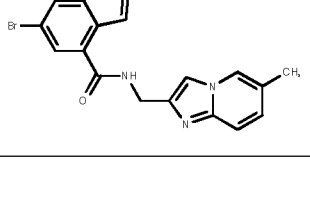
LCMS Method C (electrospray): m/z = 306.1 ($M+H$)⁺, RT = 1.99 min.

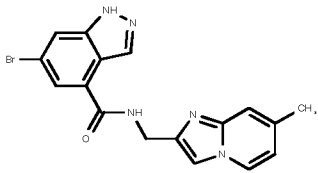
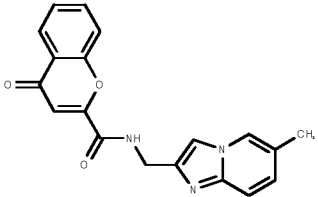
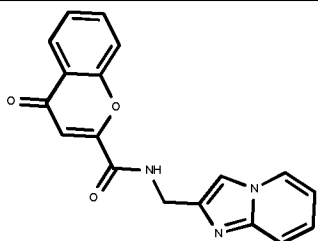
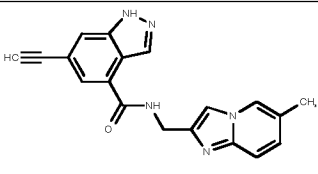
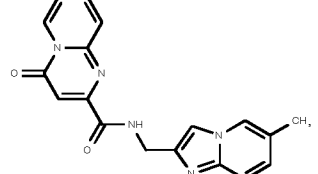
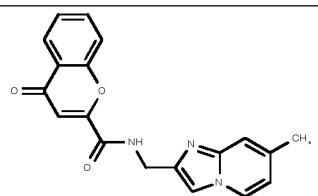
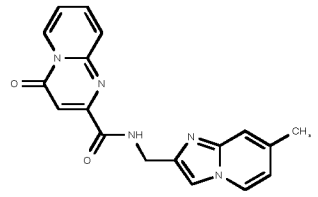
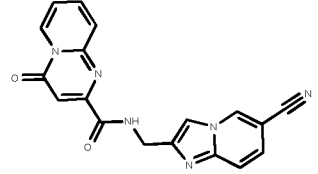
[00335] Synthesis of Compounds 2-31

[00336] The compounds in Table 2 were prepared in a similar fashion to Compound 1 using the appropriate carboxylic acid and aminomethyl imidazopyridine intermediate, or commercially available materials, including deprotection where necessary.

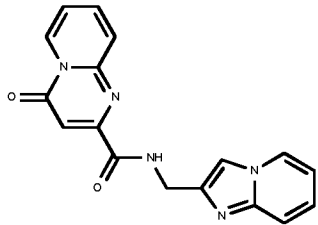
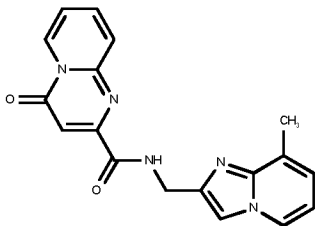
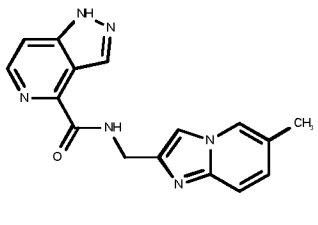
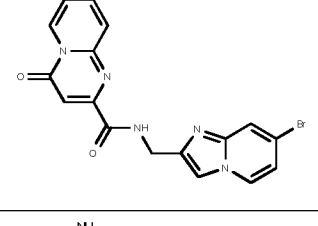
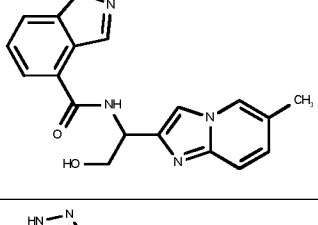
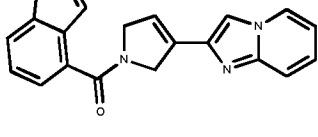
Table 2

Cpd No	Name	Structure	LCMS method	LCMS Retention time / mass ion	Inter medi ates
2	N-({7-bromoimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide		C	3.35/370.1/372.1	7

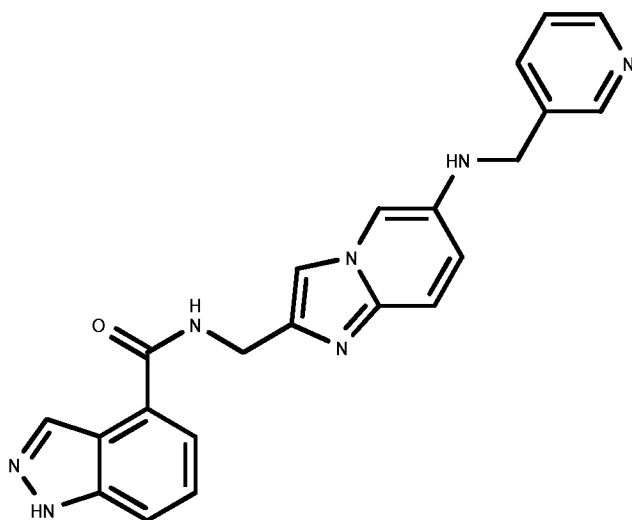
3	N-({6-bromoimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide		C	3.38/370.1/372.1	Commercially available
4	N-({6-chloroimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide		D	3.09/326.3	8
5	N-({7-fluoroimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide		D	2.76/310.2	10
6	N-({6-fluoroimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide		D	2.82/310.2	11
7	N-({7-methoxyimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide		D	2.80/322.3	12
8	N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-6-(1H-pyrazol-5-yl)-1H-indazole-4-carboxamide		D	1.17/372.2	2
9	N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide		C	1.96/306.9	9
10	6-bromo-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide		D	3.32/ 384.1/386.1	1

11	6-bromo-N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide		D	3.29/ 384.1/386.1	1, 9
12	N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide		E	1.22/334.1	Com meri cally avail able
13	N-({imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide		D	3.00/320.2	Com meri cally avail able
14	6-ethynyl-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide		D	3.15/330.2	3
15	N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.66/334.2	4
16	N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide		D	3.24/333.3	9
17	N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.96/334.3	9
18	N-({6-cyanoimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		E	1.14/345.1	Com meri cally avail able

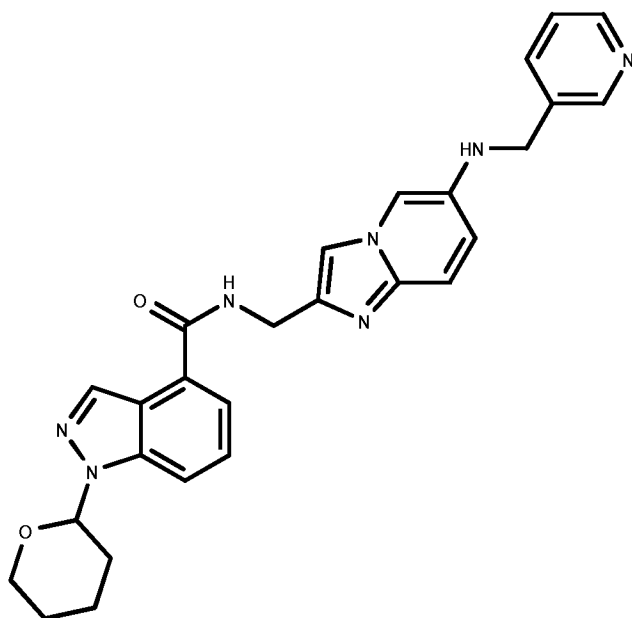
19	8-methoxy-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.20/364.3	5
20	N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-5-carboxamide		D	2.84/306.3	Com meri cally avail able
21	7-chloro-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.39/368.1	6
22	N-({6-fluoroimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.93/338.2	11
23	N-({6-bromoimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.35/ 398.1/400.1	Com meri cally avail able
24	N-({6-methoxyimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.95/350.2	13
25	N-({7-methoxyimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.55/350.3	12

26	N-({imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		MS10 7 min	2.72/320.2	Com meri cally avail able
27	N-({8-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.99/334.3	Com meri cally avail able
28	N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-pyrazolo[4,3-c]pyridine-4-carboxamide		D	2.90/307.2	Com meri cally avail able
29	N-({7-bromoimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.14/ 398.5/400.5	7
30	N-(2-hydroxy-1-({6-methylimidazo[1,2-a]pyridin-2-yl}ethyl)-1H-indazole-4-carboxamide		D	2.81/336.2	15
31	4-(3-({imidazo[1,2-a]pyridin-2-yl}-2,5-dihydro-1H-pyrrole-1-carbonyl)-1H-indazole		D	2.87/330.3	17

[00337] Synthesis of Compound 32: N-[(6-{{(pyridin-3-yl)methyl}amino}imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide

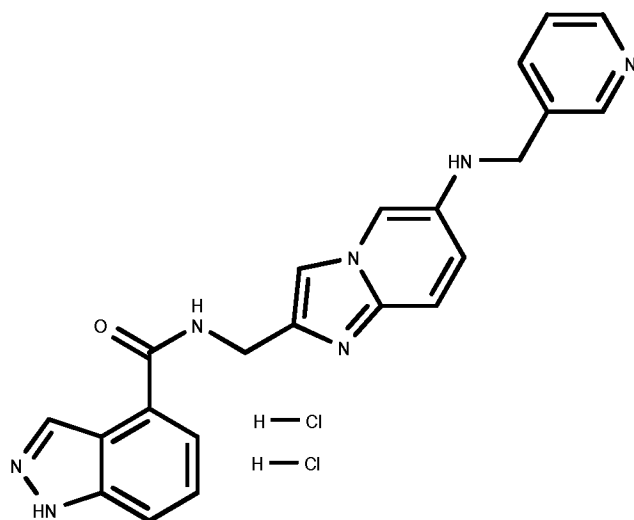


[00338] Step 1: N-[(6-(3-pyridylmethylamino)imidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide dihydrochloride



- 5 A mixture of N-[(6-bromoimidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide (100 mg, 0.220 mmol), **Intermediate 14**, 3-pyridylmethanamine (273 μ L, 2.20 mmol), copper iodide (6.3 mg, 0.0330 mmol), (2S)-pyrrolidine-2-carboxylic acid (5.1 mg, 0.0440 mmol) and potassium carbonate (61 mg, 0.440 mmol) in DMSO (0.6 mL) was heated using microwave irradiation at 150 °C for 15 min. The reaction mixture was diluted
- 10 with 10% MeOH in DCM (15 mL) and water (15 mL). The organic phase was collected and the aqueous phase was extracted with 10% MeOH in DCM (2 x 15 mL). The combined organics were evaporated to dryness under reduced pressure and purified by preparative HPLC (Method A) to afford the title compound (22 mg, 21%) as a yellow solid.
- LCMS Method A (electrospray): m/z = 482.2 (M+H)⁺, RT = 0.77 min.

[00339] Step 2: N-[(6-[(pyridin-3-yl)methyl]amino)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide dihydrochloride



The title compound was prepared from N-[[6-(3-pyridylmethylamino)imidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide using the procedure described in **Compound 1** giving (21 mg 96%) as a light brown solid.

LCMS Method D (electrospray): m/z = 398.3 ($M+H$)⁺, RT = 2.76 min.

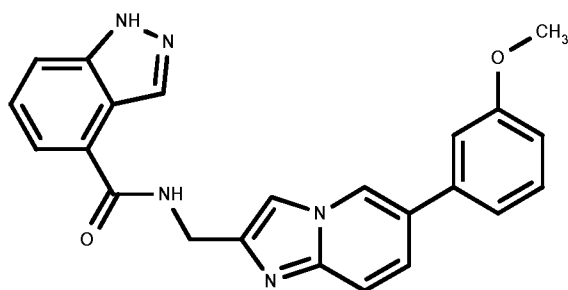
[00340] Synthesis of Compound 33: N-[(6-[(1-methyl-1H-imidazol-4-yl)methyl]amino)imidazo[1,2a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide

[00341] The compound in **table 3** was prepared in the same manner as **Compound 32**

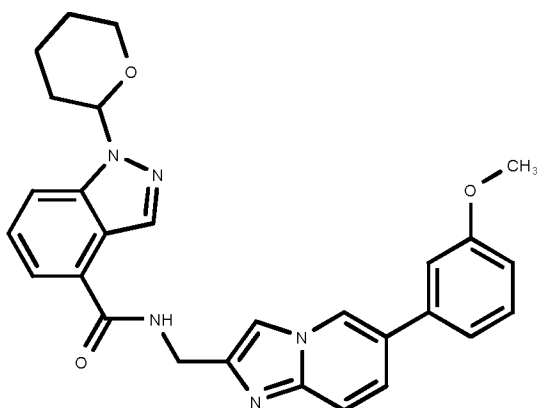
Table 3

Cpd No	Name	Structure	LCMS method	LCMS Retention time	Mass ion
33	N-[(6-[(1-methyl-1H-imidazol-4-yl)methyl]amino)imidazo[1,2a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide		D	2.53	401.3

[00342] Synthesis of Compound 34: N-[[6-(3-methoxyphenyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide



[00343] **Step 1:** N-[[6-(3-methoxyphenyl)imidazo[1,2-a]pyridin-2-yl]methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide



- 5 N-[[6-(3-methoxyphenyl)imidazo[1,2-a]pyridin-2-yl]methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide (120mg, 0.25mmol), **Intermediate 14**, (3-methoxyphenyl)boronic acid (45mg, 0.29mmol) and K_2CO_3 (1.2M aqueous, 0.61ml, 0.74mmol) were combined in 1,4-Dioxane (4ml) and the mixture sparged with nitrogen for 5mins. Dichloro[1,1'-bis(di-
10 butylphosphino)ferrocene]palladium(II) (16mg, 0.02mmol) was added and the mixture sparged for a further 5mins. The vessel was sealed and the mixture heated at 100°C for 2h. The reaction mixture was cooled to room temperature and diluted with ethyl acetate (30ml). The mixture was washed with sat. Sodium hydrogen carbonate(aq) (30ml) and brine (2 x 30ml) and the organic layer dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel [Biotage 28 g kp-NH, eluting with
15 0-100% ethyl acetate/heptane 0-100%] to afford N-[[6-(3-methoxyphenyl)imidazo[1,2-a]pyridin-2-yl]methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide (113mg, 96%) as a white solid.

LCMS Method A (electrospray): m/z = 482.25 ($M+H$)⁺, RT = 1.04 min.

- 20 **[00344]** The title compound was prepared from N-[[6-(3-methoxyphenyl)imidazo[1,2-a]pyridin-2-yl]methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide using the procedure described in **Compound 1** giving (51 mg, 54%) as a white solid.

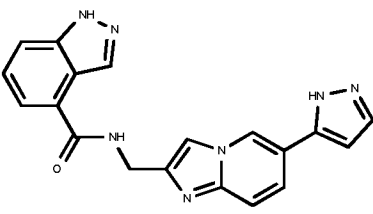
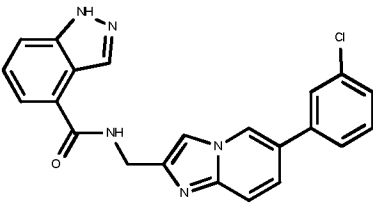
LCMS Method D (electrospray): m/z = 398.2 ($M+H$)⁺, RT = 3.50 min.

[00345] Synthesis of Compounds 35-36

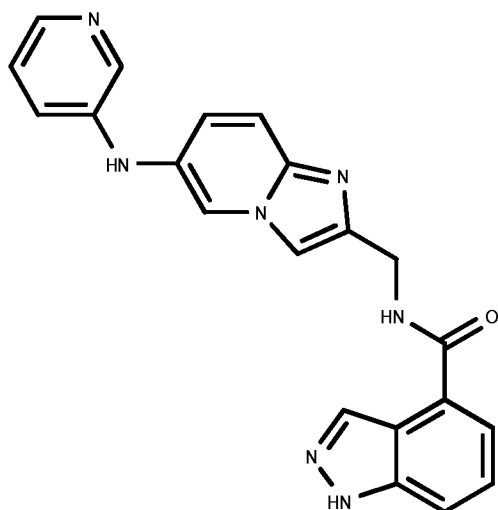
[00346] The compounds in **Table 4** were prepared by in a similar fashion to **Compound 34**.

5

Table 4

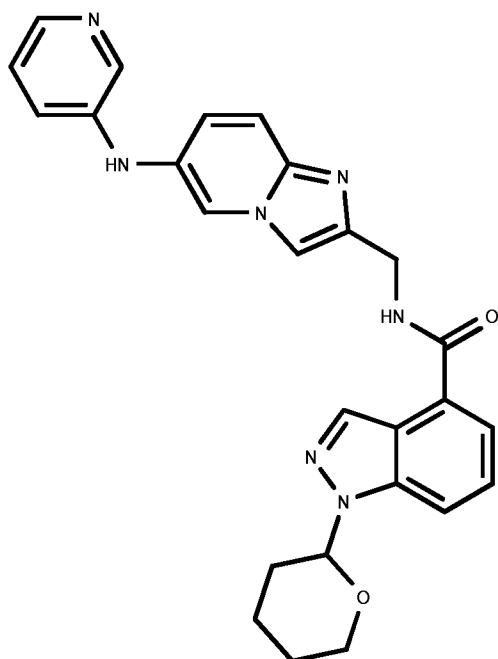
Cpd No	Name	Structure	LCMS method	LCMS Retention time	Mass ion
35	N-{{[6-(1H-pyrazol-5-yl)imidazo[1,2-a]pyridin-2-yl]methyl}-1H-indazole-4-carboxamide		D	2.64	358.2
36	N-{{[6-(3-chlorophenyl)imidazo[1,2-a]pyridin-2-yl]methyl}-1H-indazole-4-carboxamide		D	3.76	402.2

[00347] Synthesis of Compound 37: N-{{[6-{{(pyridin-3-yl)amino}}imidazo[1,2-a]pyridin-2-yl]methyl}-1H-indazole-4-carboxamide



10

[00348] Step1: 1-(oxan-2-yl)-N-({6-[(pyridin-3-yl)amino]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide



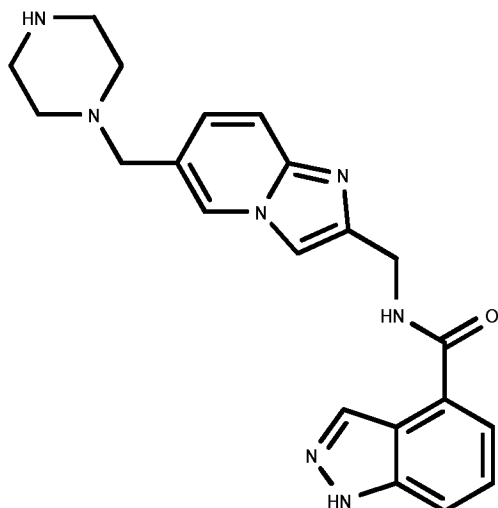
A solution of N-[(6-bromoimidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide (75 mg, 0.165 mmol), **Intermediate 14**, cesium carbonate (161 mg, 0.495 mmol), pyridin-3-amine (19 mg, 0.198 mmol) and XPhos Pd G3 (14 mg, 0.0165 mmol) in 1,4-Dioxane (2 mL) was stirred at 110 °C for 2 h. More pyridin-3-amine (19 mg, 0.198 mmol) and XPhos Pd G3 (14 mg, 0.0165 mmol) were added and the reaction mixture was stirred at 110 °C for 2 h. The reaction mixture was cooled to rt. diluted with water (25 mL) and extracted with ethyl acetate (2 x 25 mL). The combined organics were evaporated to dryness and purified by preparative HPLC [method B, followed by method A] to afford N-[[6-(3-pyridylamino)imidazo[1,2-a]pyridin-2-yl]methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide as a yellow solid.

LCMS Method A (electrospray): m/z = 468.2 (M+H)⁺, RT = 0.8 min

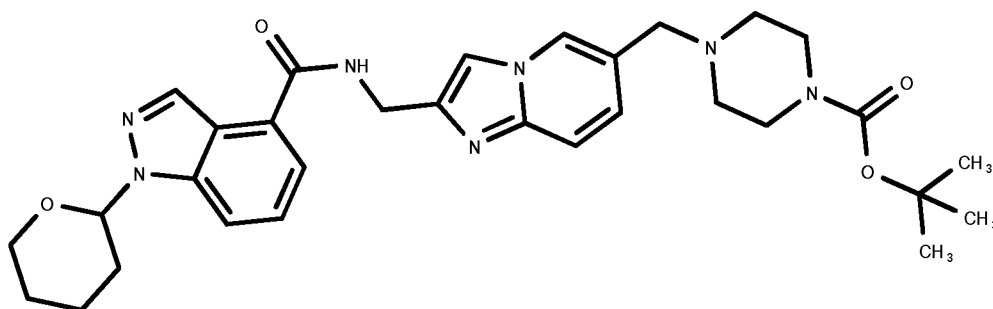
[00349] Step 2: The title compound was prepared from N-[[6-(3-methoxyphenyl)imidazo[1,2-a]pyridin-2-yl]methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide using the procedure described in **Compound 1** giving (7.5mg, 92%) as a white solid.

LCMS Method D (electrospray): m/z = 384.3 (M+H)⁺, RT = 2.75 min

[00350] **Synthesis of Compound 38:** N-({6-[(piperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide



5 [00351] **Step 1:** tert-butyl 4-[[2-[[[(1-tetrahydropyran-2-yl)indazole-4-carbonyl)amino]methyl]imidazo[1,2-a]pyridin-6-yl]methyl]piperazine-1-carboxylate



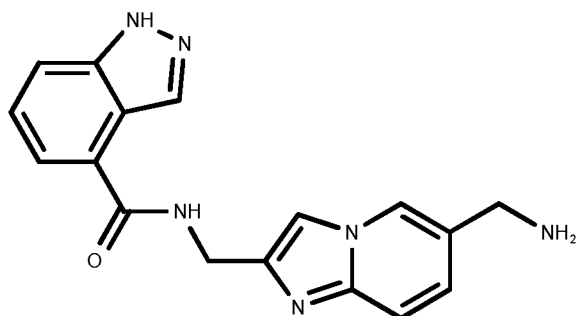
A solution of N-[(6-bromoimidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide (50 mg, 0.110 mmol), **Intermediate 14**, potassium;(4-tert-butoxycarbonylpiperazin-1-yl)methyl-trifluoro-borohydride (37 mg, 0.121 mmol), cesium carbonate (108 mg, 0.330 mmol) and Pd-118 (3.6 mg, 5.50 μ mol) in THF (3.2 mL) and Water (0.8 mL), under a nitrogen atmosphere, was stirred at 85 °C overnight. The reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organics were evaporated to dryness under reduced pressure and purified by preparative HPLC [method A] to afford the title compound (30 mg, 48%) as a white solid.
 10
 15
 LCMS Method A (electrospray): m/z = 574.4 (M+H)⁺, RT = 0.88 min.

[00352] **Step 2:** The title compound was prepared from: tert-butyl 4-[[2-[[[(1-tetrahydropyran-2-yl)indazole-4-carbonyl)amino]methyl]imidazo[1,2-a]pyridin-6-

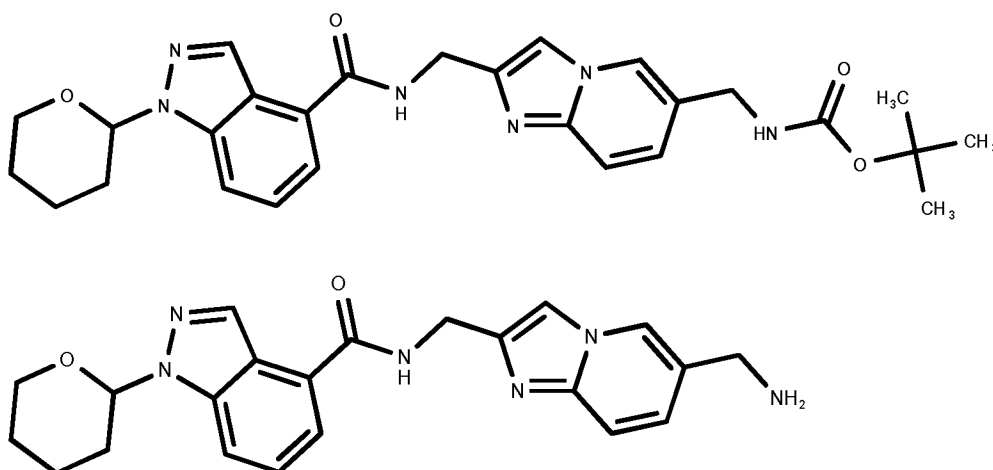
yl)methyl]piperazine-1-carboxylate using the procedure described in **Compound 1** giving (7.5mg, 92%) as a white solid.

Method C: LC-MS (electrospray): m/z = 390.3 (M+H)⁺, RT = 1.55 min.

5 **[00353] Synthesis of Compound 39: N-[[6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide**



[00354] Step 1: tert-butyl N-[[2-[[[(1-tetrahydropyran-2-yl)indazole-4-carbonyl)amino]methyl]imidazo[1,2-a]pyridin-6-yl)methyl]carbamate and N-[[6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1-(oxan-2-yl)-1H-indazole-4-carboxamide



A solution of N-[(6-cyanoimidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide (500 mg, 1.25 mmol) (**Intermediate 16**) and tert-butoxycarbonyl tert-butyl carbonate (545 mg, 2.50 mmol) in methanol (10 mL) was cooled to 0 °C and treated with nickel (II) chloride (164 mg, 1.25 mmol) followed by the addition of sodium borohydride (425 mg, 11.2 mmol) in small portions. Further NaBH₄ (212 mg, 5.5 mmol) was added in portions and the stirring was continued for an hour at 0 °C before the crude reaction was evaporated under vacuum and purified by chromatography on silica gel [Biotage; 25 g KP-NH, eluting with 40-100% ethyl acetate in heptane) to afford tert-butyl N-[[2-[[[(1-

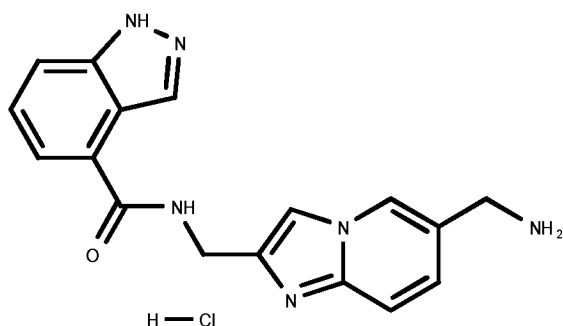
tetrahydropyran-2-ylindazole-4-carbonyl)amino]methyl]imidazo[1,2-a]pyridin-6-yl]methyl]carbamate (180 mg, 0.357 mmol, 50%) as a white solid.

LCMS Method A (electrospray): m/z = 505.2 ($M+H$)⁺, RT = 0.96 min.

- 5 **[00355]** Flushing the column with 0-20% MeOH in ethyl acetate afforded N-[[6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide (90 mg, 0.129 mmol, 18%) as a white solid.

LCMS Method A: LC-MS (electrospray): m/z = 405.1 ($M+H$)⁺, RT = 0.85 min.

- 10 **[00356]** **Step 2:** N-[[6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-1H-indazole-4-carboxamide hydrochloride

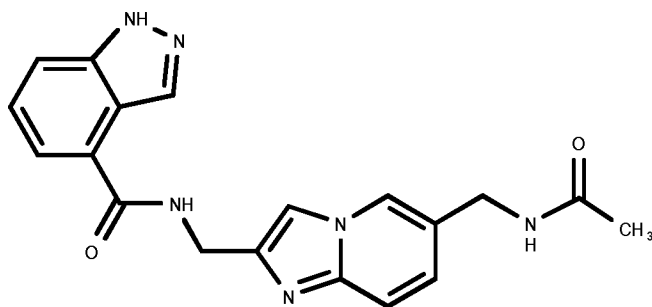


Tert-butyl N-[[2-[[[1-tetrahydropyran-2-ylindazole-4-carbonyl)amino]methyl]imidazo[1,2-a]pyridin-6-yl]methyl]carbamate (180 mg, 0.36 mmol) was treated with HCl (4M in dioxane

- 15 0.5 mL) and the mixture was stirred at room temperature for 65 hours. The mixture was evaporated to dryness and triturated from MeOH/ethyl acetate to afford the title compound (98 mg, 70%) as a white powder.

LCMS Method D (electrospray): m/z = 321.2 ($M+H$)⁺, RT = 2.38 min.

- 20 **[00357]** **Synthesis of Compound 40:** N-[[6-(acetamidomethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-1H-indazole-4-carboxamide

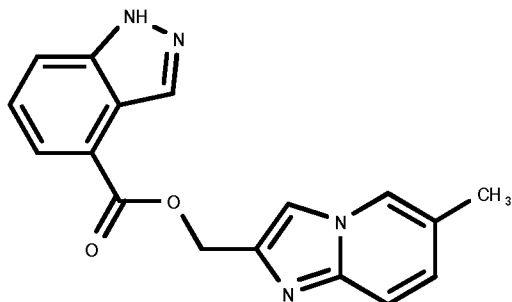


- [00358]** The title compound was prepared using the method described in **Compound 39** substituting acetic anhydride for tert-butoxycarbonyl tert-butyl carbonate to give (32 mg, 31%) as a white solid.

25

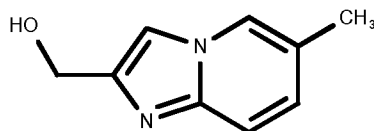
LCMS Method D: LC-MS (electrospray): $m/z = 363.2$ ($M+H$)⁺, $RT = 2.36$ min.

[00359] Synthesis of Compound 41: {6-methylimidazo[1,2-a]pyridin-2-yl}methyl 1H-indazole-4-carboxylate hydrochloride



5

[00360] Step 1: (6-methylimidazo[1,2-a]pyridin-2-yl)methanol



6-methylimidazo[1,2-a]pyridine-2-carbaldehyde (Eur. J. Org. Chem. 2015 (18), 3957)

(165mg, 1.03mmol) was dissolved in methanol (20ml) and cooled in an ice/water

10 bath. NaBH_4 (195mg, 5.15mmol) was added in a single portion and the effervescent mixture stirred under cooling for 30 minutes. The reaction mixture was quenched with sodium hydrogen carbonate (Sat, 30ml) and warmed to RT. The mixture was extracted with 3:1 chloroform/isopropanol (4 x 30ml) and the combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by Chromatography

15 on silica gel [Biotage 28 g kp-NH, eluting with 0-20% MeOH/DCM] to afford the title compound (137mg (80% yield, 98%) as a bright yellow oily residue.

LCMS Method B (electrospray): $m/z = 163.2$ ($M+H$)⁺, $RT = 1.11$ min

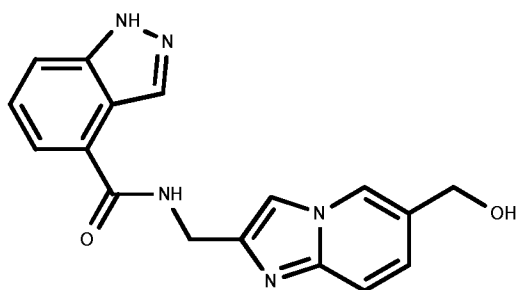
[00361] Step 2: The title compound was prepared from (6-methylimidazo[1,2-

20 a]pyridin-2-yl)methanol using the procedure described in **Compound 1** giving (187mg, 90%) as a white solid.

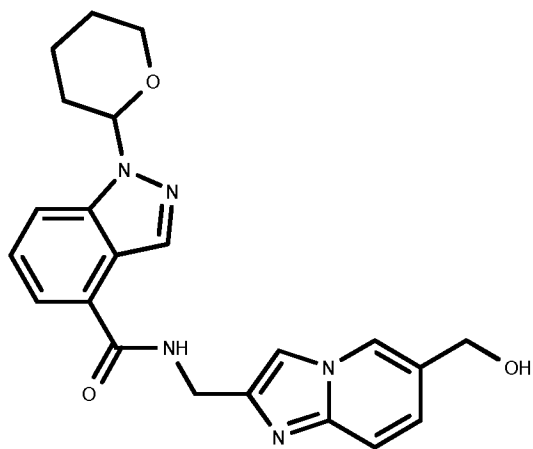
LCMS Method B: LC-MS (electrospray): $m/z = 163.2$ ($M+H$)⁺, $RT = 1.11$ min

[00362] Synthesis of Compound 42: {N-[[6-(hydroxymethyl)imidazo[1,2-

25 a]pyridin-2-yl]methyl}-1H-indazole-4-carboxamide



[00363] **Step 1:** N-[[6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide



5

A solution of N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide (**Intermediate 18**) (50% purity with N-(imidazo[1,2-a]pyridin-2-ylmethyl)-1-tetrahydropyran-2-yl-indazole-4-carboxamide, 92 mg, 0.114 mmol) in ethanol (4 mL), under a nitrogen atmosphere was treated with sodium borohydride (13 mg, 0.342 mmol) and the resultant mixture was stirred at room temperature for an hour. The reaction mixture was quenched by the addition of sodium hydrogen carbonate(sat) and concentrated under vacuum. The residue was extracted with DCM (phase sep) and the extracts were evaporated under vacuum to a residue which was purified by chromatography on silica gel [Biotage KPNH 11 g, eluting with 20-80% (10% MeOH in DCM/DCM) to give the title compound (44 mg, 95%).

15

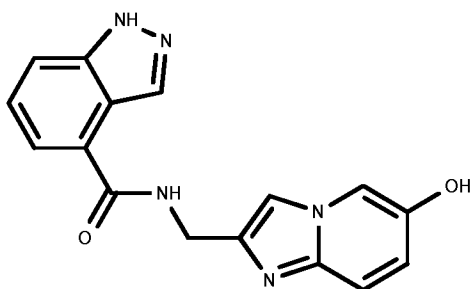
LCMS Method B (electrospray): $m/z = 406.4$ ($M+H$)⁺, RT = 1.27 min

[00364] The title compound was prepared from N-[[6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide using the procedure described in **Compound 1** giving (24 mg, 68%) as a beige solid.

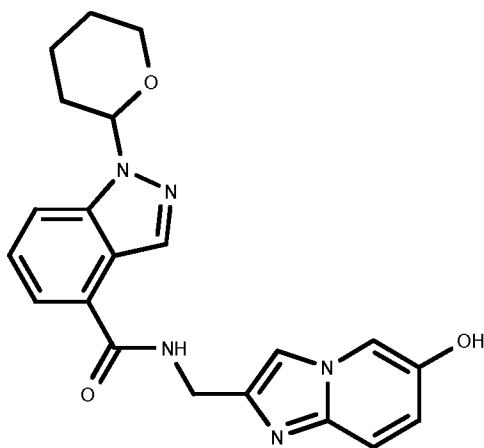
20

LCMS Method D (electrospray): $m/z = 322.3$ ($M+H$)⁺, RT = 2.30 min

[00365] **Synthesis of Compound 43: N-({6-hydroxyimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide**



5 [00366] **Step 1: N-({6-hydroxyimidazo[1,2-a]pyridin-2-yl}methyl)-1-(oxan-2-yl)-1H-indazole-4-carboxamide**

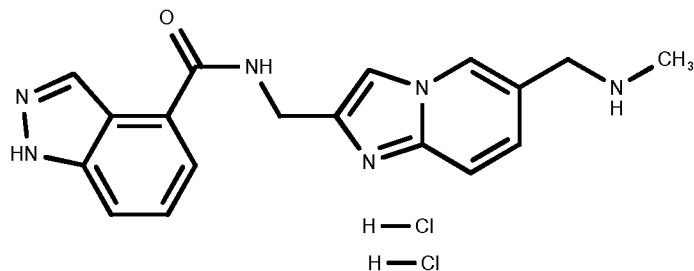


A solution of N-[(6-bromoimidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide (**Intermediate 14**) (100 mg, 0.220 mmol), 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (126 mg, 0.495 mmol), Pd(dppf)Cl₂·CH₂Cl₂ (18 mg, 0.0220 mmol) and potassium acetate (65 mg, 0.660 mmol) in 1,4-Dioxane (3 mL) was stirred at 100 °C for 2 hours. The mixture was cooled to room temperature before acetic acid (25 uL, 0.440 mmol) and Water (0.06 mL) were added. The mixture was stirred for 1 hour before hydrogen peroxide (30%, 2.86 mL, 28.0 mmol) was added and the mixture was stirred for 3 hours. The mixture was quenched with sodium thiosulfate solution (sat, 15 mL), diluted with water (15 mL), extracted with ethyl acetate (2 x 25 mL) and evaporated to dryness under reduced pressure. The residue was purified by preparative HPLC [method B] to afford the title compound (25 mg, 27%) as a white powder. LCMS Method A (electrospray): m/z = 392.1 (M+H)⁺, RT = 0.85 min

[00367] **Step 2:** The title compound was prepared from N-({6-hydroxyimidazo[1,2-a]pyridin-2-yl}methyl)-1-(oxan-2-yl)-1H-indazole-4-carboxamide using the procedure described in **Compound 1** giving (7.3mg, 37%) as a brown powder.

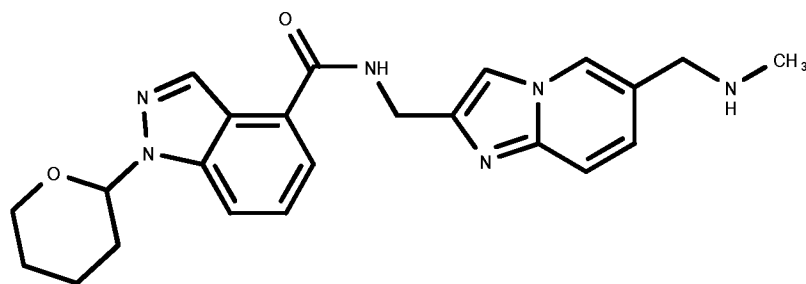
LCMS Method C (electrospray): $m/z = 308.1$ ($M+H$)⁺, RT = 1.04 min

[00368] Synthesis of Compound 44: N-({6-[(methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide dihydrochloride



5

[00369] Step 1: N-({6-[(methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1-(oxan-2-yl)-1H-indazole-4-carboxamide



A solution of N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide (**Intermediate 18**) (50%, 100 mg, 0.114 mmol), STAB (48 mg, 0.228 mmol) and methylamine (8M in ethanol, 16 μ L, 0.125 mmol) in DCM (1 mL) was stirred at rt for 3 h.

More methylamine (8M in ethanol, 16 μ L, 0.125 mmol) and STAB (48 mg, 0.228 mmol) were added in portions over 48 hours whilst stirring the reaction mixture at rt. The reaction mixture was evaporated to dryness and purified by ion exchange [SCX-2] followed by preparative HPLC [method A] to afford the title compound (46 mg, 96%) as a yellow solid.

LCMS Method A (electrospray): $m/z = 419.1$ ($M+H$)⁺, RT = 0.74 min

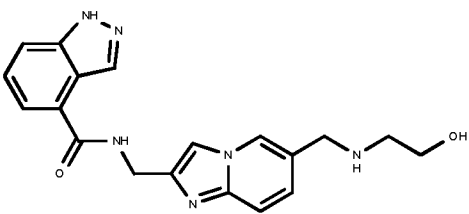
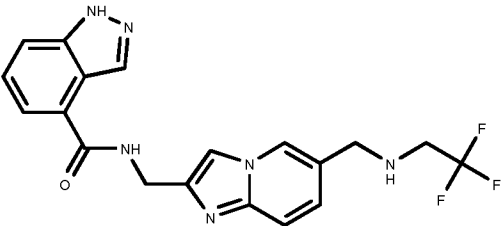
[00370] Step 2: The title compound was prepared from N-[(6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide using the procedure described in **Compound 1** giving (25 mg, 58%) as a beige solid.

LCMS Method C (electrospray): $m/z = 390.3$ ($M+H$)⁺, RT = 1.58 min

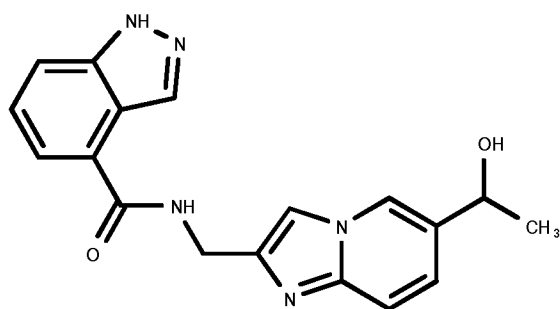
[00371] Synthesis of Compounds 45-46

[00372] The compounds in **table 4** was prepared in the same manner as **Compound 44**

Table 4

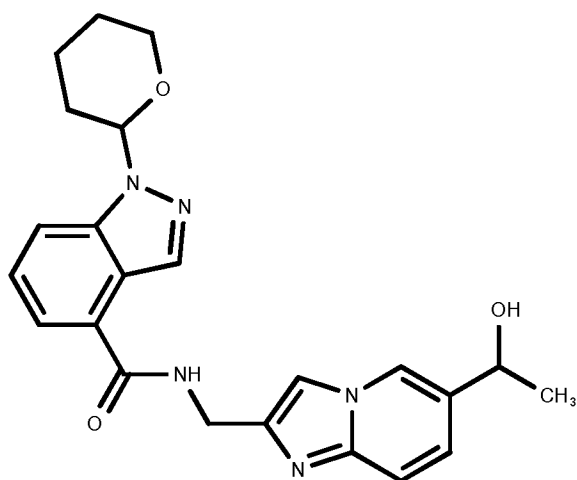
Cpd No	Name	Structure	LCMS method	LCMS Retention time	Mass ion
45	N-[(6-[(2-hydroxyethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide		C	1.40	365.2
46	N-[(6-[(2,2,2-trifluoroethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide		D	3.05	403.1

5 [00373] **Synthesis of Compound 47: N-[(6-(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide**



[00374] **Step 1: N-[(6-(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1-(oxan-2-yl)-1H-indazole-4-carboxamide**

10



A solution of magnesium bromide in ether (3M, 74 μ L, 0.22 mmol) was added dropwise over 1 min to a solution of N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]-1-tetrahydropyran-2-yl-indazole-4-carboxamide (**intermediate 18**) (75 mg, 0.186 mmol) in THF (1 mL) at -30 °C. The reaction mixture was then warmed to 0 °C and stirred for 2 h. The reaction mixture was quenched by the addition of sat. aq. NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organics were dried and evaporated to dryness and the residue was purified by preparative HPLC (method B) to afford the title compound (31 mg, 40%) as an orange solid.

[00375] The title compound was prepared from N-[[6-(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-1-(oxan-2-yl)-1H-indazole-4-carboxamide using the procedure described in **Compound 1** giving (14.6 mg, 59%) as a white powder.

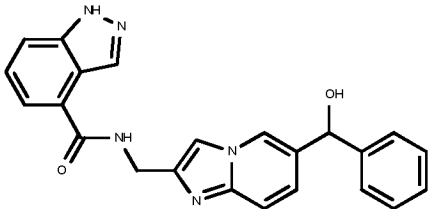
Method C: LC-MS (electrospray): m/z = 336.2 ($\text{M}+\text{H}$)⁺, RT = 1.56 min

[00376] Synthesis of Compound 48

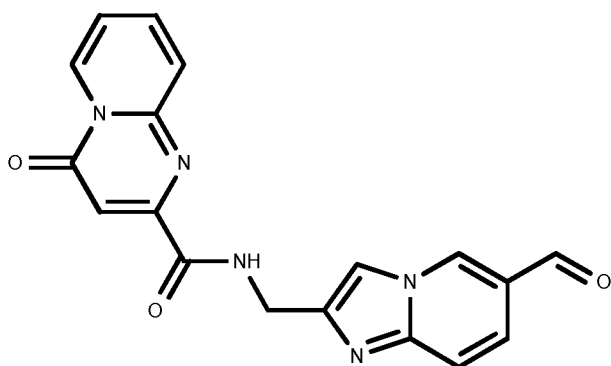
[00377] The compound in **table 5** was prepared in the same manner as **Compound 47**

[00378] Table 5

Compound No	Name	Structure	LCMS method	LCMS Retention time	Mass ion

48	N-({6-[hydroxy(phenyl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide		D	3.05	398.2

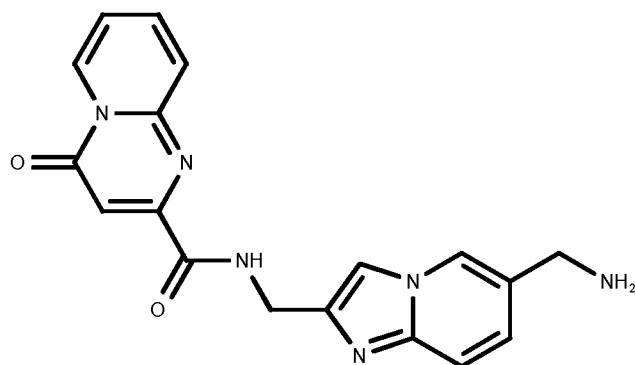
[00379] Synthesis of Compound 49: N-({6-formylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



- 5 **[00380]** A suspension of N-[(6-cyanoimidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide (**Compound 18**) (400 mg, 1.16 mmol), in a mixture of water (6 mL), pyridine (12 mL) and acetic acid (3 mL) was treated with sodium phosphinate hydrate (985 mg, 9.29 mmol) followed by Raney nickel (50%, 1.20 g, 10.2 mmol) and the mixture was heated at 100 °C, under a nitrogen atmosphere, for 4.5 hours.
- 10 Further Raney nickel (50%, 0.6 g, 5.1 mmol) was added and the heating was continued for an hour. The suspension was cooled to room temperature and the Ni (R) was removed by filtration through a bed of celite (washing with water). The filtrate was extracted with DCM (x4) and the extracts were dried (magnesium sulfate) and evaporated under vacuum to a suspension which contained pyridine. Further evaporation under vacuum gave a solid
- 15 residue which was suspended in water and the solids were collected by filtration, washed with water followed by ether and dried under vacuum to give the title compound (205 mg, 51%) as a buff solid. The aqueous was further extracted with IPA/CHCl₃ (1:3) and the extracts were evaporated under vacuum to dryness. The residue which was suspended in water and the solids were collected by filtration, washed with water followed by ether and
- 20 dried under vacuum to give the title compound (61 mg, 15%) as a buff solid.

LCMS Method E (electrospray): m/z = 348.1 (M+H)⁺, RT = 1.16 min

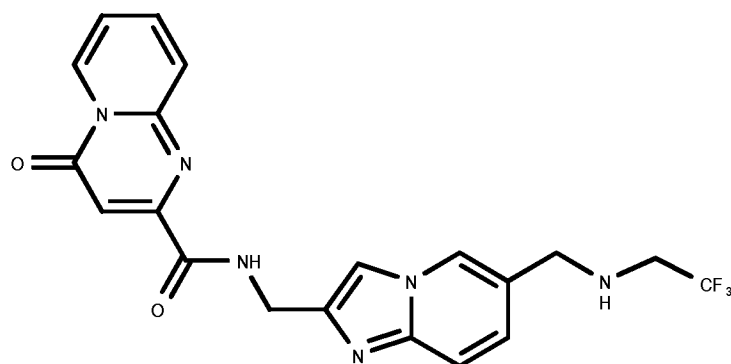
[00381] **Synthesis of Compound 50: N-[[6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide**



[00382] The residual aqueous solution from **Compound 49** was concentrated under vacuum and the residue was dissolved in MeOH and purified by ion exchange (SCX-2, 5 g) and the eluted fraction was evaporated under vacuum to a beige solid which was purified by preparative HPLC [method B] to provide the title compound (7.5 mg, 2%) as an off white solid.

LCMS Method C (electrospray): m/z = 349.2 ($M+H$)⁺, RT = 1.47 min

[00383] **Synthesis of Compound 51: 4-oxo-N-[[6-[[2,2,2-trifluoroethyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide**



[00384] A solution of N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide (**Compound 49**) (50 mg, 0.144 mmol) and 2,2,2-trifluoroethanamine (29 mg, 0.288 mmol) in DCE (2 mL) was stirred at rt for 2 hours before STAB (92 mg, 0.432 mmol) was added and the reaction mixture was stirred at 50 °C for 18 h. The reaction mixture was cooled to RT, STAB (92 mg, 0.432 mmol) was added and the reaction mixture was stirred at 50 °C for 2 h. The reaction mixture was quenched with water (5 mL) and extracted with DCM (3 x 5 mL). The combined organics were dried, evaporated

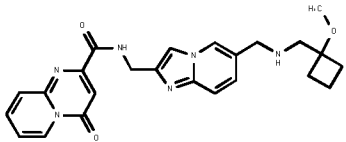
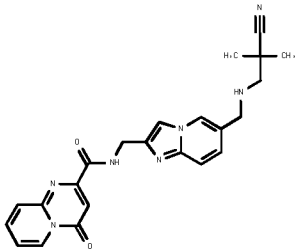
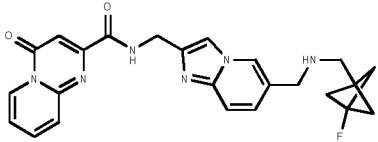
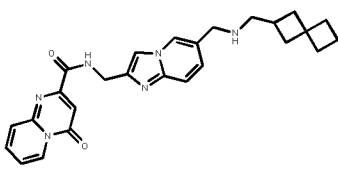
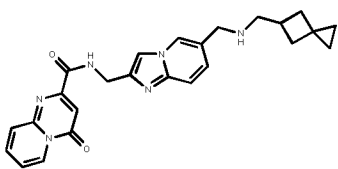
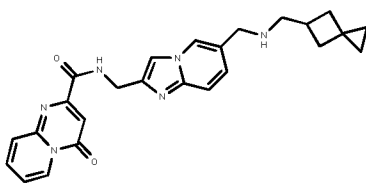
to dryness and purified by preparative HPLC [method B] to afford the title compound (34 mg, 53%) as a white powder.

LCMS Method E (electrospray): m/z = 431.3 (M+H)⁺, RT = 1.18 min

- 5 [00385] **Synthesis of Compounds 52-55**
 [00386] The compounds in **table 6** was prepared in the same manner as **Compound 47**

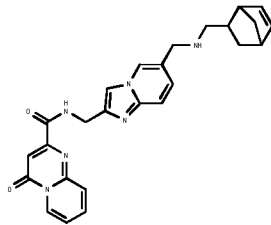
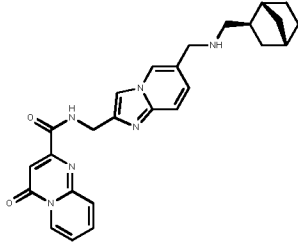
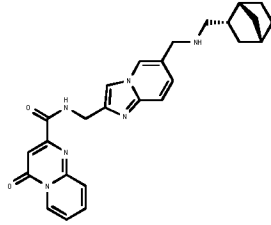
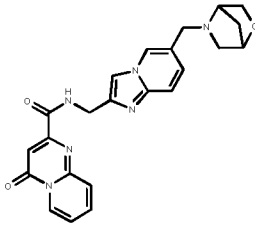
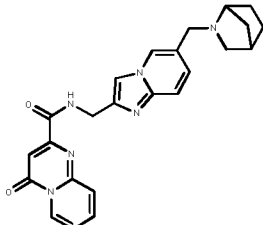
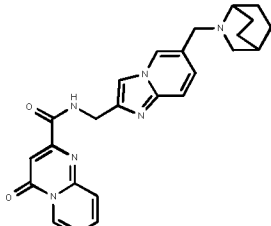
Table 6

Compound No	Name	Structure	LCMS method	LCMS Retention time	Mass ion
52	N-[(6-[(2-hydroxyethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.47	393.2
53	4-oxo-N-[(6-[(2-phenylethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.43	453.3
54	N-[(6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.37	439.3
55	4-oxo-N-[(6-[(3-phenylpropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.64	467.3

	4H-pyrido[1,2-a]pyrimidine-2-carboxamide				
273	N-[[6-[(1-methoxycyclobutyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.04	447.4
275	N-[[6-[(2-cyano-2-methylpropyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.19	430.1
276	N-[[6-[(3-fluoro-1-bicyclo[1.1.1]pentanyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.36	447.3
277	4-oxo-N-[[6-[(spiro[3.3]heptan-2-yl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]pyrido[1,2-a]pyrimidine-2-carboxamide		C	3.12	457.4
278	4-oxo-N-[[6-[(spiro[2.3]hexan-5-yl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.79	443.4
279	N-[[6-[(1-bicyclo[1.1.1]pentanyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.33	429.4

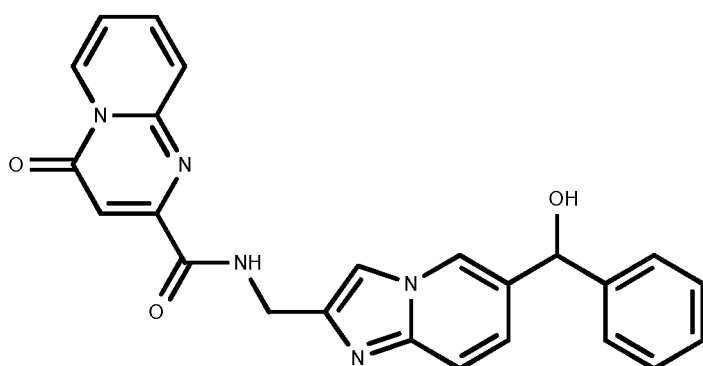
280	4-oxo-N-[[6-[(spiro[2.3]hexan-2-ylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.37	429.3
281	N-[[6-[[[(2-methoxy-2-methylpropyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.09	435.4
282	N-[[6-[[[(1-methylcyclobutyl)methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.51	431.3
283	N-[[6-(butylaminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.17	405.3
284	N-[[6-[[[(1-hydroxycyclopentyl)methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.06	447.4
285	N-[[6-[(2-methylbutylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.66	419.4
286	N-[[6-[(2-cyclobutylethylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.75	431.3

287	N-[[6-[[[(2-hydroxy-2-methylpropyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.76	421.3
288	N-[[6-[[[(1-hydroxycyclobutyl)methylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.89	433.3
289	N-[[6-[(2-hydroxybutylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.65	421.3
290	N-[[6-[[[(3-methylcyclobutyl)methylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.59	431.2
291	N-[[6-[[[(3,3-dimethylcyclobutyl)methylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.84	445.3
292	N-[[6-[(2,2-dimethylbutylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.74	433.3
293	N-[[6-[[[(2S)-2-methylbutyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.66	419.3

346	N-[(6-{[(1R,2R,4S)-bicyclo[2.2.1]hept-5-en-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.61	455.3
347	N-({6-[(1R,2R,4S)-bicyclo[2.2.1]heptan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.93	457.4
348	N-({6-[(1R,2S,4S)-bicyclo[2.2.1]heptan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	3.00	457.4
349	N-({6-({2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.75	431.4
350	N-({6-({2-azabicyclo[2.2.1]heptan-2-yl)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.45	429.4
351	N-({6-({2-azabicyclo[2.2.2]octan-2-yl)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.80	443.3

352	N-({6-[(6,6-difluorospiro[3.3]heptan-2-yl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.55	479.3
353	rac-N-({6-[(1R,2R,4R)-7-oxabicyclo[2.2.1]hept-5-en-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.97	457.4
354	rac-N-({6-[(1R,2S,4R)-7-oxabicyclo[2.2.1]hept-5-en-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.92	457.3

[00387] Synthesis of Compound 56: N-({6-[hydroxy(phenyl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



- 5 **[00388]** Phenyl magnesium bromide (1M in THF, 207 μ L, 0.207 mmol) was added dropwise over 1 min to a solution of N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide (**Compound 49**) (30 mg, 0.0864 mmol) in THF (2 mL) at -30 $^{\circ}$ C. The reaction mixture was then warmed to 0 $^{\circ}$ C and stirred for 2 hours. The stirring was continued for 16 hours during which time the reaction warmed to room
- 10 temperature. The reaction mixture was re-cooled to -30 $^{\circ}$ C and treated with Phenyl magnesium bromide (1M in THF, 103 μ L, 0.1 mmol) and the mixture was stirred at 0 $^{\circ}$ C for a

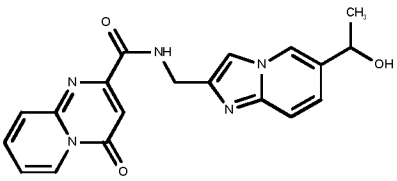
further 30 minutes. The mixture was quenched by the addition of NH_4Cl (sat 10 mL) and extracted with DCM (3 x 15 mL) and the organics were dried and evaporated to dryness to afford a residue which was purified by Preparative HPLC [method B] and the fractions were freeze dried to afford the title compound (4.4 mg, 12%) as a white foam.

- 5 LCMS Method D (electrospray): $m/z = 426.2$ ($\text{M}+\text{H}^+$), $\text{RT} = 3.10$ min

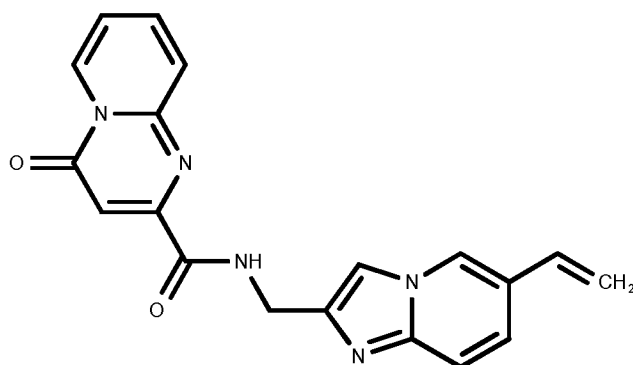
[00389] Synthesis of Compound 57

[00390] The compound in **table 7** was prepared in a similar manner to **Compound 56**

10 **Table 7**

Compound No	Name	Structure	LCMS method	LCMS Retention time	Mass ion
57	N-([6-(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.54	364.2

[00391] Synthesis of Compound 58: N-([6-ethenylimidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



- 15 **[00392]** N-([6-bromoimidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide (**Compound 23**) (150mg, 0.38mmol), potassium ethenyl(trifluoro)borate (76mg, 0.57mmol) and K_2CO_3 (1.2M aqueous, 941 μL , 1.13mmol) were combined in 1,4-Dioxane (4ml) and the mixture was sparged with nitrogen for 5mins. Pd-118 (25mg,

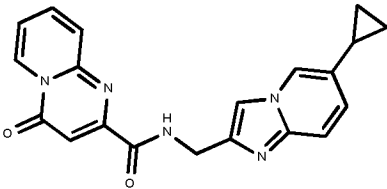
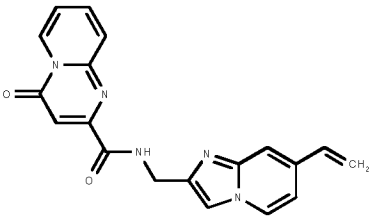
0.04mmol) was added and the mixture was sparged for a further 5mins. The vessel was sealed and the mixture heated at 100°C for 2 hours. The reaction mixture was cooled to room temperature and diluted with sodium hydrogen carbonate (sat, 30ml) and extracted with chloroform/isopropanol (3:1, 3 x 50ml) and the combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage 28 g kp-NH, eluting with 0-100% ethyl acetate/heptane). The residue after evaporation was triturated with ethyl acetate/heptane. The solids were collected by filtration, washed with heptane and dried under suction to afford the title compound (73mg, 56% yield) as a white solid.

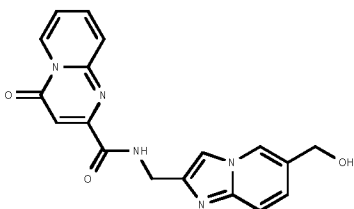
LCMS Method E (electrospray): m/z = 346.1 (M+H)⁺, RT = 1.17 min

[00393] Synthesis of Compounds 59-61

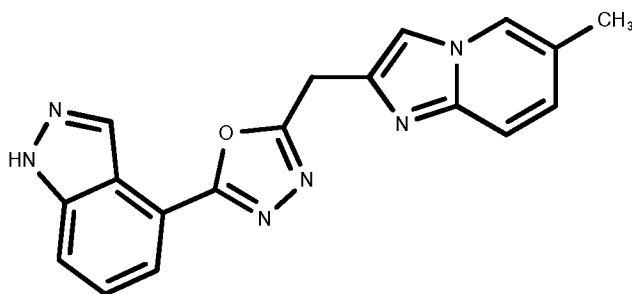
[00394] The compounds in **table 8** was prepared in a similar manner to **Compound 58**

Table 8

Compound No	Name	Structure	LCMS method	LCMS Retention time	Mass ion	catalyst
59	N-({6-cyclopropylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.27	360.3	Pd118 Followed by PddppfCl ₂
60	N-({7-ethenylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.12	346.2	

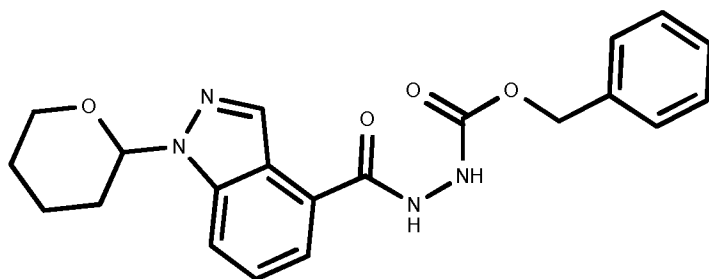
61	N-{{[6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl]methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.45	350.3	Ruphos, Acetyl protected

[00395] Synthesis of Compound 62: 2-(1H-indazol-4-yl)-5-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]-1,3,4-oxadiazole

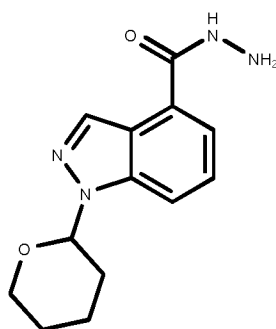


[00396]

- 5 **[00397] Step 1: ({[(benzyloxy)carbonyl]amino}amino)[1-(oxan-2-yl)-1H-indazol-4-yl]methanone**

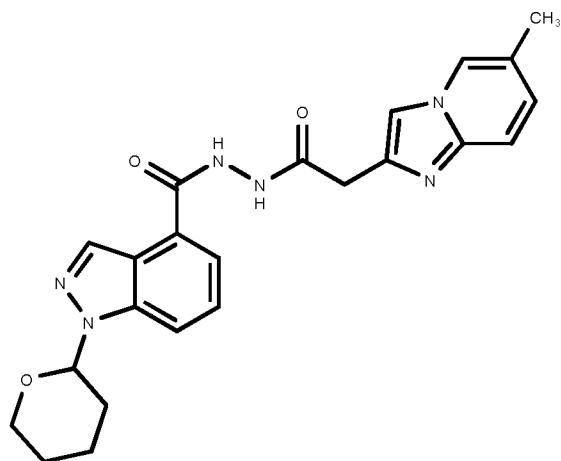


- [00398]** A solution of 1-tetrahydropyran-2-ylindazole-4-carboxylic acid (900mg, 3.65mmol), benzyl N-aminocarbamate (729mg, 4.39mmol) and triethylamine (1.53ml, 11.0mmol) were combined in DMF (10ml), HATU (2.08g, 5.48mmol) was added and the mixture was stirred at room temperature for 7 hours. The reaction mixture was diluted with ethyl acetate (100ml) and washed with sodium hydrogen carbonate (sat, 100ml) and brine (4 x 100ml). The organic layer was dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage 50 g, eluting with 0-100% ethyl acetate/heptane) to afford the title compound (1.42g, 91%) as a pale pink solid.
- LCMS Method A (electrospray): m/z = 393.15 (M-H)⁻, RT = 1.09 min

[00399] Step 2: 1-(oxan-2-yl)-1H-indazole-4-carbohydrazide

A suspension of benzyl N-[(1-tetrahydropyran-2-yl)indazole-4-carbonyl]amino]carbamate (500mg, 1.17mmol) and Palladium on carbon (10% wt, 124mg, 0.12mmol) were suspended in ethanol (50ml) and the mixture stirred vigorously under an atmosphere of hydrogen (1 atm) at room temperature for 6h. The catalyst was removed by filtration through Celite, washing with MeOH, then ammonia in MeOH (7M) and the filtrate evaporated under vacuum. The residue was purified by ion exchange [SCX-2, 10g] and the residue triturated with ethyl acetate/heptane to afford the title compound (158 mg, 52%) as a pale yellow solid.

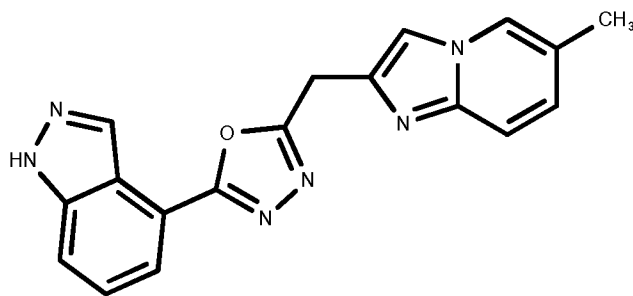
LCMS Method A (electrospray): m/z = 261.0 (M+H)⁺, RT = 0.84 min

[00400] Step 3: 2-{6-methylimidazo[1,2-a]pyridin-2-yl}-N'-[1-(oxan-2-yl)-1H-indazole-4-carbonyl]acetohydrazide

The title compound was prepared by coupling 1-(oxan-2-yl)-1H-indazole-4-carbohydrazide with **Intermediate 19** using the coupling described in **Compound 1** and DMF as solvent to give (178 mg, 67%) as yellow solid.

LCMS Method A (electrospray): m/z = 433.2 (M+H)⁺, RT = 0.84 min

[00402] Step 4: 4-[5-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1,3,4-oxadiazol-2-yl]-1H-indazole

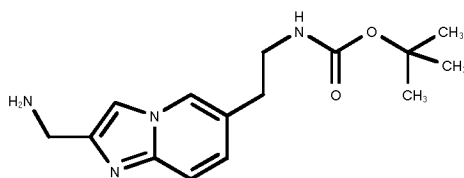


[00403] A suspension of N'-[2-(6-methylimidazo[1,2-a]pyridin-2-yl)acetyl]-1-tetrahydropyran-2-yl-indazole-4-carbohydrazide (150mg, 0.35mmol) in phosphoryl trichloride (5ml) was heated at 100°C for 1.5 hours. The reaction mixture was cooled to room temperature and poured slowly onto a slurry of solid K₂CO₃ and ice. The mixture was stirred vigorously [gas evolution; significant exotherm] until the ice had melted. The mixture was extracted with chloroform/isopropanol (3:1, 4 x 80ml). The extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by ion exchange [SCX-2, 10g]. The residue was purified by preparative HPLC (method B) and the residue was triturated with ethyl acetate/heptane, the solids were collected by filtration, washed with heptane and dried under vacuum to afford the title compound (21.3mg, 19%) as an off-white solid.

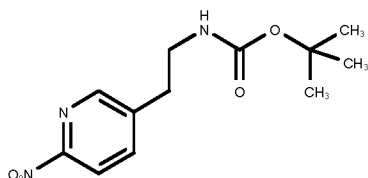
LCMS Method D (electrospray): m/z = 331.2 (M+H)⁺, RT = 3.20 min

Further Organic Synthesis

[00404] Intermediate 20: tert-butyl N-[2-[2-(aminomethyl)imidazo[1,2-a]pyridin-6-yl]ethyl]carbamate



[00405] Step 1: tert-butyl N-[2-(6-nitro-3-pyridyl)ethyl]carbamate

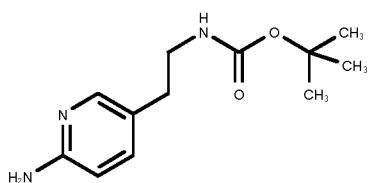


[00406] 5-bromo-2-nitro-pyridine (1000 mg, 4.93 mmol), potassium;2-(tert-butoxycarbonylamino)ethyl-trifluoro-boranuide (1.36 g, 5.41 mmol), cesium carbonate (4815

mg, 14.8 mmol) and [1,1'-Bis(diphenylphosphino)ferrocene]palladium(II) chloride dichloromethane complex (302 mg, 0.369 mmol) were combined in toluene (20 mL) and water (5 mL) and the mixture was heated at 80 °C for 16 hours. The reaction mixture was cooled to room temperature whereupon water (20 mL) was added and the aqueous were
 5 extracted with EtOAc (2 x 30 mL). The combined organic layer was washed with brine, dried over Na₂SO₄, filtered and evaporated under reduced pressure to give a brown gum, which was purified by chromatography on silica gel [Biotage 100 g, eluting by 10% - 80% EtOAc in heptane] to provide the title compound (900 mg, 55%) as an off white solid.

Method A: LC-MS (electrospray): m/z = 267.9 (M+H)⁺, RT = 1.06 min.

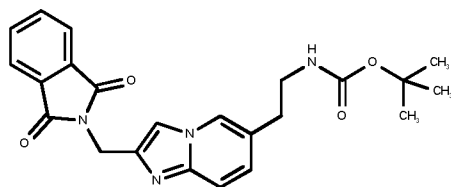
10 **Step 2: tert-butyl N-[2-(6-aminopyridin-3-yl)ethyl]carbamate**



[00407] tert-butyl N-[2-(6-nitro-3-pyridyl)ethyl]carbamate (1.07 g, 4.00 mmol) and Pd/C (10%) were combined in EtOH (25 mL). The mixture placed under an atmosphere of hydrogen and the reaction mixture was stirred at room temperature for 4 hours. The catalyst
 15 was removed by filtration washing with methanol and the filtrate was evaporated under vacuum to provide the title compound (1000 mg, 95%) as a colourless oil.

[00408] Method A: LC-MS (electrospray): m/z = 238.0 (M+H)⁺, RT = 0.66 min.

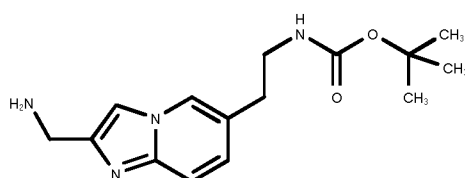
[00409] **Step 3: tert-butyl N-(2-[2-[(1,3-dioxo-2,3-dihydro-1H-isoindol-2-yl)methyl]imidazo[1,2-a]pyridin-6-yl]ethyl)carbamate**



20 [00410] The title compound was prepared using the method described for **Intermediate 7 Step 1** and triturating with MeCN to provide the title compound (600 mg, 38%) as an off white solid.

[00411] Method A: LC-MS (electrospray): m/z = 421.55 (M+H)⁺, RT = 0.94 min.

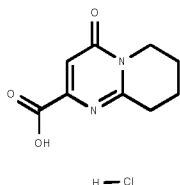
25 [00412] **Step 4: tert-butyl N-[2-[2-(aminomethyl)imidazo[1,2-a]pyridin-6-yl]ethyl]carbamate**



[00413] The title compound was prepared using the method described for **Intermediate 7 Step 2** to provide the title compound (170 mg, 41%) as a yellow solid.

[00414] Method A: LC-MS (electrospray): $m/z = 291.10$ ($M+H$)⁺, RT = 0.70 min.

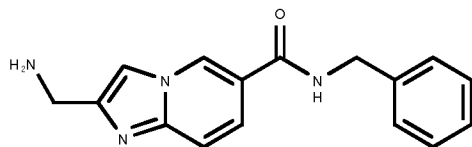
5 [00415] **Intermediate 21**: 4-oxo-6,7,8,9-tetrahydropyrido[1,2-a]pyrimidine-2-carboxylic acid hydrochloride



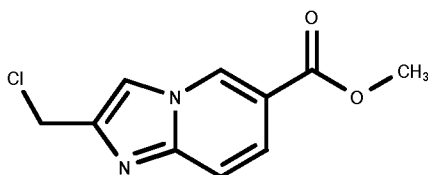
10 [00416] A suspension of rhodium (504 mg, 4.90 mmol) in ethanol (20 mL) was placed under a nitrogen atmosphere. 4-oxopyrido[1,2-a]pyrimidine-2-carboxylate hydrochloride (**Intermediate 4**, 60%, 1000 mg, 2.66 mmol) was added. The mixture was placed under an atmosphere of hydrogen and the mixture was stirred at room temperature for 4 hours. The catalyst was removed by filtration and the filtrate was evaporated under vacuum to afford a brown gum which crystallised on standing to give the title compound (600 mg, 97%) as beige solid.

15 [00417] Method B: LC-MS (electrospray): $m/z = 195.2$ ($M+H$)⁺, RT = 0.28 min.

[00418] **Intermediate 22**: 2-(aminomethyl)-N-benzylimidazo[1,2-a]pyridine-6-carboxamide



[00419] **Step 1**: methyl 2-(chloromethyl)imidazo[1,2-a]pyridine-6-carboxylate

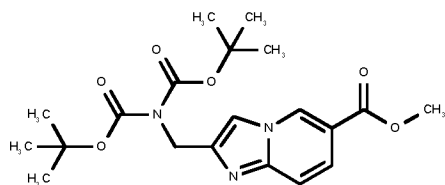


20

[00420] The title compound was prepared using the method described in **Intermediate 8 Step 1**, to provide (741 mg, 48%) as a white solid.

[00421] Method B: LC-MS (electrospray): $m/z = 225.1$ ($M+H$)⁺, RT = 1.31 min.

25 [00422] **Step 2**: methyl 2-({bis[(tert-butoxy)carbonyl]amino}methyl)imidazo[1,2-a]pyridine-6-carboxylate



[00423] A mixture of methyl 2-(chloromethyl)imidazo[1,2-a]pyridine-6-carboxylate (740 mg, 3.29 mmol), di-tert-butyl imidodicarbonate (1.07g, 4.94 mmol), NaI (50 mg, 0.33 mmol) and K₂CO₃ (1.37g, 9.88 mmol) were combined in acetonitrile (40 mL) and the mixture stirred at room temperature for an hour before water (1 mL) was added and the mixture heated at reflux for an hour. The reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was suspended in saturated aqueous sodium hydrogen carbonate (50 mL) and extracted with DCM (4 x 80 mL). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage 50 g kp-Sil, eluting with EtOAc/heptane 0-50%) to afford the title compound (1.13g 77%, 91% purity) as a viscous yellow oil which solidified on standing.

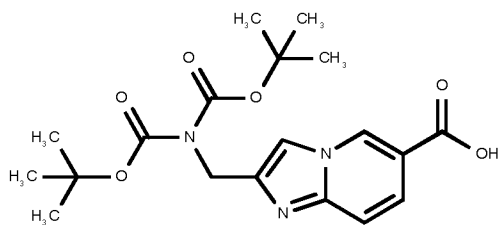
[00424] Method B: LC-MS (electrospray): m/z = 406.2 (M+H)⁺, RT = 1.72 min.

[00425] **Step 3:** 2-({bis[(tert-butoxy)carbonyl]amino}methyl)imidazo[1,2-a]pyridine-6-carboxylic acid

[00426] A mixture of methyl 2-(chloromethyl)imidazo[1,2-a]pyridine-6-carboxylate (740 mg, 3.29 mmol), di-tert-butyl imidodicarbonate (1.07g, 4.94 mmol), NaI (50 mg, 0.33 mmol) and K₂CO₃ (1.37g, 9.88 mmol) were combined in Acetonitrile (40 mL) and the mixture stirred at room temperature for an hour before water (1 mL) was added and the mixture heated at reflux for an hour. The reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was suspended in aqueous sodium hydrogen carbonate (sat, 50 mL) and extracted with DCM (4 x 80 mL). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage 50 g kp-Sil, eluting with EtOAc/heptane 0-50%) to afford the title compound (1.13g 77%, 91% purity) as a viscous yellow oil which solidified on standing.

[00427] Method B: LC-MS (electrospray): m/z = 406.2 (M+H)⁺, RT = 1.72 min.

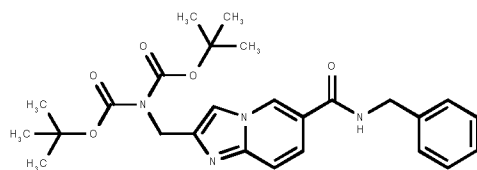
[00428] **Step 3:** 2-({bis[(tert-butoxy)carbonyl]amino}methyl)imidazo[1,2-a]pyridine-6-carboxylic acid



[00429] Methyl 2-[[bis(tert-butoxycarbonyl)amino]methyl]imidazo[1,2-a]pyridine-6-carboxylate (500 mg, 1.23 mmol) was dissolved in THF (25 mL) and water (10 mL), lithium hydroxide (240 mg, 5.98 mmol) was added which caused instant decolourisation of the yellow solution and the mixture was stirred at room temperature for 70 minutes. The reaction mixture was acidified with HCl (2M, pH~5) and extracted with chloroform/isopropanol (3:1, 3 x 80 mL). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum to afford the title compound (405 mg, 84%) as a white solid.

Method B: LC-MS (electrospray): m/z = 392.2 (M+H)⁺, RT = 1.17 min.

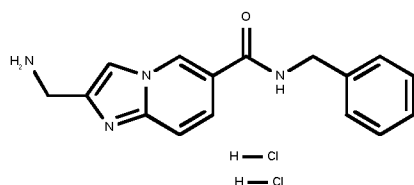
[00430] **Step 4:** tert-butyl N-[[6-(benzylcarbamoyl)imidazo[1,2-a]pyridin-2-yl]methyl]-N-[(tert-butoxy)carbonyl]carbamate



[00431] Prepared using the coupling conditions described in **Example 1** and purified by chromatography on silica gel (Biotage 25 g kp-Sil, eluting with EtOAc/heptane 0-100%) to afford the title compound (493 mg, 99%) as a pink solid.

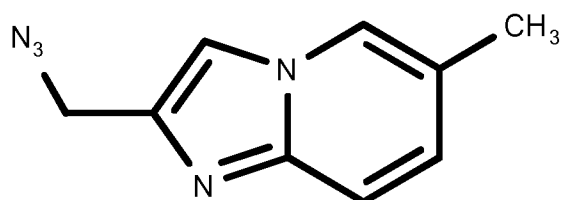
Method B: LC-MS (electrospray): m/z = 481.25 (M+H)⁺, RT = 1.13 min.

[00432] **Step 5:** 2-(aminomethyl)-N-benzylimidazo[1,2-a]pyridine-6-carboxamide dihydrochloride



[00433] A solution of tert-butyl N-[[6-(benzylcarbamoyl)imidazo[1,2-a]pyridin-2-yl]methyl]-N-tert-butoxycarbonyl-carbamate (493 mg, 1.03 mmol) in methanol (20 mL) was treated with HCl (4M in Dioxane, 3 mL, 12 mmol) and the mixture was heated at 50 °C for an hour. The reaction mixture was cooled to room temperature and evaporated to dryness under vacuum to afford the title compound (346 mg, 95%) as a white solid.

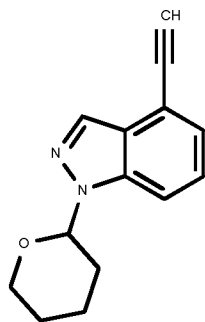
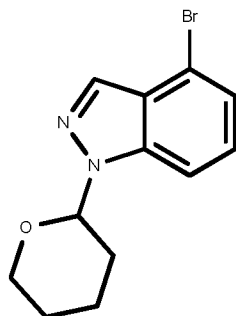
Method B: LC-MS (electrospray): m/z = 281.05 (M+H)⁺, RT = 0.71 min.

[00434] Intermediate 23: 2-(azidomethyl)-6-methylimidazo[1,2-a]pyridine**[00435]** A suspension of 2-(chloromethyl)-6-methyl-imidazo[1,2-a]pyridine

5 hydrochloride (532 mg, 2.45 mmol), triethylamine (1 mL, 7.35 mmol) and NaI (111 mg, 0.74 mmol) were suspended in DMF (5 mL) before sodium azide (175 mg, 2.70 mmol) was added and the mixture was stirred at room temperature For 16 hours. The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate (20 mL) and extracted with chloroform/isopropanol (3:1, 4 x 30 mL) and the combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography

10 on silica gel (Biotage 28 g kp-NH, eluting with EtOAc/heptane 0-100%) to afford the title compound (291 mg, 63%) as a colourless oil.

Method B: LC-MS (electrospray): m/z = 188.2 ($M+H$)⁺, RT = 1.33 min.

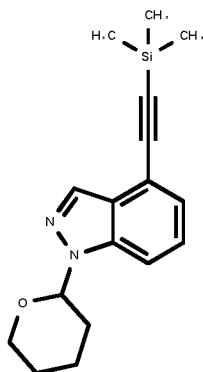
[00436] Intermediate 24: 4-ethynyl-1-(oxan-2-yl)-1H-indazole**[00437] Step 1: 4-bromo-1-(tetrahydropyran-2-yl)-1H-indazole****[00438]** A solution of 4-bromo-1H-indazole (2.3g, 11.7 mmol) and tosic acid

20 monohydrate (444 mg, 2.33 mmol) in DCM (50 mL) was treated with 3,4-dihydro-2H-pyran (1.60 mL, 17.5 mmol) and the mixture was stirred at room temperature for 2 hours during

which time the solution turned brown. The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate (50 mL) the phases were separated and the aqueous phase was extracted with DCM (2 x 80 mL) and the combined organic layers were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage 50 g kp-Sil, eluting with EtOAc/heptane 0-50%) to afford the title compound (3.4 g, 91%) as a pale yellow oil which solidified on standing to a white solid.

Method B: LC-MS (electrospray): m/z = 281.1/283.1 ($M+H$)⁺, RT = 1.74 min.

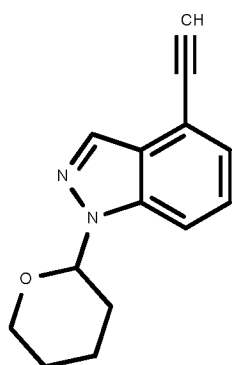
[00439] Step 2: 1-(oxan-2-yl)-4-[2-(trimethylsilyl)ethynyl]-1H-indazole



[00440] 4-bromo-1-tetrahydropyran-2-yl-indazole (1g, 3.56 mmol), CuI (68 mg, 0.36 mmol), PdCl₂(PPh₃)₂ (125 mg, 0.18 mmol) and triethylamine (1.5 mL, 3.03 mmol) were combined in anhydrous THF (7.5 mL) and the mixture sparged with nitrogen for 5 minutes. Ethynyl(trimethyl)silane (739 μ L, 5.34 mmol) was added, the vessel was sealed and the mixture heated at 80 °C for 48 hours. The reaction mixture was cooled to room temperature and diluted with EtOAc (100 mL). The mixture was washed with saturated aqueous sodium hydrogen carbonate (80 mL) and brine (2 x 80 mL) and the organic phase was dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage 50 g kp-Sil, eluting with EtOAc/heptane 0-50%) to afford the crude title compound contaminated with starting material (1.15g, 52%, 48% purity) as a brown oil.

Method B: LC-MS (electrospray): m/z = 299.0 ($M+H$)⁺, RT = 1.52 min.

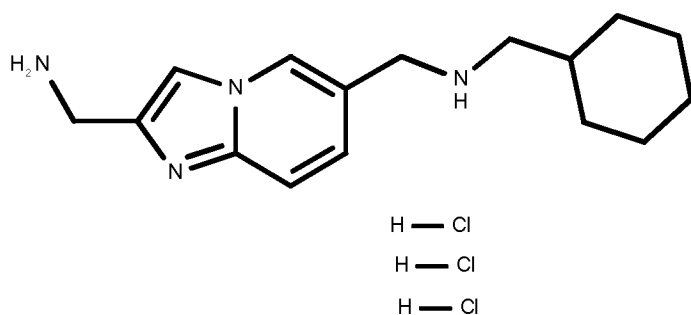
[00441] Step 3: 4-ethynyl-1-(oxan-2-yl)-1H-indazole



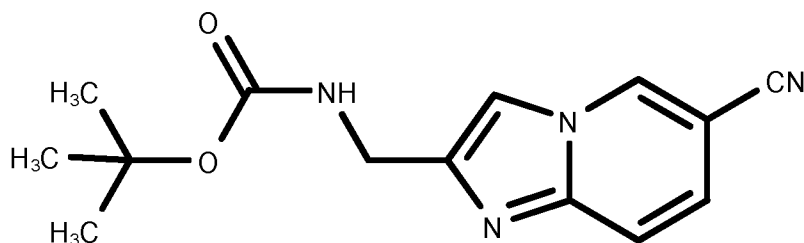
[00442] A solution of trimethyl-[2-(1-tetrahydropyran-2-ylindazol-4-yl)ethynyl]silane (1.15g, 1.93 mmol) in methanol (30 mL) was treated with K₂CO₃ (100 mg, 0.72 mmol) and the mixture was stirred at room temperature for 16 hours. The reaction mixture was filtered and the filtrate were evaporated under vacuum. The resultant residue was purified by chromatography on silica gel (Biotage 25 g kp-Sil, eluting with TMBE/heptane 0-40%) to afford the title compound (207 mg, 39%) of as a pale yellow oil which slowly solidified on standing.

Method B: LC-MS (electrospray): m/z = 226.95 (M+H)⁺, RT = 1.23 min.

[00443] Intermediate 25: (6-((cyclohexylmethyl)amino)methyl)imidazo[1,2-a]pyridin-2-yl)methanamine trihydrochloride



[00444] Step 1: tert-butyl N-({6-cyanoimidazo[1,2-a]pyridin-2-yl)methyl}carbamate

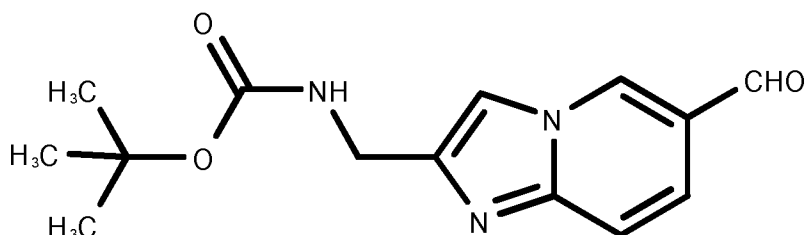


[00445] A suspension of 2-(aminomethyl)imidazo[1,2-a]pyridine-6-carbonitrile (2.60 g, 15.1 mmol) and N-ethyl-N-isopropyl-propan-2-amine (3.7 mL, 20.9 mmol) in THF (35 mL) and DCM (35 mL) was treated with N,N-dimethylpyridin-4-amine (0.085 g, 0.697 mmol) and tert-butoxycarbonyl tert-butyl carbonate (3.40 g, 15.6 mmol) at 0 °C and the mixture was allowed to warm to room temperature and stirred at room temperature for 65 hours. The reaction mixture was concentrated under vacuum, the residue was suspended in water-CH₃CN (1:1, 15 mL), and sonicated for 20 min. The solid was filtered, and then treated with water-MeCN again. The obtained solid was dried under vacuum to give the title compound (2.78 g, 63%) as an off white solid. The filtrate was purified by reverse phase

chromatography (Biotage 400 g eluting with 5-100% (0.1% formic acid in MeCN) in 0.1% formic acid to provide a further crop of title compound (414 mg, 10%).

Method B: LC-MS (electrospray): m/z = 273.3 (M+H)⁺, RT = 1.38 min.

[00446] Step 2: tert-butyl N-({6-formylimidazo[1,2-a]pyridin-2-yl)methyl}carbamate

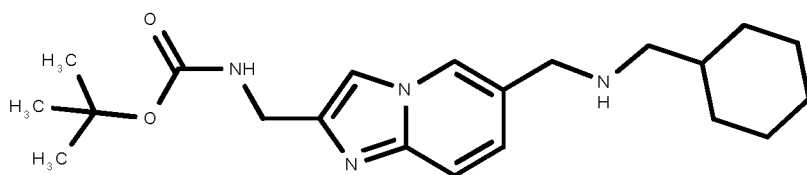


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[00447] A suspension of tert-butyl N-[(6-cyanoimidazo[1,2-a]pyridin-2-yl)methyl]carbamate (5.00 g, 18.4 mmol) and sodium phosphinate hydrate (15.57 g, 0.147 mol) in a mixture of water (50 mL), Pyridine (100 mL) and Acetic acid (50 mL) was treated with Raney nickel (50%, 18.97 g, 0.162 mol) and the mixture was heated at 100 °C under a nitrogen atmosphere for an hour. The Raney nickel was removed by hot filtration through a bed of Celite (washing with water, followed by methanol). The filtrate was concentrated under vacuum to remove the methanol and the blue solution was extracted with DCM (50 mL x 4). The extracts evaporated under vacuum to afford a beige gum which was triturated with water to furnish a white solid. The solid was collected by filtration, washed with water followed by ether and dried under vacuum overnight to provide the title compound (4.13 g, 82%) as an off white solid.

Method B: LC-MS (electrospray): m/z = 276.2 (M+H)⁺, RT = 1.33 min.

Step 3: tert-butyl N-[(6-[(cyclohexylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]carbamate

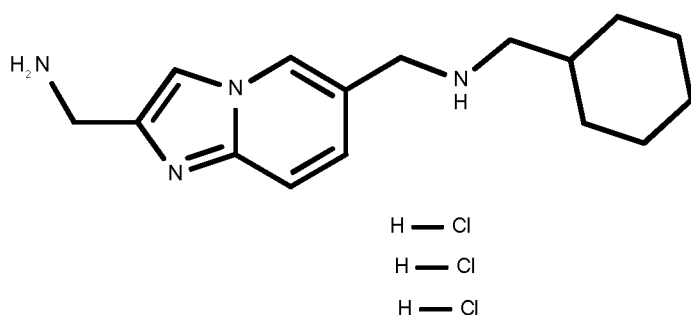


[00448] A solution of tert-butyl N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]carbamate (340 mg, 0.988 mmol) and cyclohexylmethanamine (224 mg, 1.98 mmol) in ethanol (6.8 mL) was stirred at 50 ° C for an hour. The reaction mixture was cooled

to 0 °C and NaBH₄ (75 mg, 1.98 mmol) was added in portions. The reaction mixture was allowed to warm to room temperature and stirring was continued for 2 hours. The reaction mixture was partitioned between DCM (80 mL) and saturated aqueous sodium hydrogen carbonate (30 mL). The organic layer was separated, washed with brine (30 mL), dried (MgSO₄), concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (Biotage KP-NH 28 g, eluting with 0-20% methanol in EtOAc) to afford the title compound (360 mg, 97%) as a pale yellow oil.

Method B: LC-MS (electrospray): m/z = 373.3 (M+H)⁺, RT = 1.76 min.

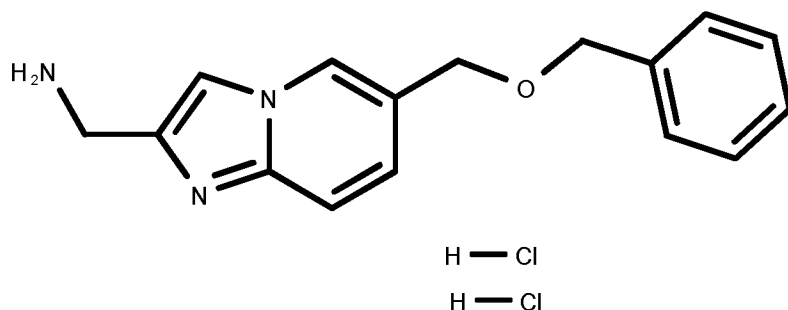
[00449] Step 4: (6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methanamine trihydrochloride

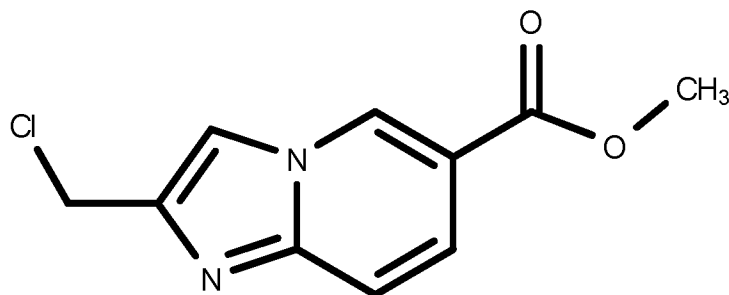


[00450] To a solution of tert-butyl N-[[6-[(cyclohexylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate (360 mg, 0.908 mmol) in methanol (4.1379 mL) was added HCl (4M in dioxane, 2.4 mL, 9.6 mmol) at room temperature. The solution was stirred at 50 °C for 1 hour. The solution was cooled to room temperature, and concentrated to dryness under reduced pressure. The residue (pale yellow glass) was dissolved in methanol (~3 mL) and diethyl ether (~20 mL) was added drop-wise to the stirred solution. The resulting precipitate was collected by filtration and dried in the vacuum oven at 40 °C for 4 hours to afford the title compound (359 mg, 100%) as white solid.

Method B: LC-MS (electrospray): m/z = 273.3 (M+H)⁺, RT = 1.77 min.

[00451] Intermediate 28: {6-[(benzyloxy)methyl]imidazo[1,2-a]pyridin-2-yl)methanamine dihydrochloride

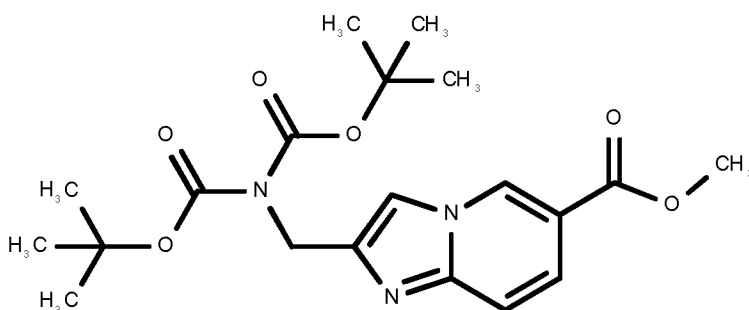


[00452] Step 1: Methyl 2-(chloromethyl)imidazo[1,2-a]pyridine-6-carboxylate

- 5 **[00453]** Methyl 6-aminopyridine-3-carboxylate (8.8g, 57.8 mmol) and 1,3-dichloropropan-2-one (11.0g, 86.8 mmol) were combined in acetonitrile (120 mL) and the mixture heated at reflux. The reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was basified using saturated aqueous sodium hydrogen carbonate (~150 mL) and extracted with chloroform/isopropanol (3:1, 4 x 80 mL).
- 10 The combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage, 100 g kp-Sil, eluting with EtOAc/heptane 0-100%) to afford the title compound (6.33g, 49%) of as an off-white solid.

Method B: LC-MS (electrospray): m/z = 225.1 ($M+H$)⁺, RT = 1.33 min.

- 15 **[00454] Step 2: methyl 2-({bis[(tert-butoxy)carbonyl]amino}methyl)imidazo[1,2-a]pyridine-6-carboxylate**



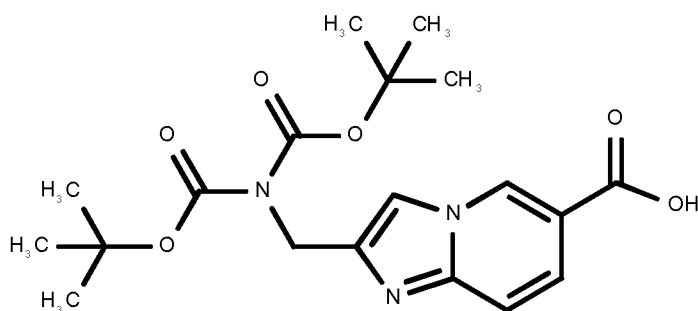
- 20 **[00455]** Methyl 2-(chloromethyl)imidazo[1,2-a]pyridine-6-carboxylate (6.33g, 28.2 mmol), di-tert-butyl imidodicarbonate (9.80g, 45.1 mmol), NaI (425 mg, 2.82 mmol) and K₂CO₃ (11.7g, 84.5 mmol) were combined in acetonitrile (200 mL) and water (5 mL) and the mixture heated at 70 °C for 3 hours.

- [00456]** The reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was diluted with water (100 mL) and extracted with DCM (3 x
- 25

150 mL) and the combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage 340 g kp-Sil, eluting with EtOAc/heptane 0-50%) to afford the title compound (8.51g, 74%) as a very pale yellow oil.

5 Method B: LC-MS (electrospray): m/z = 406.2 ($M+H$)⁺, RT = 1.71 min.

[00457] Step 3: 2-({bis[(tert-butoxy)carbonyl]amino}methyl)imidazo[1,2-a]pyridine-6-carboxylic acid

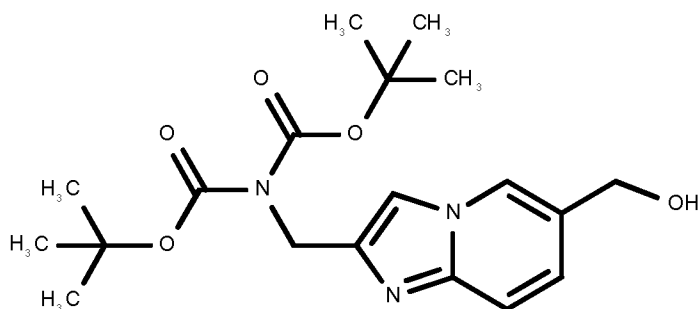


10 **[00458]** Methyl 2-[[bis(tert-butoxycarbonyl)amino]methyl]imidazo[1,2-a]pyridine-6-carboxylate (2.12g, 5.23 mmol) was dissolved in THF (30 mL) and water (10 mL) and lithium hydroxide (455 mg, 18.2 mmol) was added. The mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated under vacuum to remove THF. The residue was acidified carefully using HCl(1M) to ~pH2 and extracted with chloroform/isopropanol

15 (3:1, 3 x 80 mL). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum to afford the title compound (1.99g, 97%) as a white solid. Method B: LC-MS (electrospray): m/z = 392.3 ($M+H$)⁺, RT = 1.13 min.

[00459] Step 4: 2-({bis[(tert-butoxy)carbonyl]amino}methyl)imidazo[1,2-a]pyridine-6-carboxylic acid

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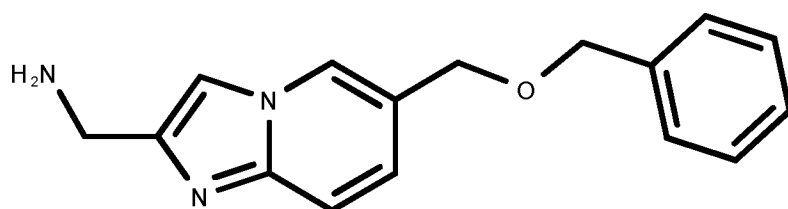
[00460] 2-[[bis(tert-butoxycarbonyl)amino]methyl]imidazo[1,2-a]pyridine-6-carboxylic acid (800 mg, 2.04 mmol) was dissolved in THF (anhydrous, 40 mL) and borane in THF (1M, 4.7 mL, 4.7 mmol) was added. The mixture was stirred at room temperature. Further borane

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THF (1M, 4.7 mL, 4.7 mmol) added and stirring continued overnight. Yellow solution after 2nd addition. The reaction mixture was quenched with methanol (40 mL) and the mixture stirred at room temperature for 30 minutes and was heated at reflux for 24 hours. The reaction mixture was cooled to room temperature and evaporated under vacuum. The residue was suspended in saturated aqueous sodium hydrogen carbonate (50 mL) and extracted with chloroform/isopropanol (3:1 4 x 50 mL). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage 28 g kp-NH, eluting with methanol/DCM 0-20%) to afford the title compound (356 mg, 44%) of the title compound as a colourless oily residue.

Method B: LC-MS (electrospray): m/z = 378.3 (M+H)⁺, RT = 1.49 min.

[00461] Step 5: {6-[(benzyloxy)methyl]imidazo[1,2-a]pyridin-2-yl}methanamine dihydrochloride



H — Cl

H — Cl

[00462] tert-butyl N-tert-butoxycarbonyl-N-[[6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl]methyl]carbamate (350 mg, 0.93 mmol) was dissolved in THF (anhydrous 30 mL) and cooled in an ice/water bath. Sodium hydride (60% wt in mineral oil, 371 mg, 9.27 mmol) was added and the mixture stirred under cooling for 15 minutes. Benzyl bromide (220 μ L, 1.85 mmol) was added and the mixture stirred whilst warming to room temperature.

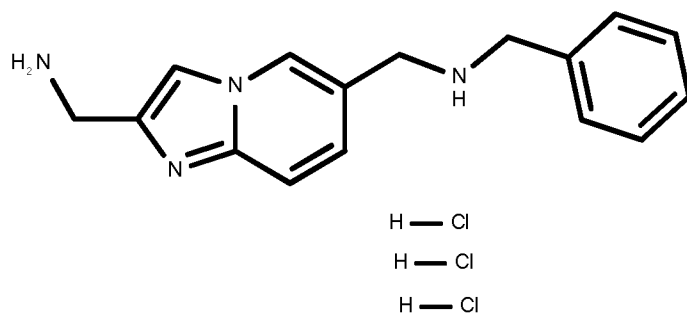
Further sodium hydride (60% wt in mineral oil, 371 mg, 9.27 mmol) was added and mixture continued to stir for 16 hours. The reaction mixture was slowly quenched with water (20 mL) - gas evolution - and the mixture stirred for 5 minutes, then extracted with chloroform/isopropanol (3:1, 4 x 30 mL) and the combined organic extracts dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage 28 g kp-NH, eluting with EtOAc/heptane 0-100%) to afford the crude

intermediate (356 mg, 37%, 41% purity) of as an amorphous solid. tert-butyl N-[[6-(benzyloxymethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-N-tert-butoxycarbonyl-carbamate (356 mg, 0.31 mmol, 41% purity) was dissolved in methanol (5 mL) and HCl (4M in Dioxane 1 mL, 4 mmol) was added and the mixture was stirred at room temperature for an hour and at 60 °C for 3 hours. The reaction mixture was cooled to room temperature and evaporated under

vacuum to afford the title compound (252 mg, 97%, 41% purity) as a colourless foamy residue which was used without further purification.

Method B: LC-MS (electrospray): m/z = 268.3 (M+H)⁺, RT = 1.26 min.

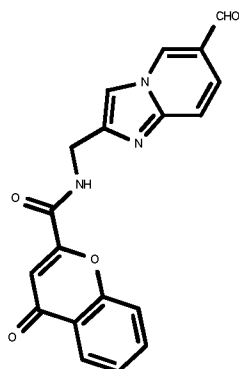
[00463] Intermediate 29: {6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl}methanamine dihydrochloride



[00464] The title compound was prepared in the same manner as **Intermediate 25** using benzylamine to provide (99 mg, 98%) as a white solid.

Method B: LC-MS (electrospray): m/z = 267.2 (M+H)⁺, RT = 1.32 min.

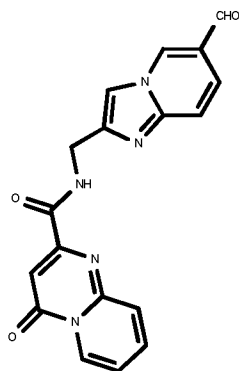
[00465] Intermediate 30: N-({6-formylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-chromene-2-carboxamide



[00466] The intermediate was prepared in the same manner as **Compound 49** starting from 2-(aminomethyl)imidazo[1,2-a]pyridine-7-carbonitrile and acid giving (349 mg, 49%) as a beige solid.

Method B: LC-MS (electrospray): m/z = 348.1 (M+H)⁺, RT = 1.29 min.

[00467] Intermediate 31: N-({7-formylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide

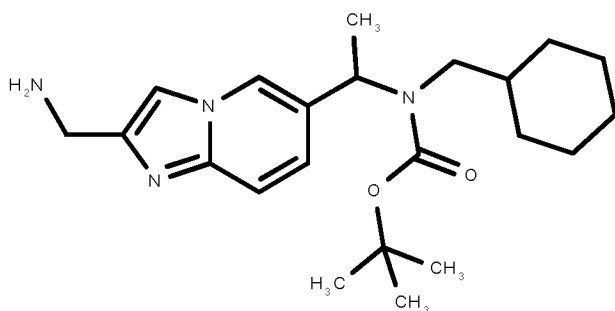


[00468] The intermediate was prepared in the same manner as **Compound 49** starting from 2-(aminomethyl)imidazo[1,2-a]pyridine-7-carbonitrile and coupling with

5 **Intermediate 4** to give the title compound as a beige solid.

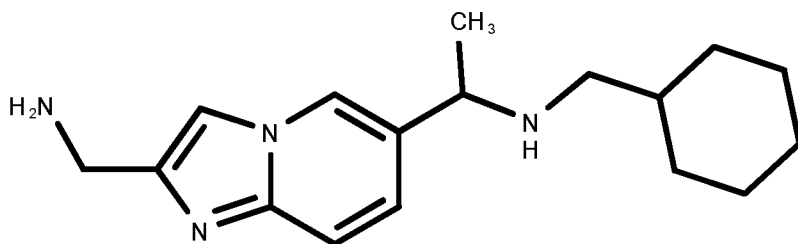
Method B: LC-MS (electrospray): m/z = 348.2 ($M+H$)⁺, RT = 1.19 min.

[00469] **Intermediate 32**: tert-butyl N-{1-[2-(aminomethyl)imidazo[1,2-a]pyridin-6-yl]ethyl}-N-(cyclohexylmethyl)carbamate



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[00470] **Step 1**: 5-{1-[(cyclohexylmethyl)amino]ethyl}pyridin-2-amine



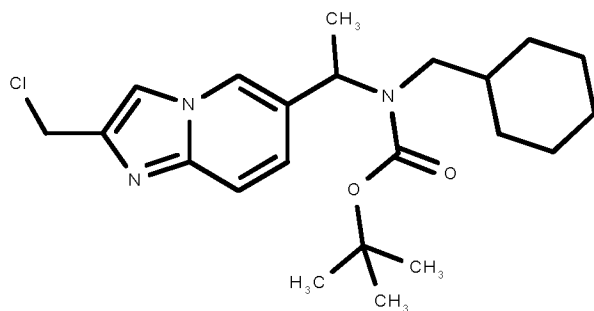
[00471] A mixture of 1-(6-amino-3-pyridyl)ethanone (1.05 g, 7.71 mmol)

15 and cyclohexylmethanamine (5.24 g, 46.3 mmol) in ethanol (20 mL) was stirred at 90 °C for 36 hours. The reaction mixture was cooled to 0 °C, and then NaBH₄ (584 mg, 15.4 mmol) was added. The reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was cooled to 0 °C and quenched with water and NaOH (1M). The aqueous were

extracted with IPA-CHCl₃ (1:4, 3 x 30 mL). The combined organic layer was dried over Na₂SO₄, filtered and evaporated under reduced pressure to give a yellow gum, which was purified by acidic reverse phase chromatography (biotage100 g) to give the title compound as a pale brown gum(1.00 g, 48%).

5 Method B: LC-MS (electrospray): m/z = 234.3 (M+H)⁺, RT = 1.51 min

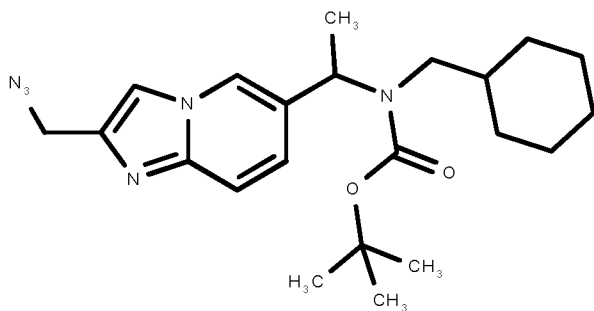
[00472] Step 2: tert-butyl N-[1-[2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl]ethyl]-N-(cyclohexylmethyl)carbamate



[00473] A solution of 1,3-dichloropropan-2-one (702 mg, 5.53 mmol) and 5-[1-(cyclohexylmethylamino)ethyl]pyridin-2-amine (1000 mg, 3.69 mmol) in acetonitrile (50 mL) was stirred at reflux for 2 hours. The reaction mixture was cooled to 0 °C and treated with tert-butoxycarbonyl tert-butyl carbonate (965 mg, 4.42 mmol), N,N-dimethylpyridin-4-amine (45 mg, 0.369 mmol) and N-ethyl-N-isopropyl-propan-2-amine (1.3 mL, 7.37 mmol) and the mixture was stirred at room temperature for 16 hours. The solvent was removed under vacuum and the residue was suspended in EtOAc (100 mL) and washed with water and brine, dried over Na₂SO₄, filtered and evaporated under reduced pressure to give a brown gum, which was purified by high pH reverse phases chromatography (biotage C18 Snap 100 g,) to give the title compound (400 mg, 27%) as a white solid.

Method B: LC-MS (electrospray): m/z = 406.3 (M+H)⁺, RT = 1.97 min.

[00474] Step 3: tert-butyl N-[1-[2-(azidomethyl)imidazo[1,2-a]pyridin-6-yl]ethyl]-N-(cyclohexylmethyl)carbamate

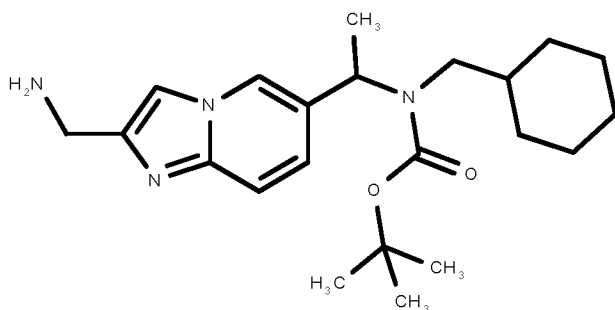


[00475] A suspension of tert-butyl N-[1-[2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl]ethyl]-N-(cyclohexylmethyl)carbamate (400 mg, 0.985 mmol) in acetonitrile (15 mL) was

treated with sodium azide (231 mg, 3.55 mmol) and sodium iodide (15 mg, 0.0985 mmol) at room temperature. The mixture was stirred at reflux for 20 hours. The reaction mixture was cooled to 0 °C and quenched with water (50 mL). The mixture was extracted with DCM (3 x 15 mL). The combined organic layer was dried over Na₂SO₄, filtered and concentrated in vacuo to give the title compound (410 mg, 98%) as a dark brown solid.

Method B: LC-MS (electrospray): m/z = 413.4 (M+H)⁺, RT = 1.98 min.

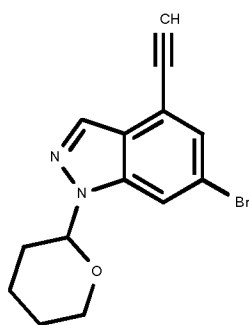
[00476] Step 4: tert-butyl N-[1-[2-(aminomethyl)imidazo[1,2-a]pyridin-6-yl]ethyl]-N-(cyclohexylmethyl)carbamate



[00477] tert-butyl N-[1-[2-(azidomethyl)imidazo[1,2-a]pyridin-6-yl]ethyl]-N-(cyclohexylmethyl)carbamate (300 mg, 0.727 mmol) and Pd/C (10%, 50 mg, 0.0470 mmol) were combined in EtOH (10 mL). The mixture was flushed three times with nitrogen, placed under a hydrogen atmosphere and stirred at room temperature for 16 hours. The reaction mixture was filtered through a pad of celite and the solid residue was washed with methanol. The filtrate was concentrated to dryness under vacuum to provide the title compound (280 mg, 100%) as yellow solid.

Method B: LC-MS (electrospray): m/z = 387.3 (M+H)⁺, RT = 1.95 min.

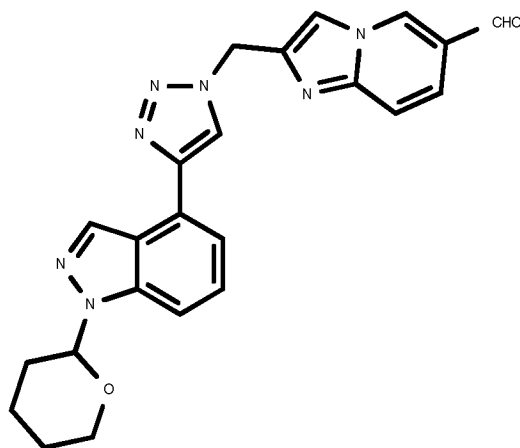
[00478] Intermediate 33: 6-bromo-4-ethynyl-1-(oxan-2-yl)-1H-indazole



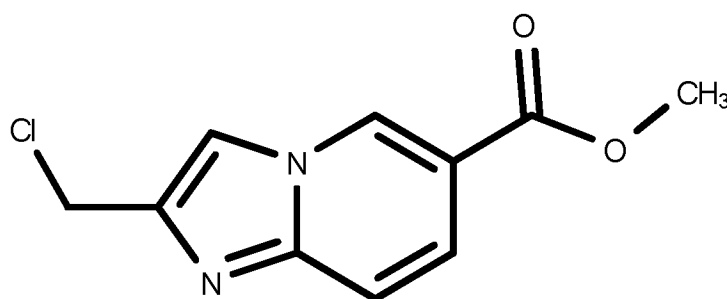
[00479] The title compound starting from was prepared from 6-bromo-4-iodo-1H-indazole using the steps described in **Intermediate 24** to give (737 mg, 96%).

Method A: LC-MS (electrospray): m/z = 304.95/306.95 (M+H)⁺, RT = 1.39 min

[00480] Intermediate 34: 2-[[4-(1-tetrahydropyran-2-yl)indazol-4-yl]triazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carbaldehyde



[00481] **Step 1:** methyl 2-(chloromethyl)imidazo[1,2-a]pyridine-6-carboxylate

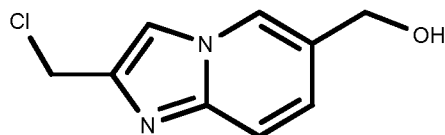


[00482] Methyl 6-aminopyridine-3-carboxylate (5.3g, 34.8 mmol) and 1,3-

5 dichloropropan-2-one (6.63 g, 52.3 mmol) were combined in acetonitrile (50 mL) and the mixture heated at reflux for 6 hours. The reaction mixture was cooled to room temperature and the residue suspended in saturated aqueous sodium hydrogen carbonate (80 mL). The mixture was extracted with 3:1 chloroform/isopropanol (3 x 100 mL) and the combined organic extracts dried over sodium sulfate and evaporated under vacuum. The residue was purified by Biotage Isolera™ chromatography (100 g kp-Sil, eluting with EtOAc/heptane 0-100%) to afford a crude material which was triturated with EtOAc/heptane. The solids were collected by filtration and dried under suction to afford 3.35g (43%) of the title compound as a white solid.

Method B: LC-MS (electrospray): m/z = 225.1 ($M+H$)⁺, RT = 1.32 min

15 [00483] **Step 2:** [2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl]methanol



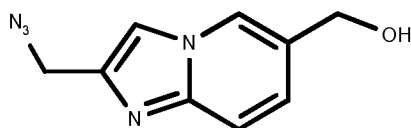
[00484] A solution of methyl 2-(chloromethyl)imidazo[1,2-a]pyridine-6-carboxylate (700 mg, 3.12 mmol) in anhydrous THF (20 mL) and cooled in an ice/water bath. DIBAL (1M in PhMe, 8.6 mL, 8.6 mmol) was added slowly to give a yellow solution and the mixture

stirred under cooling for 2 hours. The reaction mixture was quenched by dropwise addition of methanol (5 mL), then diluted with DCM (70 mL) and saturated aqueous sodium hydrogen carbonate (50 mL). The mixture was filtered through Celite and the residue rinsed well with DCM. The filtrates were phase-separated, the aqueous layer extracted with DCM (80 mL).

- 5 The combined organic layers dried over sodium sulfate and evaporated under vacuum. The resultant residue was triturated with Et₂O and the solids collected by filtration to afford (384 mg 60%) of the title compound as a pale yellow solid

[00485] MS16 IPC: LC-MS (electrospray): m/z = 196.8 (M+H)⁺, RT = 0.31 min

[00486] **Step 3:** [2-(azidomethyl)imidazo[1,2-a]pyridin-6-yl]methanol



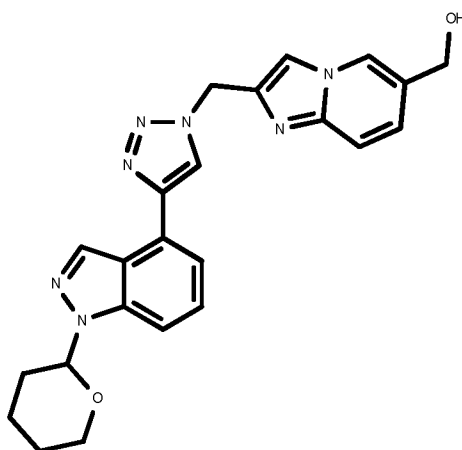
10 **[00487]**

[00488] [2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl]methanol (380 mg, 1.93 mmol), NaI (29 mg, 0.19 mmol) and NaN₃ (300 mg, 4.61 mmol) were combined in DMF (2 mL) and the mixture stirred at room temperature for 3 hours. The reaction mixture was diluted with saturated aqueous sodium hydrogen carbonate (30 mL) and extracted with DCM (3 x 50 mL). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The solids were carefully triturated with EtOAc/heptane and the solids collected by filtration to afford 309 mg, 79%) of the title compound as a pale yellow solid

Method B: LC-MS (electrospray): m/z = 204.2 (M+H)⁺, RT = 1.10 min

[00489] **Step 4:** [2-[[4-(1-tetrahydropyran-2-yl)indazol-4-yl]triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanol

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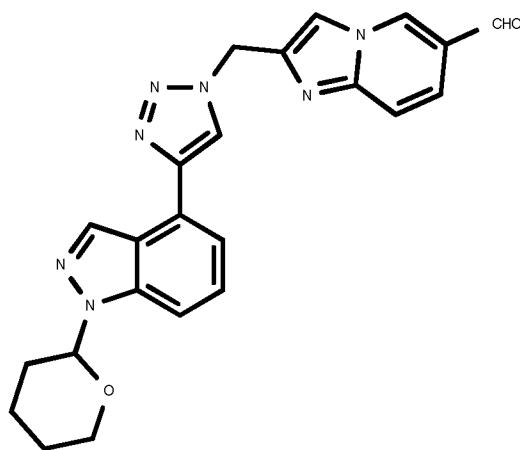
[00490] 4-ethynyl-1-tetrahydropyran-2-yl-indazole **Intermediate 24** (280 mg, 1.19 mmol), [2-(azidomethyl)imidazo[1,2-a]pyridin-6-yl]methanol (265 mg, 1.31 mmol) and copper sulfate (40 mg, 0.25 mmol) were combined in DMF (3 mL) and water (1 mL), and sodium

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ascorbate (261 mg, 1.31 mmol) was added. The mixture was stirred at room temperature for 45 minutes. The reaction mixture was diluted with 3:1 chloroform/isopropanol (50 mL) and water (30 mL) and the phases separated. The aqueous phase was extracted with 3:1 chloroform/isopropanol (2 x 30 mL) and the combined organic layers dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage, 28 g kp-NH, eluting with EtOAc/heptane 0-100% followed by 0-20% methanol/EtOAc) to afford a crude material which was triturated with methanol/Et₂O/heptane and the resultant flocculant solid collected by filtration to afford the title compound (376 mg (71%)) of as a white solid.

10 Method B: LC-MS (electrospray): $m/z = 430.3$ ($M+H$)⁺, RT = 1.38 min

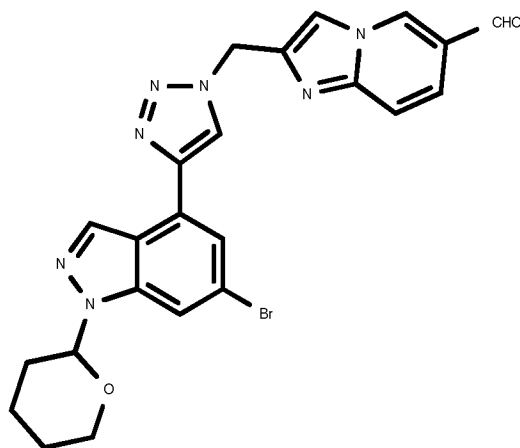
[00491] Step 5: 2-[[4-(1-tetrahydropyran-2-ylindazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carbaldehyde



15 **[00492]** [2-[[4-(1-tetrahydropyran-2-yl)indazol-4-yl]triazol-1-yl]methyl]imidazo[1,2-
a]pyridin-6-yl]methanol (380 mg, 0.88 mmol) was suspended in DCE (30 mL) and Dess-
Martin periodinane (1.13g, 2.65 mmol) was added. The mixture was stirred at 60 °C for 2
hours. The reaction mixture was cooled to room temperature, quenched with saturated
aqueous sodium hydrogen carbonate (40 mL) and extracted with 3:1 chloroform/isopropanol
20 (4 x 50 mL). The combined organic extracts were dried over sodium sulfate and evaporated
under vacuum. The residue was triturated with EtOAc/heptane and the solids collected by
filtration to afford the title compound (371 mg, 94%) as a beige solid

Method B: LC-MS (electrospray): $m/z = 428.2$ ($M+H$)⁺, RT = 1.45 min

25 **[00493]** **Intermediate 35:** 2-[[4-(6-bromo-1-tetrahydropyran-2-yl-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carbaldehyde



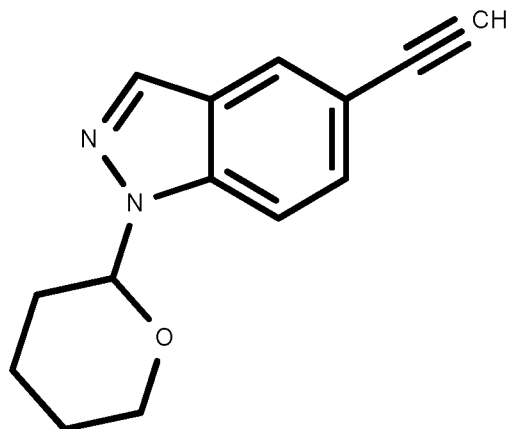
[00494] The title compound was prepared from **Intermediate 33** in a similar fashion to **Intermediate 34** giving (906 mg, 99%) as a pale yellow solid.

Method B: LC-MS (electrospray): m/z = 506.2/508.2 ($M+H$)⁺, RT = 1.58 min

5 [00495] The title compound was prepared in a similar fashion to **Intermediate 34** starting from 5-iodo-1H-indazole

Method B: LC-MS (electrospray): m/z = 428.2 ($M+H$)⁺, RT = 1.42 min

[00496] **Intermediate 36**: 5-ethynyl-1-(oxan-2-yl)-1H-indazole



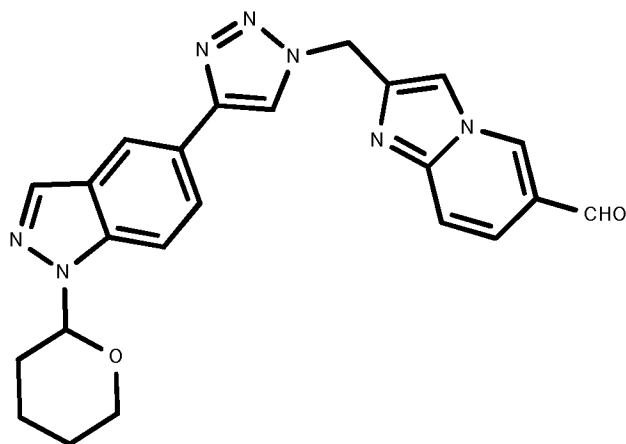
10

[00497] The title compound was prepared from 5-iodo-1H-indazole using the steps described in **Intermediate 24** giving (1.03 g, 94%) as a yellow oil.

Method A: LC-MS (electrospray): m/z = 227.10 ($M+H$)⁺, RT = 1.22 min.

[00498] **Intermediate 37**: 2-({4-[1-(oxan-2-yl)-1H-indazol-5-yl]-1H-1,2,3-triazol-1-yl}methyl)imidazo[1,2-a]pyridine-6-carbaldehyde

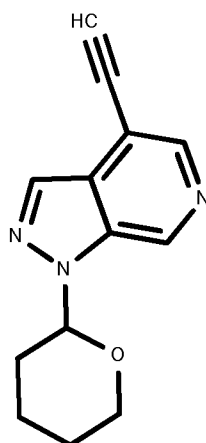
15



[00499] The title compound was prepared from **Intermediate 36** using the steps described in **Intermediate 24** giving (143 mg, 98%) as a pale yellow solid.

5 Method B: LC-MS (electrospray): m/z = 428.2 ($M+H$)⁺, RT = 1.42 min

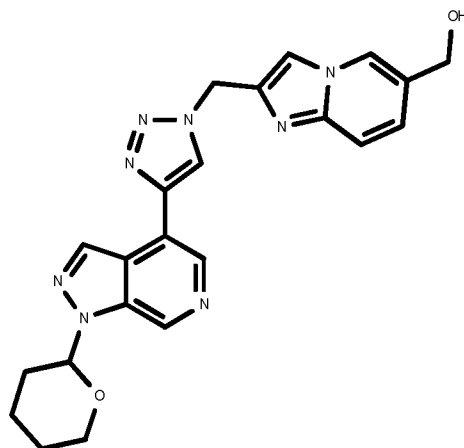
[00500] **Intermediate 38**: 4-ethynyl-1-(oxan-2-yl)-1H-pyrazolo[3,4-c]pyridine



[00501] The title compound was prepared from 4-bromo-1H-pyrazolo[3,4-c]pyridine using the method described for **Intermediate 24** giving

10 Method A: LC-MS (electrospray): m/z = 228.15 ($M+H$)⁺, RT = 1.078 min

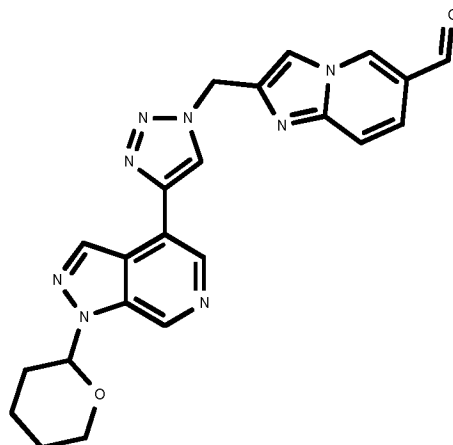
[00502] **Intermediate 39**: [2-({4-[1-(oxan-2-yl)-1H-pyrazolo[3,4-c]pyridin-4-yl]-1H-1,2,3-triazol-1-yl}methyl)imidazo[1,2-a]pyridin-6-yl]methanol



[00503] The intermediate was prepared from **Intermediate 38** using the methods described in **Intermediate 34 Step 4** giving (314 mg, 73%) as an off white solid.

Method A: LC-MS (electrospray): m/z = 431.05 ($M+H$)⁺, RT = 0.78 min

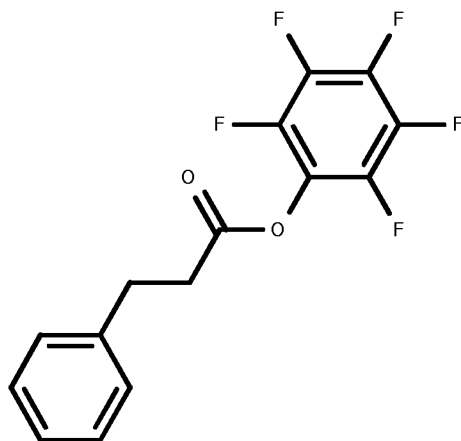
- 5 [00504] **Intermediate 40**: 2-({4-[1-(oxan-2-yl)-1H-pyrazolo[3,4-c]pyridin-4-yl]-1H-1,2,3-triazol-1-yl}methyl)imidazo[1,2-a]pyridine-6-carbaldehyde



[00505] The intermediate was prepared from **Intermediate 39** using the methods described in **Intermediate 34 Step 5** giving (249 mg, 77%) as a pale yellow solid.

Method A: LC-MS (electrospray): m/z = 429.65 ($M+H$)⁺, RT = 0.95 min

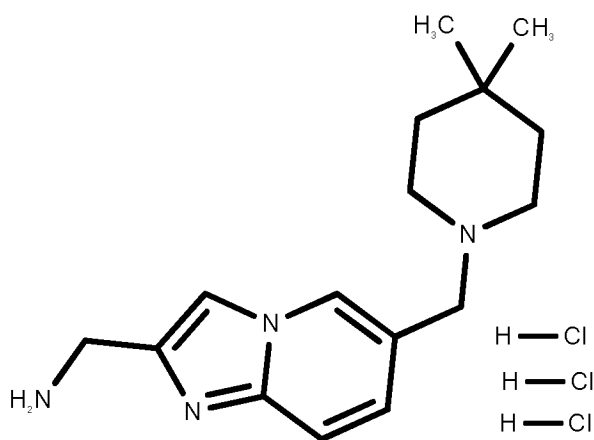
- 10 [00506] **Intermediate 42**: (2,3,4,5,6-pentafluorophenyl) 3-phenylpropanoate



[00507] pentafluorophenol (135 mg, 0.732 mmol) was added to a mixture of 3-phenylpropanoic acid (100 mg, 0.666 mmol), N,N'-dicyclohexylmethanediimine (0.18 mL, 0.799 mmol) and N,N-dimethylpyridin-4-amine (8.1 mg, 0.0666 mmol) in anhydrous THF (4 mL) under nitrogen and the reaction mixture was stirred at room temperature for 24 hours. The reaction mixture was filtered and the filtrates concentrated under vacuum. The resultant residue was purified by chromatography on silica gel (Biotage kp-Sil, eluting with EtOAc/heptane 0-30%) to afford (135 mg, 64%) as a colourless oil.

Method A: LC-MS (electrospray): does not ionise, RT = 1.46 min

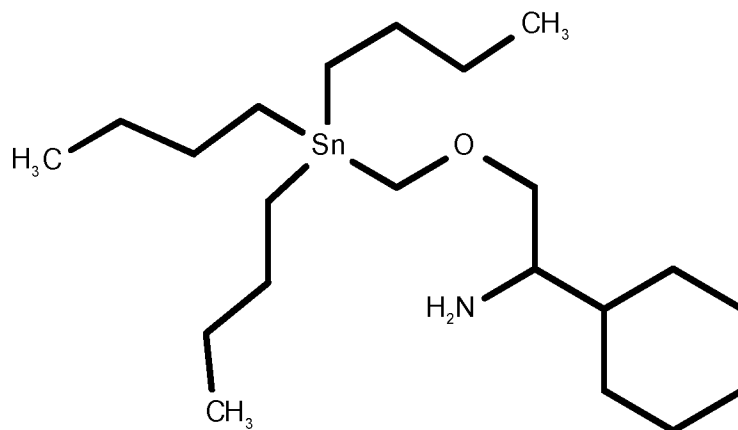
[00508] **Intermediate 43:** {6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl}methanamine trihydrochloride



[00509] The intermediate was prepared in the same manner as **Intermediate 29** to give the title compound (390 mg, 97%) as a white solid.

Method B: LC-MS (electrospray): m/z = 273.3 (M+H)⁺, RT = 1.52 min

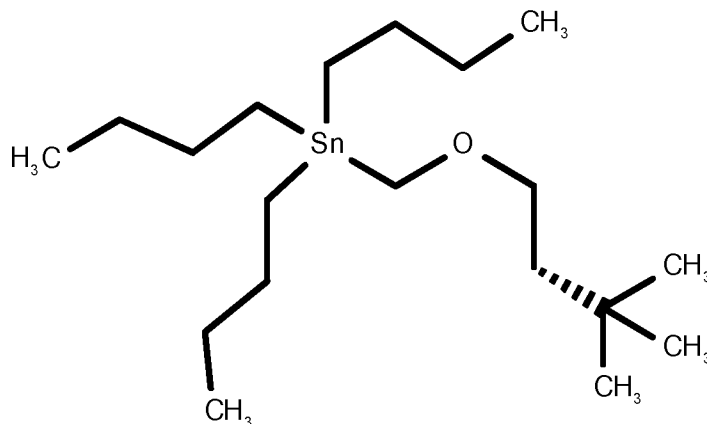
[00510] **Intermediate 44:** 1-Cyclohexyl-2-(tributylstannylmethoxy)ethanamine:



[00511] To a solution of 2-amino-2-cyclohexyl-ethanol (150 mg, 1.05 mmol) in anhydrous THF (3 mL) was added potassium-2-methylpropan-2-olate (153 mg, 1.36 mmol) at room temperature. The mixture stirred for 30 minutes before a solution of tributyl(iodomethyl)stannane (451 mg, 1.05 mmol) in THF (2 mL) was added drop-wise and stirring was continued for 72 hours. The reaction mixture was cooled to 0 °C and slowly quenched with sat aq NH₄Cl (5 mL) before being poured onto a mixture of EtOAc/water (4:1, 50 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with water (2 x 15 mL), brine (30 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica (Biotage KP-Sil 25 g; 0-10% 2M ammonia in methanol/DCM) to afford the title compound (330 mg, 64%) as yellow oil.

[00512] ¹HNMR(500 MHz, Chloroform-d) δ 0.80 – 0.97 (m, 15H), 0.98 – 1.56 (m, 18H), 1.60 – 1.84 (m, 5H), 2.02 (s, 2H), 2.67 – 2.76 (m, 1H), 3.15 – 3.23 (m, 1H), 3.38 (dd, J = 9.1, 3.6 Hz, 1H), 3.68 (d, J = 10.3 Hz, 1H), 3.74 (d, J = 10.3 Hz, 1H).

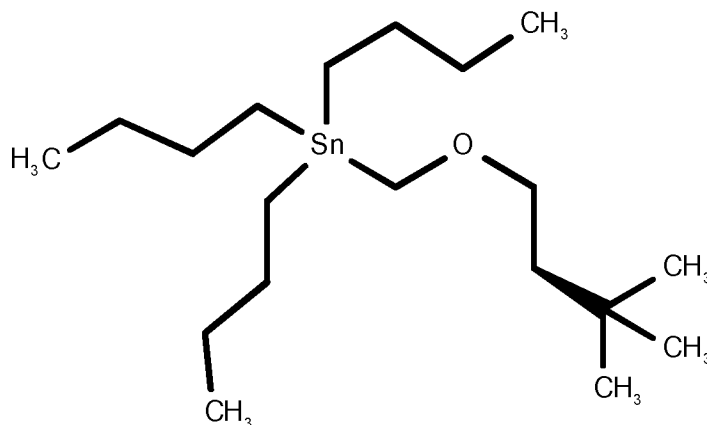
[00513] **Intermediate 45:** (2S)-3,3-Dimethyl-1-(tributylstannylmethoxy)butan-2-amine:



[00514] The title compound was prepared in the same manner as **Intermediate 44** from (2S)-2-amino-3,3-dimethylbutan-1-ol giving (465 mg, 85%) as a yellow oil.

[00515] ^1H NMR(500 MHz, Chloroform-d) δ 0.85 – 0.93 (m, 24H), 1.24 – 1.35 (m, 7H), 1.42 – 1.59 (m, 7H), 2.65 (dd, J = 9.1, 2.9 Hz, 1H), 3.06 – 3.14 (m, 1H), 3.43 (dd, J = 9.0, 2.9 Hz, 1H), 3.65 – 3.71 (m, 1H), 3.72 – 3.77 (m, 1H).

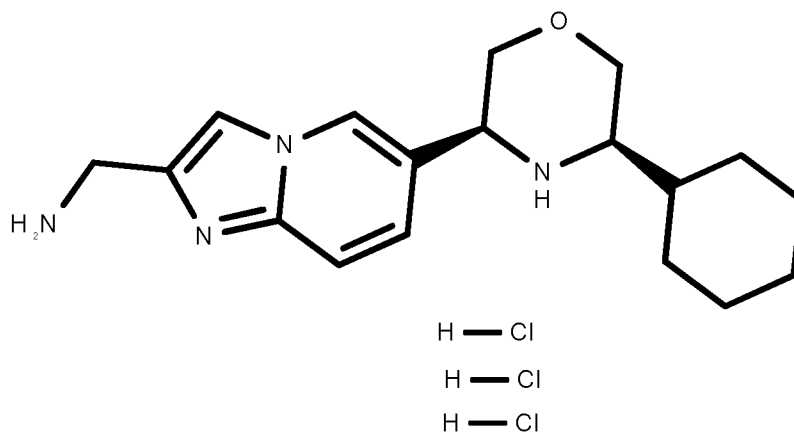
[00516] **Intermediate 46:** (2R)-3,3-Dimethyl-1-(tributylstannylmethoxy)butan-2-amine:



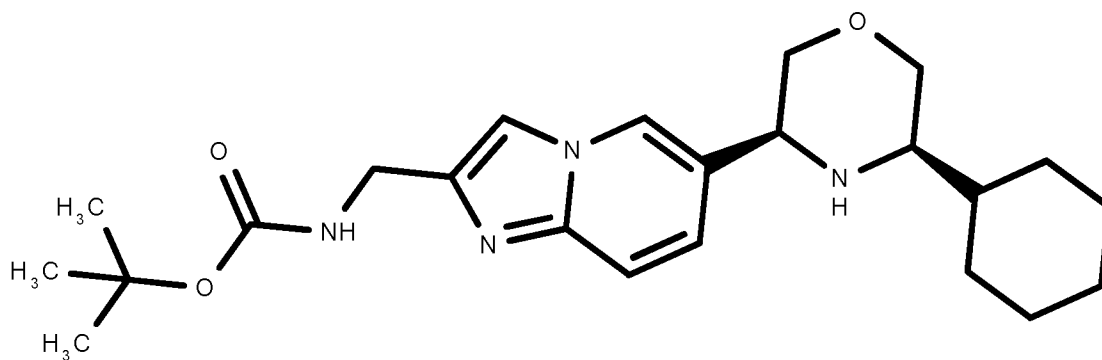
[00517] The title compound was prepared in the same manner as **Intermediate 44** from (2R)-2-amino-3,3-dimethylbutan-1-ol giving (470 mg, 87%) as a yellow oil.

[00518] ^1H NMR(500 MHz, Chloroform-d) δ 0.81 – 0.98 (m, 24H), 1.25 – 1.34 (m, 6H), 1.35 – 1.61 (m, 8H), 2.65 (dd, J = 9.1, 2.9 Hz, 1H), 3.05 – 3.15 (m, 1H), 3.44 (dd, J = 8.9, 2.9 Hz, 1H), 3.64 – 3.70 (m, 1H), 3.70 – 3.78 (m, 1H).

[00519] **Intermediate 47:** [6-[rac-(3S,5R)-5-Cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl]methanamine trihydrochloride.



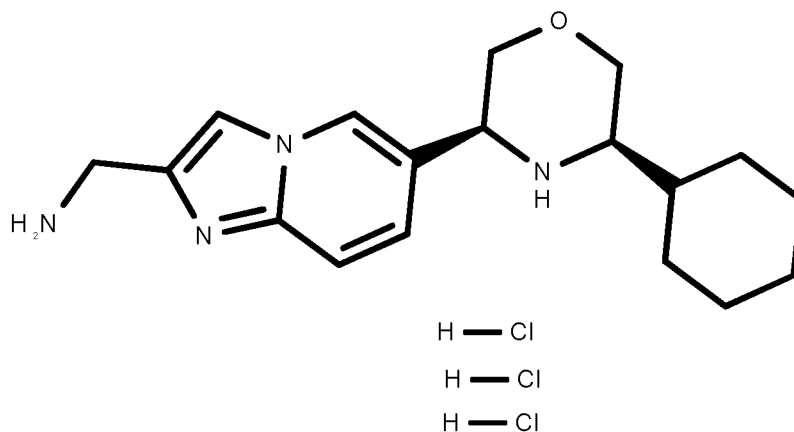
[00520] **Step 1:** tert-Butyl N-[[6-[rac-(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate



[00521] To a solution of tert-butyl N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]carbamate (**Intermediate 25 step 2**) (183 mg, 0.67 mmol) in 1,1,1,3,3,3-Hexafluoro-2-propanol (2.5 mL) was added a solution of 1-cyclohexyl-2-(tributylstannylmethoxy)ethanamine (90%, 330 mg, 0.665 mmol) in DCE (4 mL). The reaction mixture was stirred at 80 °C for 16 hours. Meanwhile a mixture of 2,6-dimethylpyridine (0.16 mL, 1.33 mmol), copper(2+) bis(trifluoromethanesulfonate) (484 mg, 1.33 mmol) and 1,1,1,3,3,3-Hexafluoro-2-propanol (2.5 mL) was stirred separately at room temperature for 1 hour. After cooling to room temperature, the solution of the imine was added drop-wise to the solution of the catalyst. The resulting mixture was stirred at room temperature for 3 hours forming a clear, dark green solution. The reaction mixture was diluted with DCM (25 mL) and quenched with 10% aq. NH₄OH (10 mL) solution. The organic layer was separated, washed with brine (10 mL), dried (Na₂SO₄), filtered and concentrated under reduced pressure. The residue was purified by preparative HPLC (method B) to afford the title compound (152 mg, 55%) as pale yellow oil.

Method C: LC-MS (electrospray): m/z = 415.4 (M+H)⁺, RT = 3.66 min

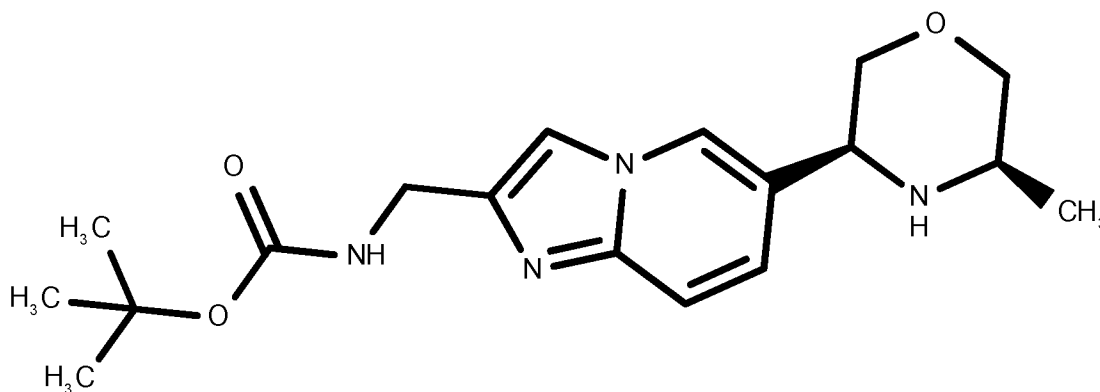
[00522] **Step 2:** [6-[rac-(3S,5R)-5-Cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl]methanamine trihydrochloride.



[00523] To a solution of tert-butyl N-[[6-[rac-(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate (153 mg, 0.368 mmol) in methanol (2 mL) was added 4M HCl in dioxane (1 mL) at room temperature. The solution was stirred at 50 °C for 1 hour. After cooling to room temperature, the reaction mixture was concentrated to dryness under reduced pressure. The residue was dissolved in methanol (3 mL) and diethyl ether (20 mL) was added drop-wise to the stirred solution. The resulting precipitate was collected by filtration and dried in the vacuum oven at 40 °C for 4 hours to afford the title compound (129 mg, 78%) as an off-white solid.

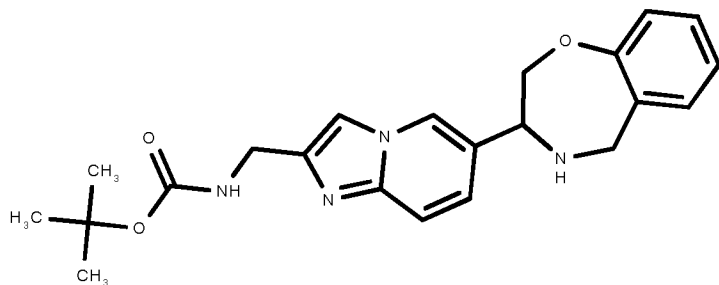
Method C: LC-MS (electrospray): m/z = 315.3 (M+H)⁺ for freebase, RT = 2.80 min.

[00524] **Intermediate 48:** tert-butyl N-[[6-[rac-(3S,5R)-5-methylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate



[00525] A glass vial (40 mL clear, screw cap) was charged with tert-butyl N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]carbamate (**Intermediate 25 step 2**) (138 mg, 0.500 mmol) and loaded into a SYNPLEChem capsule based synthesizer, using a H007 3-Methylmorpholine cartridge. After the reaction mixture was complete (11 hour), the product containing solution was concentrated under reduced pressure. The residue was purified by preparative HPLC (method B) to afford the title compound (82 mg, 45%) as colourless oil. Method C: LC-MS (electrospray): m/z = 347.3 (M+H), RT = 2.28 min.

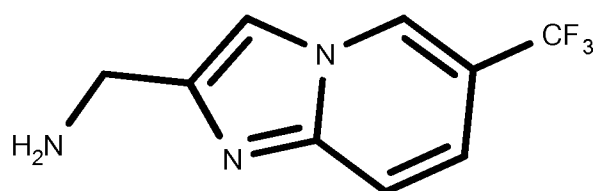
[00526] **Intermediate 49:** tert-Butyl N-[[6-(9-methoxy-2,3,4,5-tetrahydro-1,4-benzoxazepin-3-yl)imidazo[1,2-a]pyridin-2-yl]methyl]carbamate.



[00527] The intermediate was prepared in the same manner as **Intermediate 48** to afford the title compound (105 mg, 49%) as colourless oil.

Method C: LC-MS (electrospray): m/z = 425.3 (M+H), RT = 2.75 min

[00528] **Intermediate 50**: [6-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]methanamine



5

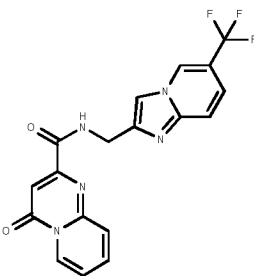
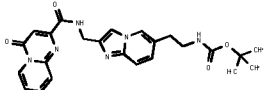
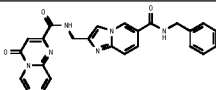
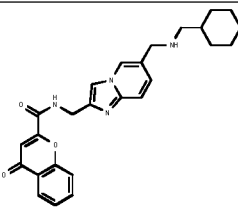
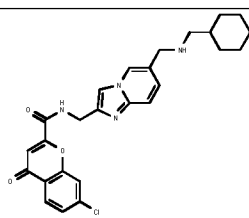
[00529] The title compound was prepared from 2-amino-5-(trifluoromethyl)pyridine in a similar manner to **Intermediate 7** to give (650 mg, 65%) as a light brown solid.

Method B: LC-MS (electrospray): m/z = 216.2 (M+H)⁺, RT = 1.29 min.

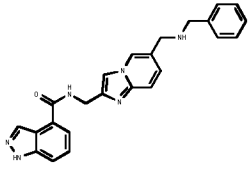
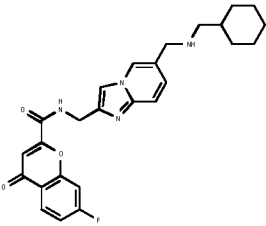
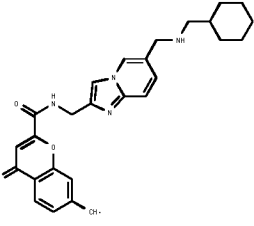
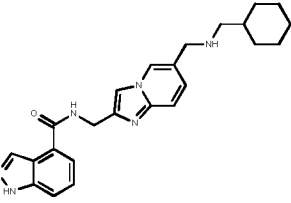
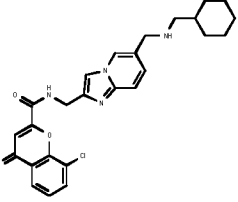
10 [00530] The compounds in **Table 9** were prepared in a similar fashion to **Compound 1** using the appropriate carboxylic acid and aminomethyl imidazopyridine intermediate, or commercially available materials, including deprotection where necessary.

15 **Table 9**

Compound No	Name	Structure	LCMS method	LCMS Retention time / mass ion	Intermediates
63	N-([6-(2-aminoethyl)imidazo[1,2-a]pyridin-2-yl]methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.69	20
64	N-([6-methylimidazo[1,2-a]pyridin-2-yl]methyl)-4-oxo-4H,6H,7H,8H,9H-pyrido[1,2-a]pyrimidine-		C	2.41/338.2	21

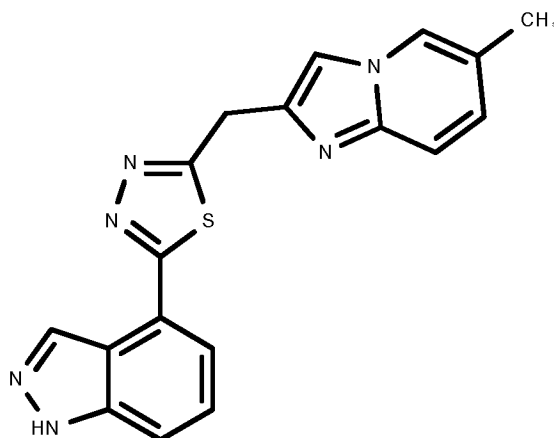
	2-carboxamide				
65	4-oxo-N-[[6-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.48/388.1	50
67	tert-butyl N-(2-{2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridin-6-yl}ethyl)carbamate		D	3.34/463.2	20
68	N-benzyl-2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridine-6-carboxamide		D	3.21/453.2	22
170	N-[(6-{[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide		C	3.20/445.4	25
171	7-chloro-N-[(6-{[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-		C	3.56/479.3	25

	chromene-2-carboxamide				
172	6-chloro-N-[(6-[(cyclohexylmethyl)amino]methyl]imido[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide		C	3.59/479.2	25
175	N-[(6-[(cyclohexylmethyl)amino]methyl]imido[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H,6H,7H,8H,9H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.97/449.4	175
176	6-amino-N-[(6-[(cyclohexylmethyl)amino]methyl]imido[1,2-a]pyridin-2-yl)methyl]pyridine-3-carboxamide		D	3.41/ 393.3	176
177	N-({6-[(benzyloxy)methyl]imido[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.68/440.1	28

178	N-({6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide		C	2.39/411.3	29
180	N-[(6-{[(cyclohexylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-7-fluoro-4-oxo-4H-chromene-2-carboxamide		C	3.33/463.4	25
181	N-[(6-{[(cyclohexylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-7-methyl-4-oxo-4H-chromene-2-carboxamide		C	3.39/459.4	25
182	N-[(6-{[(cyclohexylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide		E	0.93/417.3	25
185	8-chloro-N-[(6-{[(cyclohexylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-		C	3.56/479.3	

	chromene-2-carboxamide				
187	6-bromo-N-[(6-[(cyclohexylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide		D	3.99/ 495.2/497.2	1, 25
188	N-[(6-[(cyclohexylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]quinoline-3-carboxamide		C	3.14/428.4	25
189	N-[(6-{1-[(cyclohexylmethyl)amino]ethyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.90/459.3	32
190	6-chloro-N-[(6-[(cyclohexylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide		D	3.94/451.2	25

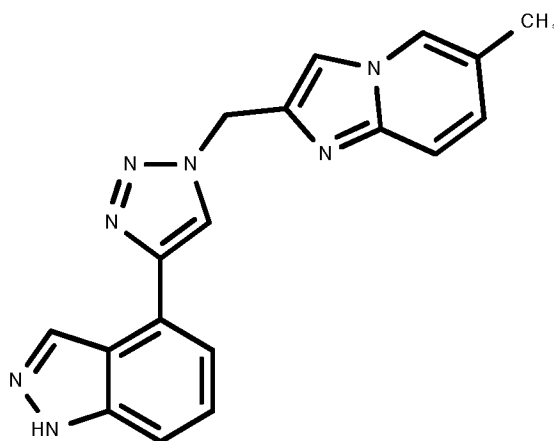
[00531] Compound 66: 4-[5-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1,3,4-thiadiazol-2-yl]-1H-indazole



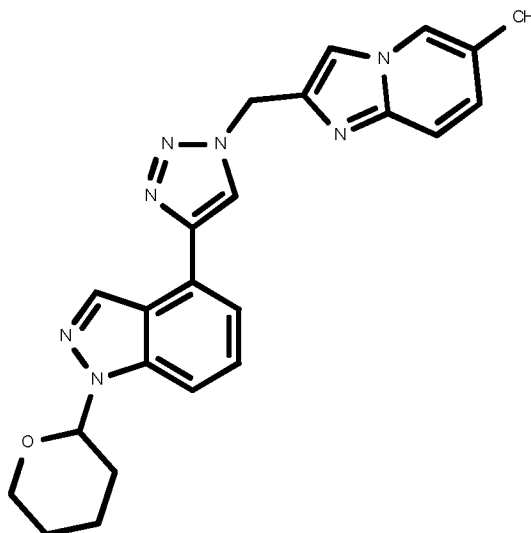
[00532] N'-[2-(6-methylimidazo[1,2-a]pyridin-2-yl)acetyl]-1-tetrahydropyran-2-yl-indazole-4-carbohydrazide (**Compound 62 Step 3**), (250 mg, 0.58 mmol) was suspended in 1,4-Dioxane (10 mL) and Lawesson's reagent (1.17g, 2.89 mmol) was added. The vessel was sealed and the mixture heated at 110°C and the solids dissolved upon heating. The reaction mixture was cooled to room temperature and left standing overnight. The reaction mixture was diluted with saturated aqueous sodium hydrogen carbonate (50 mL) and extracted with chloroform/isopropanol (3:1, 4 x 50 mL). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage kp-NH 28 g, eluting with EtOAc/heptane 0-100% followed by 0-20% methanol/EtOAc) to afford a crude material which was triturated with EtOAc. The solids were collected by filtration and rinsed with heptane to afford the title compound (112 mg, 56%) as a white solid.

Method D: LC-MS (electrospray): m/z = 347.2 ($M+H$)⁺, R_T = 3.33 min

Compound 69: 4-[1-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-1,2,3-triazol-4-yl]-1H-indazole



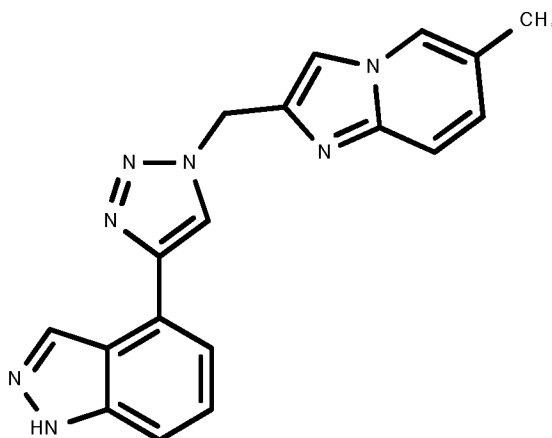
Step1: 4-[1-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1-(oxan-2-yl)-1H-indazole



- 5 **[00533]** A solution of 2-(azidomethyl)-6-methyl-imidazo[1,2-a]pyridine (**Intermediate 23**, 120 mg, 0.64 mmol) and 4-ethynyl-1-tetrahydropyran-2-yl-indazole (**intermediate 24**, 189 mg, 0.83 mmol) in DMF (3 mL) and water (0.5 mL) was treated with CuSO₄ (31 mg, 0.19 mmol) and sodium ascorbate (38 mg, 0.19 mmol) and the mixture was stirred at room temperature for an hour. Precipitation noted within 30 minutes. The reaction mixture was
- 10 diluted with water (20 mL), the solid was collected by filtration washed with water, then triturated successively with methanol, EtOAc and heptane and dried under suction to afford the title compound (209 mg, 79%) as a white solid.

Method D: LC-MS (electrospray): m/z = 414.3 (M+H)⁺, RT = 3.93 min.

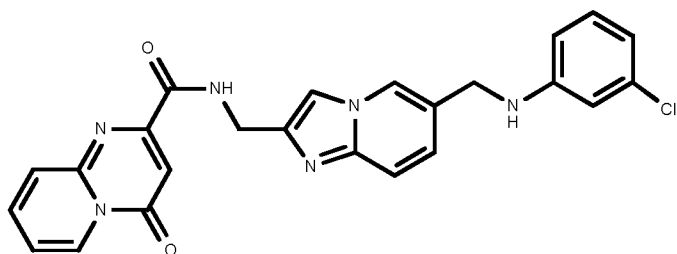
- 15 **Step 2:** 4-[1-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole



[00534] A suspension of 4-[1-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]triazol-4-yl]-1-tetrahydropyran-2-yl-indazole (100 mg, 0.24 mmol) in methanol (5 mL) was treated with HCl (4M in Dioxane, 2 mL, 8 mmol) which caused dissolution. The mixture was stirred at room temperature for two hours. The reaction mixture was evaporated under vacuum and the residue was triturated with methanol/EtOAc/heptane and the solids collected by filtration. The residue was purified by preparative HPLC (method B) and the fractions evaporated to afford the title compound (13 mg, 16%) as a white solid.

Method D: LC-MS (electrospray): m/z = 330.2 ($M+H$)⁺, RT = 3.15 min.

[00535] Compound 158: N-[(6-[(3-chlorophenyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide

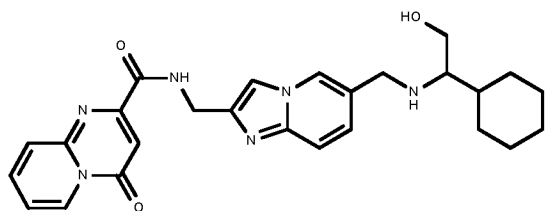


[00536] N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide (**Compound 49**) (70 mg, 0.20 mmol) and 3-chloroaniline (51 mg, 0.40 mmol) were combined in 1,1,1,3,3,3-Hexfluoro-2-propanol (2 mL) and the mixture stirred at room temperature. NaBH₄ (70 mg, 1.85 mmol) was added with a few drops of methanol - gas evolution - and the mixture stirred briefly at room temperature. The reaction mixture was quenched with methanol (20 mL) - gas evolution - and the mixture evaporated under vacuum. The residue was suspended in saturated aqueous sodium hydrogen carbonate (20 mL) and extracted with chloroform/isopropanol (3:1, 3 x 30 mL). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum.

[00537] The residue was purified by preparative HPLC (method B) and the clean product-containing fractions combined and evaporated under vacuum. The residue was dried in the genevac and under vacuum at 40 °C to afford the title compound (47 mg, 50%) as a pale yellow solid.

Method C: LC-MS (electrospray): m/z = 459.3 ($M+H$)⁺, RT = 2.96 min.

[00538] Compound 168: N-[(6-[(1-cyclohexyl-2-hydroxyethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;



[00539] To a solution of N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-

pyrido[1,2-a]pyrimidine-2-carboxamide (**Compound 49**) (100 mg, 0.288 mmol) in 1,1,1,3,3,3-Hexafluoro-2-propanol (2 mL) was added 2-amino-2-cyclohexyl-ethanol (0.062 mL, 0.317 mmol) at room temperature. The mixture was stirred at room temperature overnight. The reaction mixture was concentrated under reduced pressure and the residue (pale yellow oil) was purified by preparative HPLC (Method B). The product containing fractions were combined and concentrated under reduced pressure to afford the intermediate imine (55 mg, 38%) as white solid. To a solution of the imine (52 mg, 0.105 mmol) in ethanol (3 mL) was added NaBH₄ (36 mg, 0.96 mmol) at room temperature. The mixture was stirred at room temperature for 3 hours. The reaction mixture was partitioned between ethyl acetate (40 mL) and Na₂CO₃ (2M, 30 mL). The organic layer was separated, washed with brine (20 mL), dried (Na₂SO₄), filtered and concentrated under reduced pressure. The residue was purified by preparative HPLC (method B) to afford the title compound (16 mg, 31%) as white solid.

Method C: LC-MS (electrospray): m/z = 475.3 (M+H)⁺, RT = 2.56 min.

[00540] The compounds in **table 10** was prepared in the same manner as

Compounds 51, 158 or 168 and purified by method B.

Table 10

Compound No	Name	Structure	LCMS method	LCMS Retention time	Mass ion
70	4-oxo-N-{[6-({[(pyridin-3-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.74	440.1
71	N-{[6-({[(4-methoxyphenyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-		D	3.33	469.2

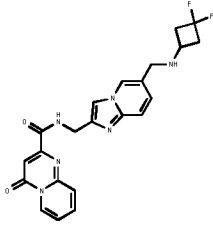
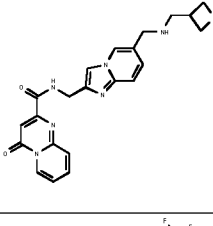
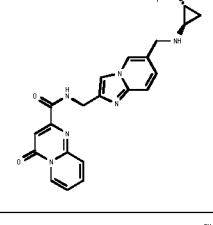
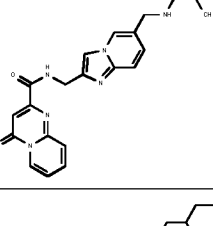
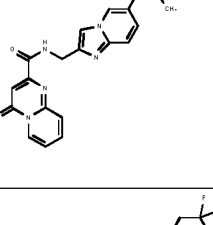
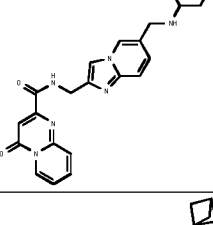
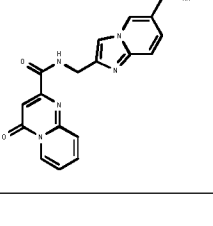
	a]pyrimidine-2-carboxamide				
72	N-[(6- {[(cyclohexylmethyl)amino methyl]imidazo[1,2- a]pyridin-2-yl)methyl]-4- oxo-4H-pyrido[1,2- a]pyrimidine-2- carboxamide		D	3.84	445.2
73	N-[(6-({[(4- chlorophenyl)methyl]amin o)methyl]imidazo[1,2- a]pyridin-2-yl)methyl]-4- oxo-4H-pyrido[1,2- a]pyrimidine-2- carboxamide		D	3.65	473.2
74	N-[(6- {[benzyl(methyl)amino]me thyl]imidazo[1,2-a]pyridin- 2-yl)methyl]-4-oxo-4H- pyrido[1,2-a]pyrimidine-2- carboxamide		D	3.80	453.3
75	4-oxo-N-[(6-({[(1R)-1- phenylethyl]amino}methyl) imidazo[1,2-a]pyridin-2- yl)methyl]-4H-pyrido[1,2- a]pyrimidine-2- carboxamide		C	2.76	453.3
76	4-oxo-N-[(6-({[(1S)-1- phenylethyl]amino}methyl) imidazo[1,2-a]pyridin-2- yl)methyl]-4H-pyrido[1,2- a]pyrimidine-2- carboxamide		C	2.76	453.3
77	N-[(6-({[(2- fluorophenyl)methyl]amin o)methyl]imidazo[1,2- a]pyridin-2-yl)methyl]-4- oxo-4H-pyrido[1,2- a]pyrimidine-2- carboxamide		D	3.40	457.1
78	4-oxo-N-[(6-({[(2- phenylpropan-2- yl)amino]methyl]imidazo[1 ,2-a]pyridin-2-yl)methyl]- 4H-pyrido[1,2- a]pyrimidine-2- carboxamide		D	3.80	467.3
79	N-[(6-({[(3- fluorophenyl)methyl]amin o)methyl]imidazo[1,2- a]pyridin-2-yl)methyl]-4- oxo-4H-pyrido[1,2- a]pyrimidine-2- carboxamide		D	3.47	457.1

80	N-([6-([[(4-fluorophenyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.43	457.1
81	4-oxo-N-([6-([[(4,4,4-trifluorobutyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.44	459.3
82	N-([6-([[(oxan-4-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.91	447.3
83	N-([6-([[(3,3-difluorocyclobutyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.33	453.3
84	N-([6-([[(cyclopropylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.11	403.2
85	4-oxo-N-([6-([[(3,3,3-trifluoropropyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.26	445.3
86	N-([6-([[(cyclohexylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.60	431.2
87	4-oxo-N-([6-([[(3-(trifluoromethyl)bicyclo[1.1.1]pentan-1-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-		D	3.75	497.2

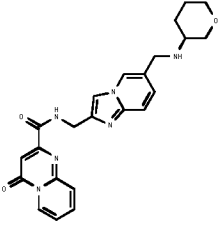
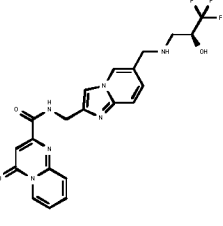
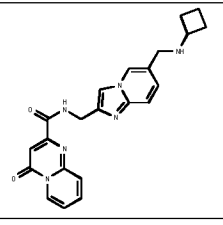
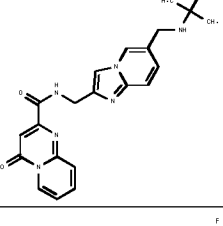
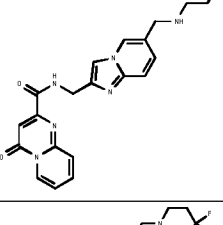
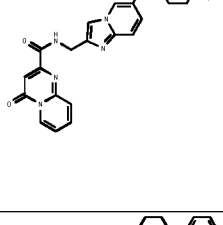
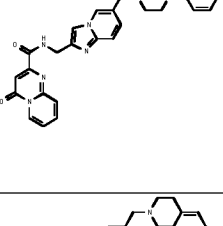
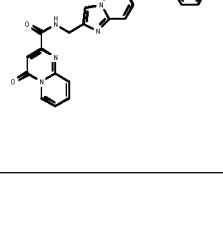
	a]pyrimidine-2-carboxamide				
88	N-[[6-([[(oxan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.05	447.2
89	4-oxo-N-[[6-([[(3-phenyloxetan-3-yl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.40	481.3
90	N-[[6-([[(oxan-3-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.90	447.2
91	N-[[6-([[(1-fluorocyclohexyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.82	463.4
92	N-[[6-([[(3-cyclopropylphenyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.96	479.4
93	N-[[6-([[(3,3-dimethylbutyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.77	433.4
94	4-oxo-N-[[6-([[(2-(trifluoromethoxy)ethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.37	461.3

95	4-oxo-N-({[6-({[(oxolan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.93	433.3
96	N-([6-({[(2-methanesulfonyl)ethyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.59	455.3
97	4-oxo-N-({[6-({[(3-phenylpyrrolidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	3.36	479.4
98	N-([6-({[(1-cyclohexylcyclopropyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	4.35	471.2
99	4-oxo-N-({[6-({[(1,3-thiazol-5-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.83	446.2
100	tert-butyl 3-({[(2-({[4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amino)methyl]piperidine-1-carboxylate		D	3.63	546.3
101	N-({[6-({[(4,4-difluorocyclohexyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.48	481.2
102	tert-butyl 2-({[(2-({[4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amino)methyl]piperidine-1-carboxylate		D	3.68	546.3

	yl)methyl]amino)methyl]piperidine-1-carboxylate				
103	N-[(6-[(2-cyclopropylethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.38	417.3
104	4-oxo-N-[(6-[(piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.49	417.3
105	4-oxo-N-[(6-[(1-(2,2,2-trifluoroethyl)-1H-pyrazol-3-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.13	511.3
106	N-[(6-[(1-methylcyclohexyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	3.29	459.4
107	4-oxo-N-[(6-[(2-(pyridin-3-yl)ethyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.88	454.3
108	N-[(6-[(1,4-dioxan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.73	449.3
109	N-[(6-[(cyclopropylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.97	389.2

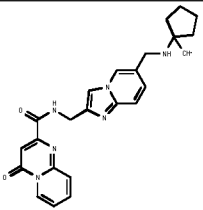
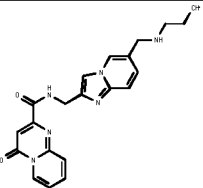
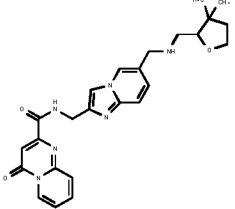
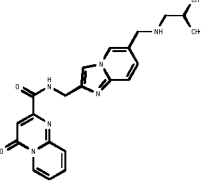
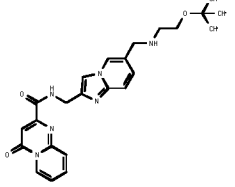
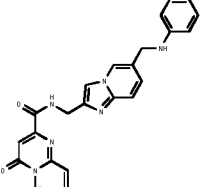
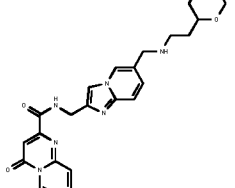
110	N-[(6-[(3,3-difluorocyclobutyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.16	439.3
111	N-[(6-[(oxetan-3-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.62	419.3
112	4-oxo-N-[(6-[(1R,2R)-2-(trifluoromethyl)cyclopropyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.43	457.3
113	N-[(6-[(2,2-dimethylpropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.70	419.3
114	N-[(6-[(cyclohexylmethyl)(methyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	4.43	459.3
115	N-[(6-[(4,4-difluorocyclohexyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.43	467.3
116	N-[(6-[(bicyclo[1.1.1]pentan-1-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.34	415.3

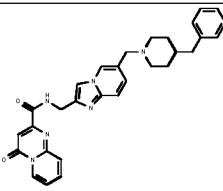
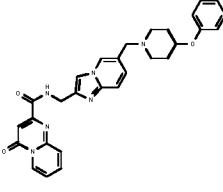
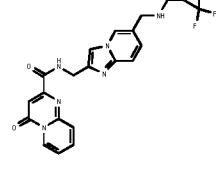
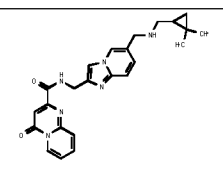
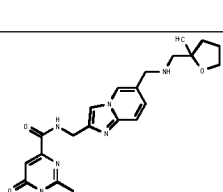
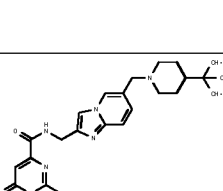
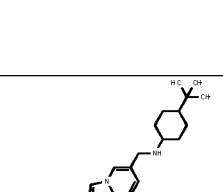
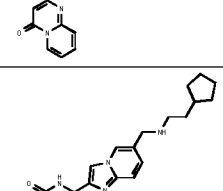
117	4-oxo-N-({6-([[(2S)-oxolan-2-yl]methyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.93	433.3
118	4-oxo-N-({6-([[(2R)-oxolan-2-yl]methyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.93	433.3
119	N-[(6-{[(2,2-difluoroethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.93	413.2
120	4-oxo-N-({6-([[(oxolan-3-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.68	433.2
121	N-[(6-([[(1-methylcyclopropyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.43	417.3
122	4-oxo-N-[(6-{[(oxolan-3-yl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.58	419.3
123	methyl 3-methyl-2-[(2-{[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amino]butanoate		C	2.53	463.3

124	N-[(6-[(oxan-3-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.74	433.3
125	4-oxo-N-{[6-[(2S)-3,3,3-trifluoro-2-hydroxypropyl]amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.98	461.3
126	N-({6-[(cyclobutylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.16	403.3
127	N-({6-[(tert-butylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.31	405.3
128	N-[(6-[(2-fluoroethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.67	395.3
129	N-({6-[(4,4-difluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.36	453.3
130	4-oxo-N-({6-[(4-phenylpiperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.83	494.4
131	4-oxo-N-({6-[(1,2,3,4-tetrahydroisoquinolin-2-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.89	465.4

132	N-({6-[(diethylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.43	405.3
133	4-oxo-N-({6-[(pyrrolidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.18	403.3
134	4-oxo-N-[(6-{[3-(pyridin-2-yl)azetidin-1-yl]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.96	466.2
135	N-[(6-{[(dicyclopropylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.63	443.3
136	N-[(6-{[(cyclopropylmethyl)(methyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.47	417.3
137	N-({6-[(4-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.80	431.3
138	4-oxo-N-[(6-{[4-(trifluoromethyl)piperidin-1-yl]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.69	485.3
139	N-({6-[(3-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.80	431.4

140	4-oxo-N-[(6- {[(spiro[2.2]pentan-1- yl)methyl]amino)methyl}im- idazo[1,2-a]pyridin-2- yl)methyl]-4H-pyrido[1,2- a]pyrimidine-2- carboxamide		C	2.53	429.3
141	N-({6-[(3,3- dimethylpiperidin-1- yl)methyl]imidazo[1,2- a]pyridin-2-yl)methyl)-4- oxo-4H-pyrido[1,2- a]pyrimidine-2- carboxamide		C	3.45	445.3
142	4-oxo-N-[(6-({3- (trifluoromethyl)piperidin- 1-yl)methyl}imidazo[1,2- a]pyridin-2-yl)methyl)-4H- pyrido[1,2-a]pyrimidine-2- carboxamide		C	2.94	485.3
143	N-({6-({[(5,5- dimethyloxolan-2- yl)methyl]amino)methyl}im- idazo[1,2-a]pyridin-2- yl)methyl)-4-oxo-4H- pyrido[1,2-a]pyrimidine-2- carboxamide		C	2.33	461.4
144	N-({6-[(4-fluoropiperidin-1- yl)methyl]imidazo[1,2- a]pyridin-2-yl)methyl)-4- oxo-4H-pyrido[1,2- a]pyrimidine-2- carboxamide		D	3.15	435.2
145	N-[(6-({[(3- methoxypropyl)amino]met hyl}imidazo[1,2-a]pyridin- 2-yl)methyl)-4-oxo-4H- pyrido[1,2-a]pyrimidine-2- carboxamide		C	1.85	421.3
146	N-[(6-({[(1- methylcyclohexyl)amino] methyl}imidazo[1,2- a]pyridin-2-yl)methyl)-4- oxo-4H-pyrido[1,2- a]pyrimidine-2- carboxamide		C	3.04	445.3
147	N-({6-({[(4,4- dimethyloxolan-2- yl)methyl]amino)methyl}im- idazo[1,2-a]pyridin-2- yl)methyl)-4-oxo-4H-		C	2.39	461.4

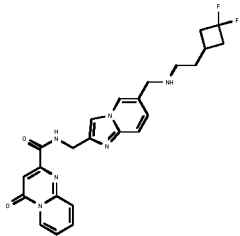
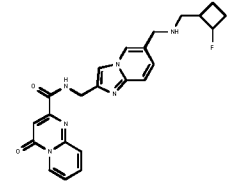
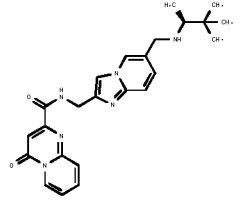
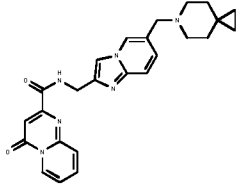
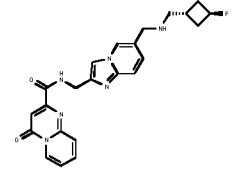
	pyrido[1,2-a]pyrimidine-2-carboxamide				
148	N-[(6-([(1-methylcyclopentyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.71	431.3
149	4-oxo-N-({6-[(propylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.10	391.3
150	N-({6-([(3,3-dimethyloxolan-2-yl)methyl]amino)methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.34	461.4
151	N-[(6-([(2-methylpropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.38	405.3
152	N-({6-([2-(tert-butoxy)ethyl]amino)methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.31	449.4
153	N-[(6-([(4-chlorophenyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.95	459.3
154	N-({6-([2-(oxan-2-yl)ethyl]amino)methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.27	461.4

155	N-({6-[(4-benzylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	4.24	507.3
156	4-oxo-N-({6-[(4-phenoxy-piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.86	509.3
157	N-({6-({[(2,2-difluorocyclopropyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.05	439.2
159	N-({6-({[(2,2-dimethylcyclopropyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.53	431.3
160	N-({6-({[(2-methyloxolan-2-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.13	447.3
161	N-({6-[(4-tert-butylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	3.55	473.4
162	N-({6-({[(4-tert-butylcyclohexyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	3.81	487.4
163	N-({6-({[(2-cyclopentylethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.95	445.4

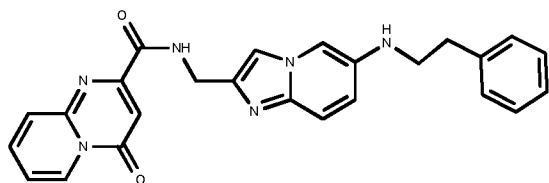
166	N-[(6-{[4-(2,2-dimethylpropanoyl)piperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.15	502.2
167	N-[(6-{[4-(4-acetylpiperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	2.60	460.1
169	N-[(6-{[7-azabicyclo[2.2.1]heptan-7-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.46	429.3
193	N-[(6-{[4-(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	3.00	445.3
194	N-[(6-{[2-(2-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	3.29	445.4
195	4-oxo-N-[(6-{[(2,3,3-trimethylbutan-2-yl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	3.54	447.4
196	N-[(6-{[(5-fluoropyridin-2-yl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.32	444.3

197	N-({6-([1,1'-bi(cyclopropane)]-1-yl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.63	429.3
198	N-([6-([1-(1-fluorocyclopentyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.56	449.4
199	N-({6-[(2,6-dimethylmorpholin-4-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.02	447.2
200	methyl 1-({2-([4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]formamido)methyl}imidazo[1,2-a]pyridin-6-yl)methyl)piperidine-3-carboxylate		D	3.25	475.2
202	N-([6-([2-fluoro-2-methylpropyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.26	423.3
203	N-([6-([1-(1-cyclohexylethyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	3.28	459.4
204	N-([6-([2-(2-cyclopropylethyl)(methyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.61	431.2
205	N-([6-([2-(2-dimethylpropyl)(methyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	4.27	433.3

206	N-([6-([[(1-fluorocyclobutyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	3.14	435.2
207	N-([6-([4-fluoro-4-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.49	449.3
208	N-([6-([3,3-difluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.52	453.3
209	N-([6-([[(1-hydroxycyclohexyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.30	461.4
210	N-([6-([(cyclopentylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.74	431.3
211	N-([6-([[(3,3-difluorocyclopentyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.32	467.4
212	N-([6-([(cyclobutylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		E	0.82	417.3

213	N-{{[6-({[2-(3,3-difluorocyclobutyl)ethyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.37	467.2
214	N-{{[6-({[2-(2-fluorocyclobutyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.06	435.2
215	N-{{[6-({[(2S)-3,3-dimethylbutan-2-yl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.69	433.2
216	N-{{[6-({[6-azaspiro[2.5]octan-6-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		D	3.63	443.3
217	4-oxo-N-({[6-({[(1R,3R)-3-fluorocyclobutyl]methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.22	435.3

[00541] Compound 191: 4-oxo-N-({[6-[(2-phenylethyl)amino]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide

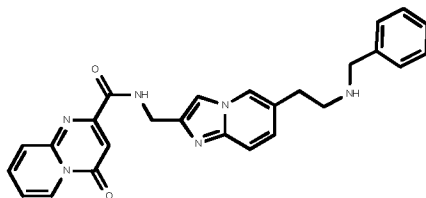


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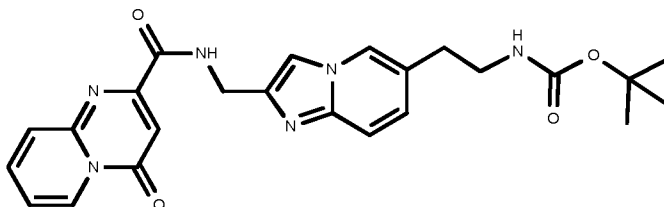
[00542] The title compound was prepared from **Compound 23** using the procedure described for **Compound 32** and purified by preparative HPLC (Method A) to give (29 mg, 22%) as a brown solid.

[00543] Method E: LC-MS (electrospray): $m/z = 439.3$ ($M+H$)⁺, $RT = 1.83$ min.

[00544] **Compound 235:** N-({6-[2-(benzylamino)ethyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide

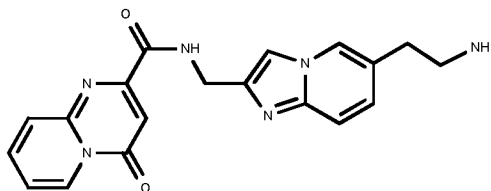


5 [00545] **Step 1:** tert-butyl N-(2-{2-[({4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl}formamido)methyl]imidazo[1,2-a]pyridin-6-yl}ethyl)carbamate



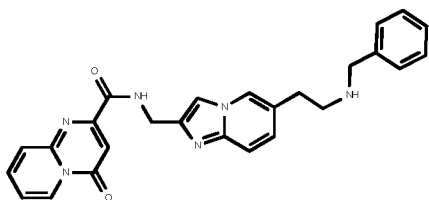
[00546] The title compound was prepared by the coupling of **Intermediate 4** with
 10 **intermediate 20** using the method described in **Compound 1** and purified by reverse phase chromatography (400 g, High pH method) to provide (900 mg, 63%) as an off white solid.
 Method B: LC-MS (electrospray): m/z = 463.3 (M+H)⁺, RT = 1.39 min.

[00547] **Step 2:** N-([6-(2-aminoethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-
 15 pyrido[1,2-a]pyrimidine-2-carboxamide



[00548] The title compound was prepared using the deprotection described in
Intermediate 22 step 5 and purified by reverse phase chromatography (60 g, High pH
 method) to provide (100 mg, 12%) as a white solid.
 20 Method D: LC-MS (electrospray): m/z = 363.2 (M+H)⁺, RT = 2.67 min.

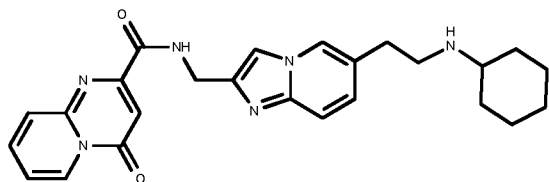
[00549] **Step 3:** N-({6-[2-(benzylamino)ethyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



[00550] The title compound was prepared from benzaldehyde using the procedure described in **Compound 51** and purified by preparative HPLC (method B) to give the title compound (7.8 mg, 8.9%) as a white solid.

5 Method D: LC-MS (electrospray): m/z = 353.2 ($M+H$)⁺, R_T = 3.44 min.

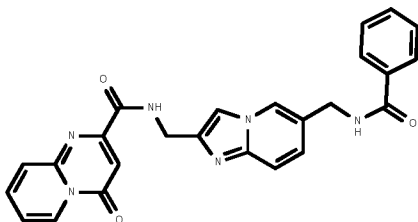
[00551] **Compound 236**: N-({6-[2-(cyclohexylamino)ethyl]imidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



10 [00552] The title compound was prepared using the method described in **Compound 51** and purified by preparative HPLC (method A) to give the title compound (48 mg, 56%) as an off white solid.

Method D: LC-MS (electrospray): m/z = 445.3 ($M+H$)⁺, R_T = 3.78 min.

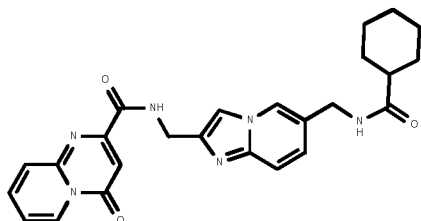
15 [00553] **Compound 237**: 4-oxo-N-({6-[(phenylformamido)methyl]imidazo[1,2-a]pyridin-2-yl}methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



[00554] A stirred solution of HATU (140 mg, 0.368 mmol), benzoic acid (30 mg, 0.246 mmol) in DMF (1 mL) was treated with N-ethyl-N-isopropyl-propan-2-amine (0.128 mL, 0.737 mmol) at 0 °C under a nitrogen atmosphere for 30 min, and then a solution of N-[[6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide **Compound 50** (122 mg, 0.245 mmol) in DMF (2 mL) was added and the reaction mixture was stirred at room temperature for 4 hours. The crude product was purified by reverse phase HPLC (method B) to provide the title product (25 mg, 21%) as an off white solid.

Method D: LC-MS (electrospray): $m/z = 453.1$ ($M+H$)⁺, RT = 3.04 min.

[00555] Compound 238: N-({6-[(cyclohexylformamido)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide

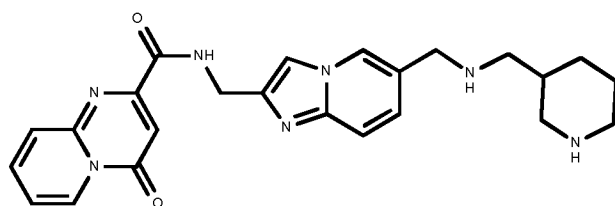


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[00556] The title compound was prepared in the same manner as **Compound 237** using cyclohexanecarboxylic acid to give the title compound (35.2 mg, 35%) as a white solid. Method D: LC-MS (electrospray): $m/z = 459.2$ ($M+H$)⁺, RT = 3.20 min.

10

[00557] Compound 239: 4-oxo-N-{{6-({[(piperidin-3-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide

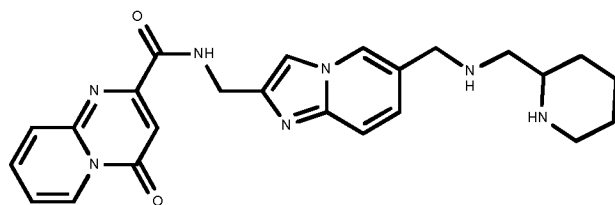


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[00558] The title compound was prepared by deprotection of **Compound 100** using the method described in **Example 1** and the product was purified by preparative HPLC (method B) followed by ion exchange (SCX-2) giving (8 mg, 19%) as a white solid. Method D: LC-MS (electrospray): $m/z = 446.2$ ($M+H$)⁺, RT = 3.18 min.

20

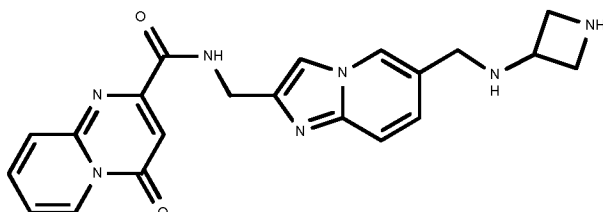
[00559] Compound 240 4-oxo-N-{{6-({[(piperidin-2-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



[00560] The title compound was prepared in the same manner as **Compound 239** to give the title compound (8 mg, 19%) as a white solid.

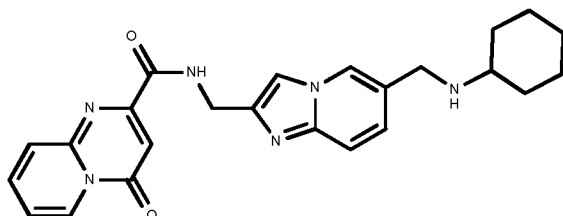
Method D: LC-MS (electrospray): m/z = 446.2 ($M+H$)⁺, RT = 3.18 min.

5 [00561] **Compound 241** N-[(6-[(azetidin-3-yl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



[00562] The title compound was prepared in the same manner as **Compound 1**
 10 starting tert-butyl 3-aminoazetidine-1-carboxylate and the deprotection outlined in **Compound 239** was used to give the title compound (24 mg, 30%) as an off white solid.
 Method D: LC-MS (electrospray): m/z = 404.3 ($M+H$)⁺, RT = 2.83 min.

[00563] **Compound 242**: N-[(6-[(cyclohexylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide
 15



[00564] The title compound was prepared in a similar manner to **Compound 51**, using **Intermediate 30** giving (16 mg, 33%) as a beige solid.

Method C: LC-MS (electrospray): m/z = 431.4 ($M+H$)⁺, RT = 2.87 min.

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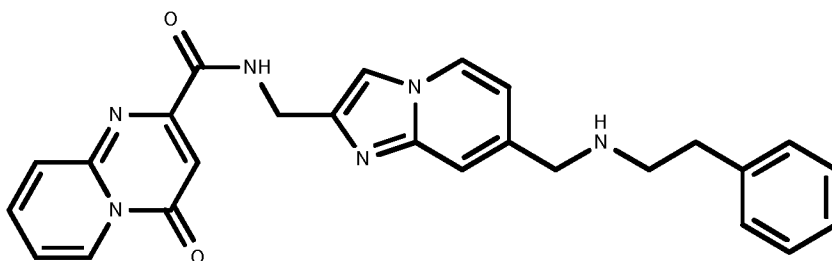
[00565] The compounds in **Table 10** were prepared in a similar manner to **Compound 242** using the appropriate amine and **Intermediate 30**.

Table 10

Compound No	Name	Structure	LCMS method	LCMS Retention time	Mass ion

218	N-[(6-[[[2-cyclopropylethyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide		E	1.00	417.2
219	4-oxo-N-({6-[(piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-chromene-2-carboxamide		E	0.87	417.2
220	N-[(6-[[[4-chlorophenyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide		E	1.26	473.1
221	N-({6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-chromene-2-carboxamide		E	1.06	439.2
222	N-[(6-[[[1-methylcyclohexyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide		E	1.35	459.3
265	N-[(6-[[[2,2-dimethylpropyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide		E	1.08	419.2

[00566] **Compound 243** 4-oxo-N-[(7-[(2-phenylethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



[00567] The title compound was prepared in a similar manner to **Compound 51**, using **Intermediate 31** giving (45 mg, 69%) as a pale yellow solid.

Method C: LC-MS (electrospray): m/z = 453.3 ($M+H$)⁺, RT = 2.58 min.

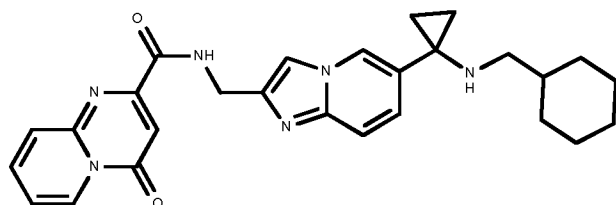
- 5 [00568] The compounds in **Table 11** were prepared in a similar manner to **Compound 243** using the appropriate amine and **Intermediate 31**.

Table 11

Compound No	Name	Structure	LCMS method	LCMS Retention time	Mass ion
223	N-[(7-[(cyclohexylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.94	445.3
224	N-[(7-[(cyclopropylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.12	403.3

10

[00569] **Compound 245**: N-[(6-{1-[(cyclohexylmethyl)amino]cyclopropyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



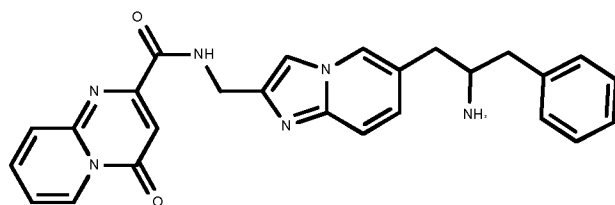
[00570] A 3 neck flask containing a suspension of N-[(6-cyanoimidazo[1,2-a]pyridin-2-

- 15 yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide **Compound 18** (300 mg, 0.871 mmol) in THF (24 mL) was cooled to -78 °C and treated with tetrakisopropoxytitanium (634 μL, 2.09 mmol) followed by bromo(ethyl)magnesium (3M, 1336 μL, 4.01 mmol) and the mixture was stirred at -78 °C for 30 minutes before (diethyl ether)(trifluoro)boron (438 μL, 3.49 mmol) was added and the mixture was stirred at -78 °C for 30 minutes before the
- 20 mixture was allowed to slowly warm to room temperature overnight. The brown mixture was

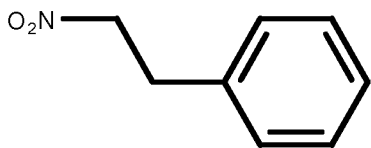
cooled to -78 °C and dropwise treated with tetraisopropoxytitanium (634 μ L, 2.09 mmol) followed by bromo(ethyl)magnesium (3M, 1336 μ L, 4.01 mmol) and the mixture was stirred at -78 °C for 30 minutes before (diethyl ether)(trifluoro)boron (438 μ L, 3.49 mmol) was added. The dark mixture was stirred at -78 °C for a further 30 minutes, allowed to warm to room temperature and left stirring for 7 days. The dark mixture was quenched by the addition of HCl (1M, 50 mL) and washed with DCM. The aqueous layer was basified (6M NaOH, pH ~12) which caused Ti salts to precipitate. The suspension was filtered through Celite (washing with DCM followed by IPA/ CHCl_3 (1:3) and the phases were separated. The extracts were evaporated under vacuum to afford a brown residue 500 mg which was further purified by ion exchange [SCX-2 washing with methanol followed by DCM and eluting with 2M ammonia in methanol]. The eluted fraction was evaporated under vacuum to afford a brown residue. The residue was suspended in DCE (2 mL) and treated with cyclohexanecarbaldehyde (17 μ L, 0.128 mmol) followed by $\text{NaB}(\text{OAc})_3\text{H}$ (41 mg, 0.192 mmol) and the mixture was stirred at room temperature for 16 hours. The mixture was quenched by the addition of aqueous sodium hydrogen carbonate and extracted with DCM (phase separation cartridge). The organics were evaporated under vacuum and the residue was purified by preparative HPLC (method B) and the relevant fraction was evaporated under vacuum to give the title compound (2.9 mg, 9%) as a brown gum.

Method C: LC-MS (electrospray): m/z = 471.4 ($\text{M}+\text{H}$)⁺, RT = 3.31 min.

[00571] Compound 247: N-[[6-(2-amino-3-phenylpropyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



[00572] Step 1: (2-nitroethyl)benzene



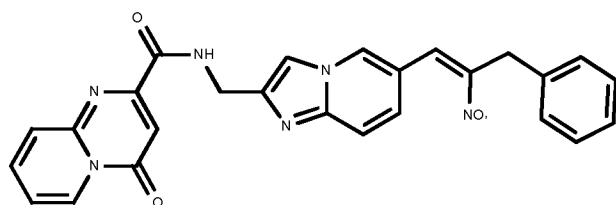
[00573] [(E)-2-nitrovinyl]benzene (1.50 g, 10.1 mmol) was added to a stirred suspension of Silica gel (604 mg, 10.1 mmol) in chloroform (75 mL) and IPA (22.5 mL). The yellow mixture was cooled to 0 °C, and NaBH_4 (837 mg, 22.1 mmol) was added in 4 portions over 20 minutes. The resulting heterogeneous mixture was stirred vigorously at 0 °C for 30

minutes, then at room temperature for 30 minutes. The suspension was cooled to 0 °C, and aqueous HCl (0.2M) was added carefully until no gas evolution was observed. The mixture was filtered and washed with DCM (30 mL). The filtrate was washed with water (50 mL), the organic phase was separated, and the aqueous phase was extracted with DCM (3 x 20 mL).

- 5 The combined organic phases were washed with brine (2 x 30 mL), dried over MgSO₄ and concentrated to give the title compound (1.15 g, 61%) as a yellow oil.

Method A: LC-MS (electrospray): m/z = no mass ion (M+H)⁺, RT = 1.13 min.

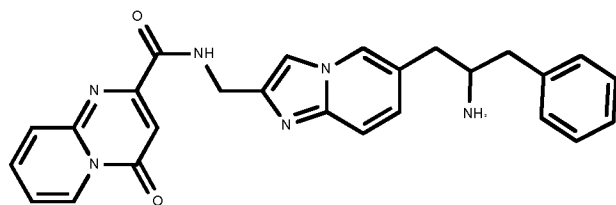
[00574] **Step 2:** N-[[6-[(E)-2-nitro-3-phenyl-prop-1-enyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide



[00575] To a stirred suspension of N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide **Compound 49** (100 mg, 0.288 mmol) and 2-nitroethylbenzene (82 mg, 0.432 mmol) in anhydrous methanol (1 mL) at 0 °C was added acetic acid (16 µL, 0.288 mmol) and butan-1-amine (28 µL, 0.288 mmol), and the reaction mixture was stirred at room temperature for 17 hours. The reaction mixture was stirred at 50 °C for 2 hours before 1,1,1,3,3,3-Hexafluoro-2-propanol (2.5 mL) was added and the solution was stirred overnight at 50 °C for 5 days. The mixture was retreated with butan-1-amine (28 µL, 0.288 mmol) and acetic acid (16 µL, 0.288 mmol), and was stirred at room temperature for 24 hours. The solvent was removed under vacuum. The mixture was diluted with water and extracted with EtOAc (4 x 10 mL), the organic layers were washed with brine, dried over MgSO₄ and concentrated under vacuum. The residue was purified by preparative HPLC (method A) to give the title compound (22 mg, 16%) as a yellow solid.

Method A: LC-MS (electrospray): m/z = 481.2 (M+H)⁺, RT = 1.00 min.

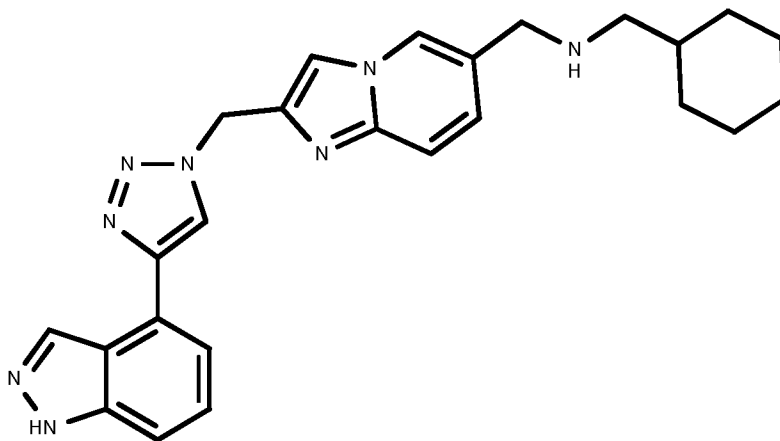
[00576] **Step 3:** N-[[6-(2-amino-3-phenyl-propyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide



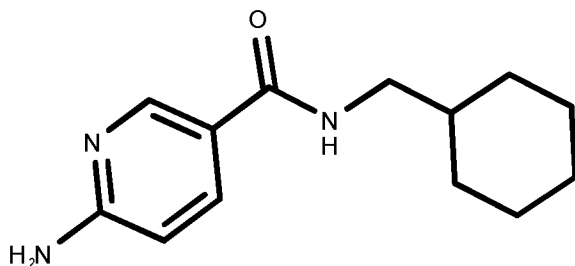
[00577] NaBH₄ (3.8 mg, 0.101 mmol) was dissolved in ethanol (1 mL) and cooled to 0 °C. To this a solution of N-[[6-[(E)-2-nitro-3-phenyl-prop-1-enyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide (22 mg, 0.05 mmol) in 1,4-Dioxane (1 mL) was added slowly, and stirred at 0 °C for 20 minutes, then at room temperature for 180 minutes. The mixture was cooled to 0 °C and was quenched with NH₄Cl (sat). The solvent was removed under vacuum, the mixture was diluted with EtOAc (10 mL) and water (10 mL), the layers were separated, the mixture was extracted with EtOAc (3 x 10 mL), the organic layers were washed with water (10 mL) and brine (10 mL), dried over MgSO₄ and concentrated to a yellow solid. Ammonium chloride (10 mg, 0.187 mmol) was then added to a mixture of N-[[6-(2-nitro-3-phenyl-propyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide (18 mg, 0.0373 mmol) in methanol (1 mL) and water (0.5 mL), the mixture was heated at 50 °C. Iron (10 mg, 0.187 mmol) was then added, and the reaction mixture was heated to 65 °C and stirred for 4.5 hours. The reaction mixture was allowed to cool to room temperature, was filtered through a pad of Celite, washed with EtOAc and the filtrate was concentrated. The mixture was purified by preparative HPLC (method A) to give the title compound (7.0 mg, 41%) as an off white solid.

Method D: LC-MS (electrospray): m/z = 453.3 (M+H)⁺, RT = 3.31 min.

[00578] **Compound 248:** (cyclohexylmethyl)[(2-[[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amine



[00579] **Step 1:** 6-amino-N-(cyclohexylmethyl)pyridine-3-carboxamide



[00580] 6-aminopyridine-3-carboxylic acid (500 mg, 3.62

mmol), cyclohexylmethanamine (820 mg, 7.24 mmol) and triethylamine (1.51 mL, 10.9

5 mmol) were combined in DMF (3 mL) and HATU (2.06g, 5.43 mmol) was added. The

mixture was stirred at room temperature for 24 hours. The reaction mixture was quenched

with saturated aqueous sodium hydrogen carbonate (30 mL) and extracted with 3:1

chloroform/isopropanol (3 x 80 mL). The combined organic extracts were dried over sodium

sulfate and evaporated under vacuum. The residue was purified by Biotage Isolera™

10 chromatography (28 g kp-NH, eluting with EtOAc/heptane 0-100% followed by

methanol/EtOAc 0-20%) to afford a crude material which was further purified by Biotage

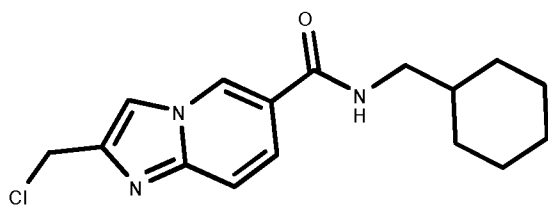
Isolera™ chromatography (60 g C18-Ultra, acetonitrile+0.1%NH₃/water +0.1% NH₃ 10-

100%) to afford (298 mg, 35%) of the title compound as a white solid

Method B: LC-MS (electrospray): m/z = 234.3 (M+H)⁺, RT = 1.36 min

[00581] **Step 2:** 2-(chloromethyl)-N-(cyclohexylmethyl)imidazo[1,2-a]pyridine-6-

carboxamide



[00582] 6-amino-N-(cyclohexylmethyl)pyridine-3-carboxamide (290 mg, 1.24 mmol)

and 1,3-dichloropropan-2-one (237 mg, 1.86 mmol) were combined in acetonitrile (10 mL)

and the mixture heated at reflux for 3 days. The reaction mixture was cooled to room

temperature and concentrated under vacuum. The residue was suspended in saturated

aqueous sodium hydrogen carbonate (30 mL) and extracted with 3:1 chloroform/isopropanol

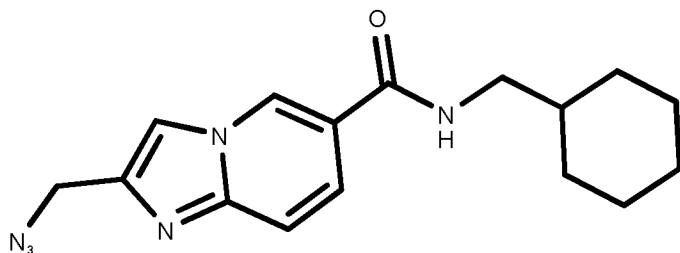
25 (4 x 30 mL). The combined organic extracts were dried over sodium sulfate and evaporated

under vacuum. The residue was purified by Biotage Isolera™ chromatography (25 g kp-Sil,

eluting with EtOAc/heptane 0-100% followed by methanol/EtOAc 0-20%) to afford (143 mg, 38%) of the title compound as an off-white solid.

Method B: LC-MS (electrospray): m/z = 306.3 (M+H)⁺, RT = 1.52 min

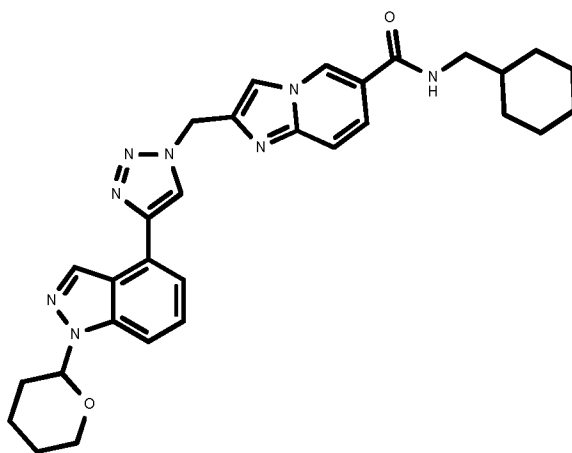
- 5 **[00583] Step 3:** 2-(azidomethyl)-N-(cyclohexylmethyl)imidazo[1,2-a]pyridine-6-carboxamide



- 10 **[00584]** 2-(chloromethyl)-N-(cyclohexylmethyl)imidazo[1,2-a]pyridine-6-carboxamide (140 mg, 0.46 mmol), sodium iodide (69 mg, 0.46 mmol) and NaN₃ (45 mg, 0.69 mmol) were combined in DMF (2 mL) and the mixture stirred at room temperature for 22 hours. The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate (30 mL) and extracted with 3:1 chloroform/isopropanol (3 x 30 mL). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was triturated
- 15 with EtOAc/heptane and the solids collected by filtration to afford (100 mg, 70%) of the title compound as a white solid

Method B: LC-MS (electrospray): m/z = 313.3 (M+H)⁺, RT = 1.52 min

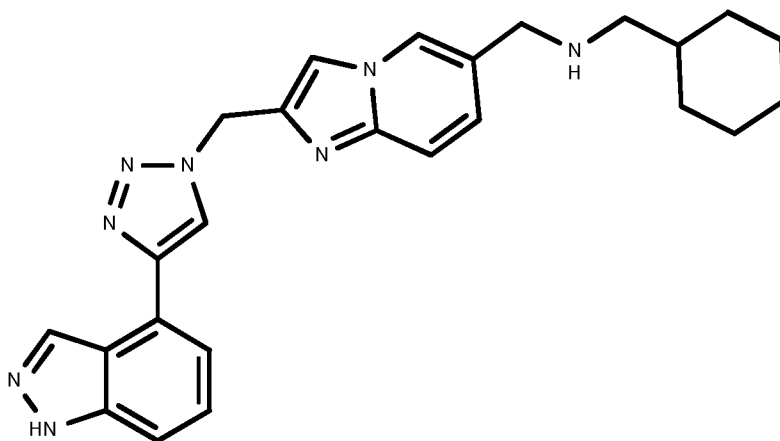
- 20 **[00585] Step 4:** N-(cyclohexylmethyl)-2-[[4-(1-tetrahydropyran-2-ylindazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carboxamide



[00586] 2-(azidomethyl)-N-(cyclohexylmethyl)imidazo[1,2-a]pyridine-6-carboxamide (100 mg, 0.32 mmol) and 4-ethynyl-1-tetrahydropyran-2-yl-indazole **Intermediate 24** (101 mg, 0.32 mmol) were dissolved in DMF (3 mL) and water (0.5 mL) and copper sulfate (10 mg, 0.06 mmol) and sodium ascorbate (64 mg, 0.32 mmol) were added. The mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with 3:1 chloroform/isopropanol (30 mL) and washed with water (20 mL). The aqueous phase was extracted with 3:1 chloroform/isopropanol (2 x 30 mL) and the combined organic layers were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on silica gel (Biotage, 11 g kp-NH, eluting with EtOAc/heptane 0-100% followed by methanol/EtOAc 0-20%) to afford the title compound (171 mg, 99%) as a white solid

Method A: LC-MS (electrospray): m/z = 589.3 (M+H)⁺, RT = 1.18 min

[00587] **Step 5:** N-(cyclohexylmethyl)-1-[2-[[4-(1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine

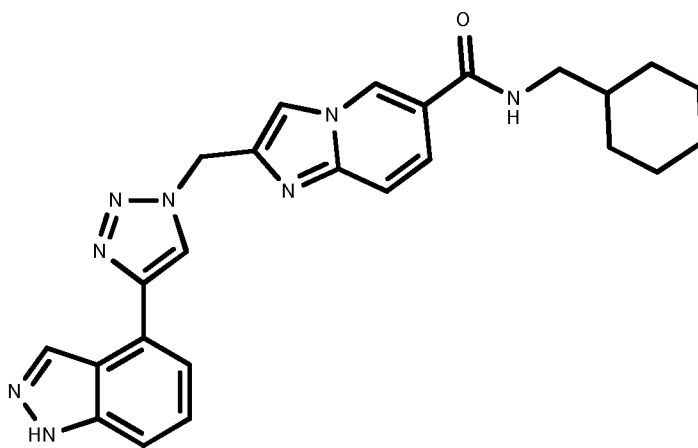


[00588] N-(cyclohexylmethyl)-2-[[4-(1-tetrahydropyran-2-ylindazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carboxamide (80 mg, 0.15 mmol) and 2-fluoropyridine (53 μ l, 0.62 mmol) were combined in DCM-Anhydrous (4 mL) and cooled in an ice/water bath. trifluoromethylsulfonyl trifluoromethanesulfonate (107 μ l, 0.63 mmol) was added dropwise to give a yellow solution which was stirred briefly, then 1,1,3,3-tetramethyldisiloxane (160 μ l, 0.91 mmol) and tris(pentafluorophenyl)borane (15 mg, 0.03 mmol) were added and the mixture stirred whilst warming to room temperature for 6 hours. K₂CO₃ (100 mg) and methanol (20 mL) were added and the mixture incubated at room temperature for 16h and at reflux for 1 hour. The reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was suspended in saturated

aqueous sodium hydrogen carbonate (20 mL) and extracted with 3:1 chloroform/isopropanol (3 x 30 mL) and the combined organic extracts dried over sodium sulfate and evaporated under vacuum. The residue was triturated with EtOAc/heptane and the solids collected by filtration. The residue was purified by reverse phase chromatography (method B) and the clean product-containing fractions combined and evaporated under vacuum to afford the title compound (17 mg (26%)) as a white solid.

Method C: LC-MS (electrospray): m/z = 441.4 (M+H)⁺, RT = 3.09 min

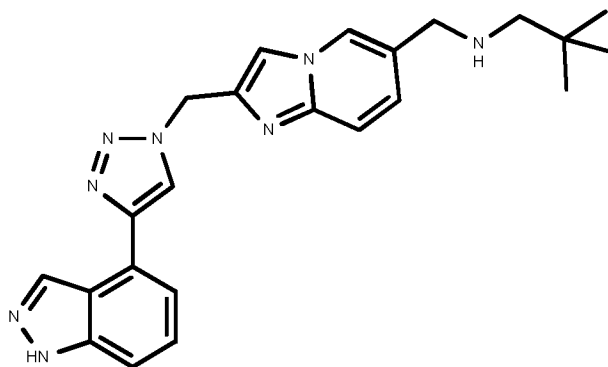
[00589] **Compound 249:** N-(cyclohexylmethyl)-2-[[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carboxamide



[00590] N-(cyclohexylmethyl)-2-[[4-(1-tetrahydropyran-2-ylindazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carboxamide **Compound 248 step 4** (40 mg, 0.07 mmol) was suspended in methanol (1 mL) and treated with 4M HCl in Dioxane (1 mL). The mixture was incubated at room temperature for 5h, then evaporated under vacuum. The residue was loaded to an SCX-2 cartridge (2g) and the cartridge rinsed with DCM and methanol, then eluted with 7M NH₃/methanol. The basic eluent was evaporated under vacuum and the residue dried in the Genevac to afford the title compound (8 mg (23%)) as an off-white solid.

Method C: LC-MS (electrospray): m/z = 455.3 (M+H)⁺, RT = 2.88 min

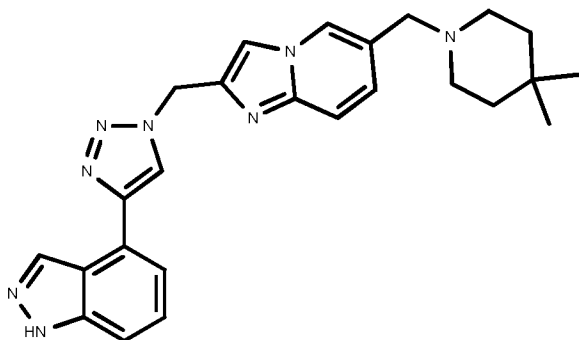
[00591] **Compound 250:** (2,2-dimethylpropyl)((2-[[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl)methyl)amine



[00592] 2-[[4-(1-tetrahydropyran-2-yl)indazol-4-yl]triazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carbaldehyde (**Intermediate 34**) (70 mg, 0.16 mmol) and 2,2-dimethylpropan-1-amine (57 mg, 0.66 mmol) were combined in 1,1,1,3,3,3-Hexafluoroisopropanol (2 mL) and the mixture stirred at room temperature for 1 hour. NaBH₄ (70 mg, 1.85 mmol) was added with a few drops methanol then quenched with methanol (20 mL) and the mixture evaporated under vacuum. The residue was suspended in saturated aqueous sodium hydrogen carbonate (40 mL) and extracted with 3:1 chloroform/isopropanol (3 x 40 mL). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was dissolved in methanol (3 mL) and treated with 4M HCl in Dioxane (3 mL) and the mixture incubated at room temperature for 2h, then evaporated under vacuum. The residue was redissolved in methanol and loaded to an SCX-2 cartridge (5g). The system was rinsed with DCM and methanol, then eluted with 7N NH₃/methanol. The basic eluent was evaporated under vacuum. The residue was triturated with EtOAc/heptane and the solids collected by filtration to afford (45 mg, 64%) of the title compound as a white solid.

Method D: LC-MS (electrospray): m/z = 415.3 (M+H)⁺, RT = 3.69 min

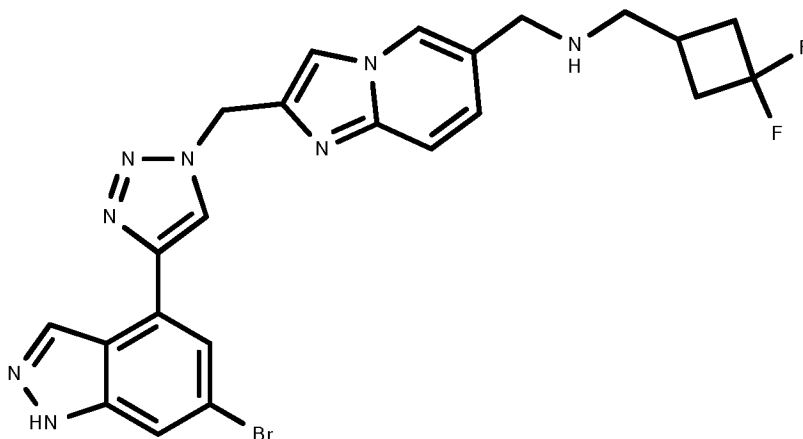
[00593] **Compound 251:** 4-[1-({6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole



[00594] **Step 1:** 4-[1-({6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole

[00595] A mixture of 2-[[4-(1-tetrahydropyran-2-ylindazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carbaldehyde (**Intermediate 34**) (70 mg, 0.164 mmol) and 4,4-dimethylpiperidine (43 μ L, 0.328 mmol) in DCE (1.8 mL) was stirred at 50 °C for 5 minutes, NaB(OAc)₃H (104 mg, 0.49 mmol) was added, and the mixture was stirred at 50 °C for 4 hours. The reaction mixture was quenched with aqueous sodium hydrogen carbonate, diluted with 3:1 CHCl₃/IPA and the phases were separated, the aqueous mixture was extracted with CHCl₃/IPA, the organic layers were dried by passage through a TELOS phase separation cartridge and concentrated under vacuum. The residue was dissolved in methanol (2.5 mL) and 4M HCl in dioxane (2.5 mL), and stirred at room temperature for 2 h, then evaporated under vacuum. The residue was purified by reverse phase chromatography (Method B) to afford the title compound (23 mg, 32%) as a white solid. Method C: LC-MS (electrospray): m/z = 441.4 (M+H)⁺, RT = 3.17 min

[00596] **Compound 252**: [(2-[[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl)methyl][(3,3-difluorocyclobutyl)methyl]amine



[00597] 2-[[4-(6-bromo-1-tetrahydropyran-2-ylindazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carbaldehyde **Intermediate 35** (70 mg, 0.12 mmol), (3,3-difluorocyclobutyl)methanamine hydrochloride (37 mg, 0.24 mmol) and triethylamine (50 μ L, 0.36 mmol) were combined in 1,1,1,3,3,3-Hexafluoro-2-propanol (2 mL) and the mixture stirred at room temperature for 30 minutes. NaBH₄ (70 mg, 1.85 mmol) was added with a few drops methanol and the mixture stirred briefly, then quenched with methanol (20 mL) and the mixture evaporated under vacuum. The residue was suspended in saturated aqueous sodium hydrogen carbonate (30 mL) and extracted with 3:1 chloroform/isopropanol (3 x 30 mL). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was redissolved in methanol (3 mL), treated with 4M HCl in Dioxane (3 mL) and incubated at room temperature for 16 hours. The reaction mixture was

evaporated under vacuum. The residue was loaded to an SCX-2 cartridge (2g) and the system rinsed with DCM and methanol, then eluted with 7M NH₃/methanol. The basic eluent was evaporated under vacuum. The resultant residue was purified by reverse phase chromatography (Method B) to afford the title compound (17 mg, 27%) as an off-white solid.

5 Method D: LC-MS (electrospray): m/z = 527.2/529.2 (M+H)⁺, RT = 3.69 min

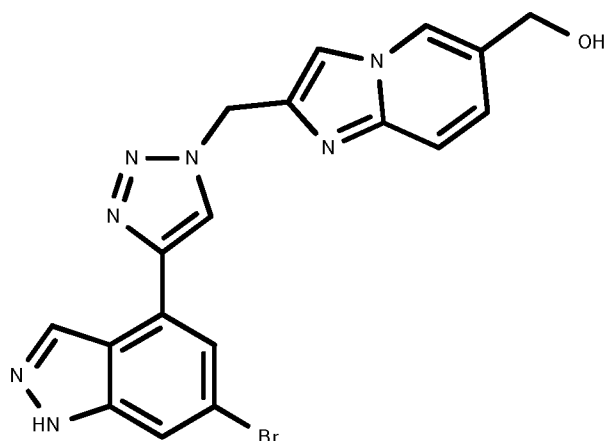
[00598] The compounds in **Table 12** were prepared in a similar fashion to **Compound 252**

Table 12

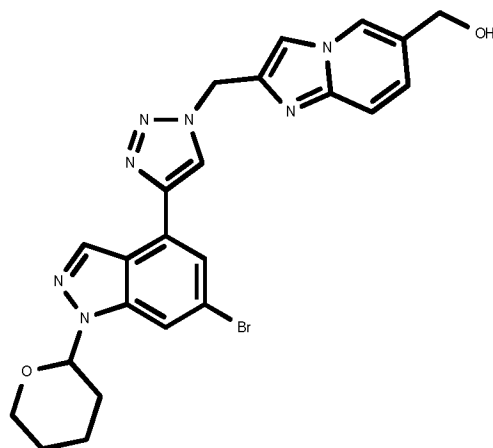
Cpd No	Name	Structure	LCMS method	LCMS Retention time	Mass ion	Reductive amination conditions
225	[(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methyl](2,2-dimethylpropyl)amine		D	4.09	493.2/ 495.2	252
226	[(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methyl](cyclohexylmethyl)amine		C	3.54	519.3/ 521.3	Compound 252
227	6-bromo-4-[1-({[4-(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-1,2,3-triazol-4-yl]-1H-indazole		C	1.64	519.2/ 521.2	Compound 251

10

[00599] **Compound 253:** (2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methanol



[00600] **Step 1:** [2-({4-[6-bromo-1-(oxan-2-yl)-1H-indazol-4-yl]-1H-1,2,3-triazol-1-yl}methyl)imidazo[1,2-a]pyridin-6-yl]methanol



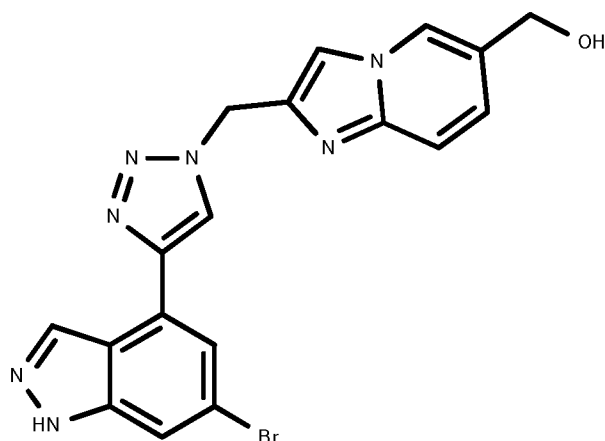
5

[00601] The title compound was prepared in the same manner as **Intermediate 34 Step 4** to give (795 mg, 68%) as a grey solid.

Method A: LC-MS (electrospray): m/z = 508.15/510.15 ($M+H$)⁺, RT = 1.00 min

10

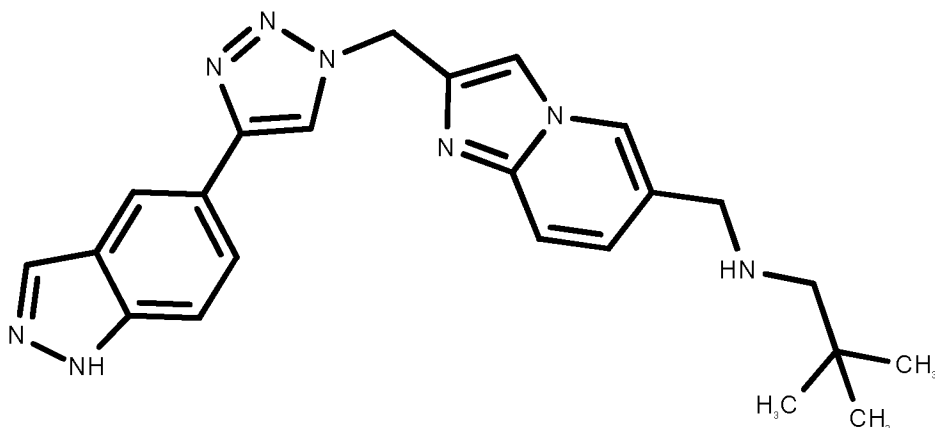
[00602] **Step 2:** (2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methanol



[00603] [2-[[4-(6-bromo-1-tetrahydropyran-2-yl-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanol (87 mg, 0.17 mmol) was suspended in methanol (3 mL) and treated with HCl (4M in Dioxane, 3 mL, 12 mmol). The mixture was stirred at room temperature for 1h, then evaporated under vacuum. The residue was triturated with methanol/Et₂O and the solids collected by filtration. The residue was purified by preparative HPLC (method B) to afford the title compound (14 mg, 19%) as an off-white solid.

Method C: LC-MS (electrospray): m/z = 424.1/426.1 (M+H)⁺, RT = 2.14 min

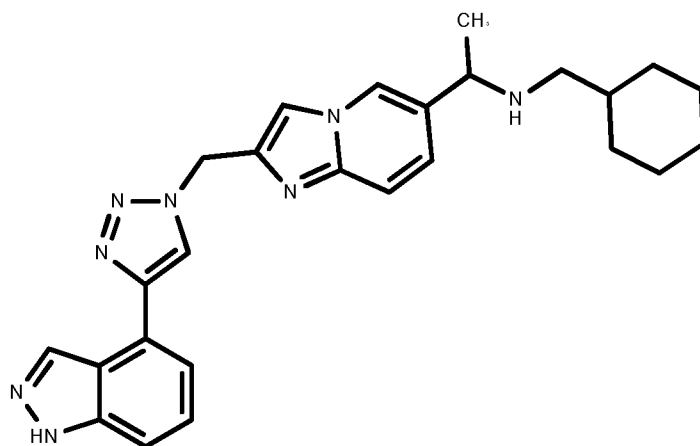
[00604] **Compound 254:** (2,2-dimethylpropyl)[(2-[[4-(1H-indazol-5-yl)-1H-1,2,3-triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amine



[00605] The title compound was prepared from **intermediate 37** using the method described in **Compound 250** giving (42 mg, 65%) as an off white solid.

Method D: LC-MS (electrospray): m/z = 415.3 (M+H)⁺, RT = 3.57 min

[00606] **Compound 255:** ((cyclohexylmethyl)[1-(2-[[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl)ethyl]amine



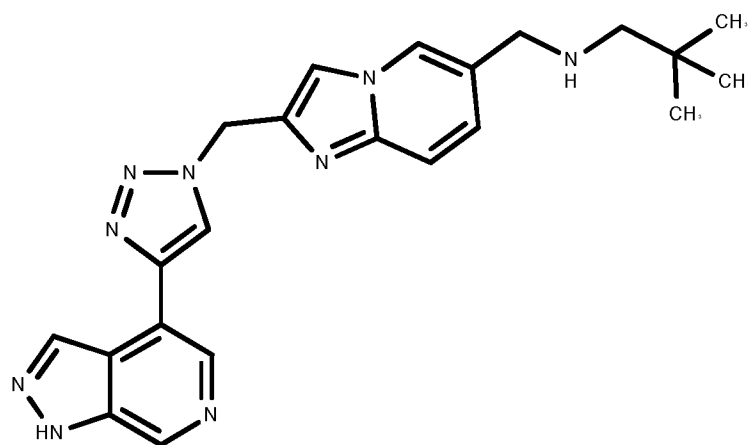
n

[00607] The title compound was prepared from **Intermediate 32 Step 3** and **Intermediate 24** using the method described in **Compound 248** giving (27 mg, 25%) as an off-white solid.

Method D: LC-MS (electrospray): $m/z = 455.4$ ($M+H$)⁺, $RT = 4.03$ min.

[00608] **Compound 256**: (2,2-dimethylpropyl)({2-[(4-{1H-pyrazolo[3,4-c]pyridin-4-yl}-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl)amine

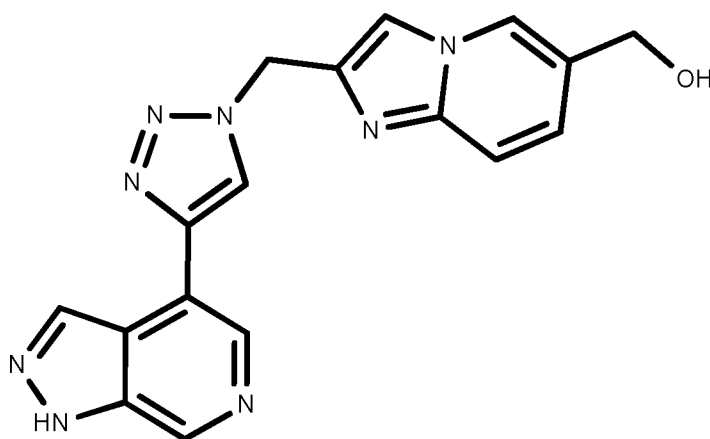
[00609]



[00610] The title compound was prepared from **Intermediate 40** using the procedure described (**Compound 250**) giving (31 mg, 32%) as a pale yellow solid.

Method D: LC-MS (electrospray): $m/z = 416.3$ ($M+H$)⁺, $RT = 3.09$ min

[00611] **Compound 257**: {2-[(4-{1H-pyrazolo[3,4-c]pyridin-4-yl}-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methanol

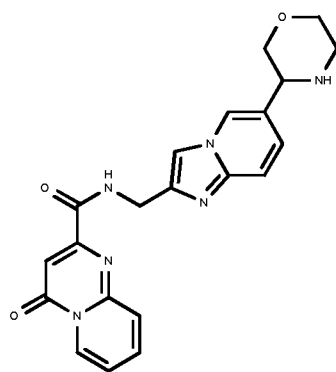


[00612] The title compound was prepared from **Intermediate 39** using the procedure described in **Compound 253** giving (1 mg, 2%) as a white solid.

Method D: LC-MS (electrospray): m/z = 347.2 ($M+H$)⁺, RT = 2.30 min.

[00613] $\mu\mu$

[00614] **Compound 263**: N-[[6-(morpholin-3-yl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



[00615] To solution of N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide (**Compound 49**) (119 mg, 0.343 mmol) in 1,1,1,3,3,3-Hexafluoro-2-propanol (0.5 mL) was added a solution of [(2-

aminoethoxy)methyl]tributylstannane (125 mg, 0.343 mmol) in DCE (4 mL). The mixture was stirred at 80 °C for 2 hours. Meanwhile a mixture of 2,6-dimethylpyridine (0.080 mL, 0.685 mmol), copper(II) bis(trifluoromethanesulfonate) (249 mg, 0.685 mmol) and 1,1,1,3,3,3-Hexafluoro-2-propanol (2 mL) was stirred separately at room temperature for 1 hour. After cooling to room temperature, the solution of the imine was added drop-wise to the solution of the catalyst. The resulting mixture was stirred at room temperature for 3 hours forming a clear, dark green solution. The reaction mixture was diluted with DCM (25 mL) and

quenched with 10% aq. NH_4OH (10 mL) solution. The organic layer was separated, washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue was purified by preparative HPLC (method B) to afford the title compound (39 mg, 28%) as greenish solid.

5 Method C: LC-MS (electrospray): $m/z = 405.3$ ($\text{M}+\text{H}^+$), $\text{RT} = 1.59$ min

[00616] The compounds in Table 12 were prepared in the same manner as

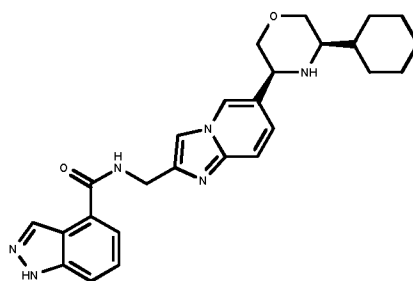
Compound 263

Table 13

Compound No	Name	Structure	LCMS method	LCMS Retention time	Mass ion
228	N-({6-[(3R,5S)-5-tert-butylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.91	461.4
229	N-({6-[(3S,5R)-5-tert-butylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.89	461.4
230	N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide		C	3.05	487.4

10

[00617] **Compound 231:** N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide

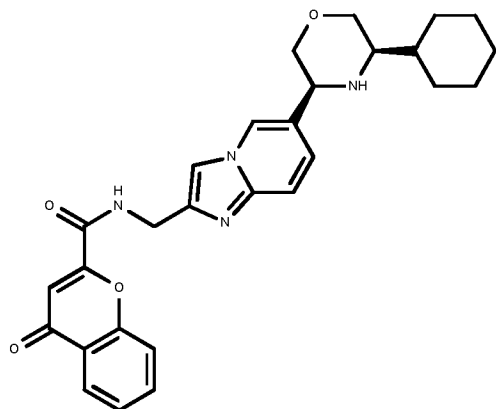


trans racemate

[00618] To a solution of 1-[rac-(2R)-tetrahydropyran-2-yl]indazole-4-carboxylic acid (35 mg, 0.142 mmol), [6-[rac-(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl]methanamine trihydrochloride (**Intermediate 47**) (60 mg, 0.142 mmol) and DIPEA (0.12 mL, 0.708 mmol) in DMF (3 mL) was added HATU (65 mg, 0.170 mmol). The reaction mixture was stirred at room temperature overnight. The reaction mixture was partitioned between EtOAc (30 mL) and saturated aqueous sodium hydrogen carbonate (20 mL). The organic layer was separated, washed with brine (10 mL), dried (Na₂SO₄), filtered and concentrated under reduced pressure to dryness. The residue was dissolved in methanol (3 mL) and 4M HCl in dioxane (1 mL) was added. The mixture was stirred at room temperature overnight. The volatiles were removed under reduced pressure and the residue was purified by preparative HPLC (method B) to afford the title compound (30 mg, 46%) as white solid.

Method C: LC-MS (electrospray): m/z = 459.4 (M+H)⁺, RT = 2.96 min

[00619] **Compound 264:** N-((6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide:

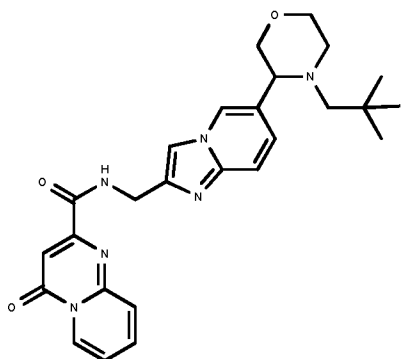


[00620] To a solution of 4-oxochromene-2-carboxylic acid (22 mg, 0.118 mmol), [6-[rac-(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl]methanamine-

trihydrochloride (50 mg, 0.118 mmol) and DIPEA (0.10 mL, 0.590 mmol) in DMF (1 mL) was added HATU (54 mg, 0.142 mmol). The reaction mixture was stirred at room temperature overnight. The reaction mixture was partitioned between EtOAc (30 mL) and saturated aqueous sodium hydrogen carbonate (20 mL). The organic layer was separated, washed with brine (10 mL), dried (Na₂SO₄), filtered and concentrated under reduced pressure. The residue was purified by preparative HPLC (method B) to afford the title compound (15 mg, 26%) as off-white solid.

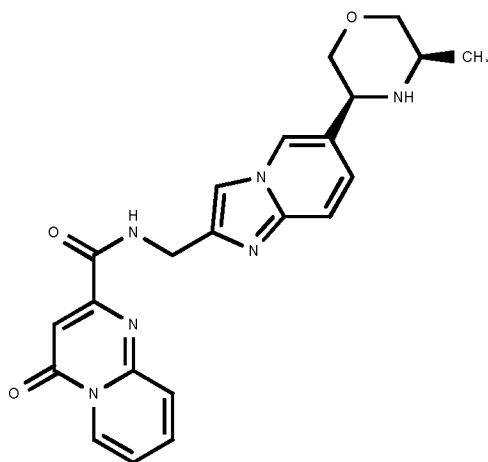
Method C: LC-MS (electrospray): m/z = 487.4 (M+H)⁺, RT = 3.33 min

- 10 **[00621] Compound 232:** N-({6-[4-(2,2-dimethylpropyl)morpholin-3-yl]imidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide:



- [00622]** To a solution of N-[(6-morpholin-3-yl)imidazo[1,2-a]pyridin-2-yl]methyl-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide (**Compound 263**) (38 mg, 0.09 mmol) in DCE (1.5 mL) was added 2,2-dimethylpropanal (0.04 mL, 0.38 mmol) and acetic acid (0.011 mL, 0.188 mmol) at room temperature. The mixture was stirred for 15 minutes before NaB(OAc)₃H (100 mg, 0.470 mmol) was added in small portions over a period of 2 hours. The reaction mixture was then stirred at 40 °C overnight. More 2,2-dimethylpropanal (0.041 mL, 0.376 mmol) and NaB(OAc)₃H (100 mg, 0.470 mmol) were added and the reaction mixture was stirred for another 24 hours at 40 °C. The reaction mixture was diluted with DCE (20 mL), washed with saturated aqueous sodium hydrogen carbonate (10 mL) and brine (10 mL), dried (Na₂SO₄), filtered and concentrated under reduced pressure. The residue was purified by preparative HPLC (method B) to afford the title compound (14 mg, 31%) as off-white solid.
- 25 Method C: LC-MS (electrospray): m/z = 475.4 (M+H)⁺, RT = 3.17 min

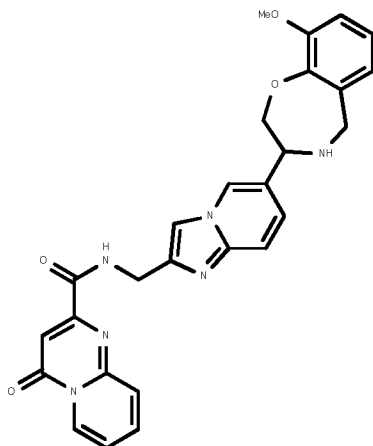
- [00623] Compound 233:** N-({6-[(3S,5R)-5-methylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide.



[00624] To a solution of tert-butyl N-[[6-[rac-(3S,5R)-5-methylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate (**Intermediate 48**) (80 mg, 0.231 mmol) in methanol (1 mL) was added HCl (4M in dioxane, 1 mL, 4 mmol) at room temperature. The solution was stirred at 50 °C for 1 hour. After cooling to room temperature, the reaction mixture was concentrated to dryness under reduced pressure. To the residue was added DMF (2 mL), 4-oxopyrido[1,2-a]pyrimidine-2-carboxylic acid **Intermediate 4** (60%, 73 mg, 0.231 mmol) and N-ethyl-N-isopropyl-propan-2-amine (0.20 mL, 1.15 mmol). The mixture was stirred for 15 minutes at room temperature before HATU (105 mg, 0.277 mmol) was added and stirring was continued overnight. The reaction mixture was then diluted with EtOAc (30 mL), washed with saturated aqueous sodium hydrogen carbonate (20 mL) and brine (10 mL), dried (Na₂SO₄), filtered and concentrated under reduced pressure. The residue was purified by preparative HPLC (method B) to afford the title compound (41 mg, 42%) as white solid.

Method C: LC-MS (electrospray): m/z = 419.3 (M+H)⁺, RT = 1.81 min

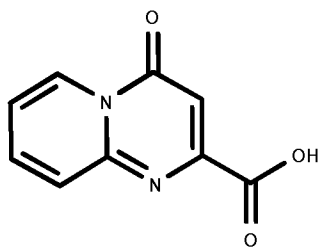
[00625] **Compound 234:** N-[[6-(9-methoxy-2,3,4,5-tetrahydro-1,4-benzoxazepin-3-yl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide:



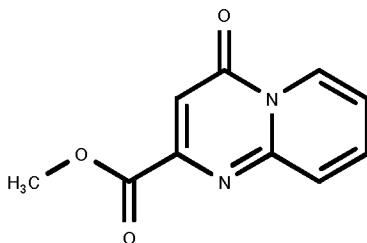
[00626] The title compound was prepared in a similar manner to **Compound 233** using **Intermediate 49** to afford the title compound (415 mg, 38%) as white solid.

5 Method C: LC-MS (electrospray): $m/z = 497.3$ ($M+H$)⁺, RT = 2.27 min

[00627] Improved synthesis of **Intermediate 4**: 4-oxopyrido[1,2-a]pyrimidine-2-carboxylic acid



[00628] **Step 1:** methyl 4-oxopyrido[1,2-a]pyrimidine-2-carboxylate



10

[00629] Dimethyl but-2-ynedioate (16 mL, 0.126 mol) was added slowly to a vigorously stirred solution of pyridin-2-amine (10.00 g, 0.105 mol) in water (1000 mL), and the reaction mixture was stirred at room temperature for 18 hours.

[00630] The mixture was worked up in two batches. Each half of the material was
15 extracted with DCM (3x100 mL), passed through a TELOS phase separator and concentrated.

[00631] The material was also purified in two batches. One half of the material was dry loaded onto KP-NH silica, loaded onto a plug of KP-NH silica, and was eluted, with

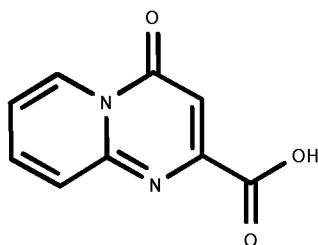
EtOAc in heptane, 50%, 70% and 100% and the yellow solution was concentrated to give a pale yellow solid.

[00632] The second half of the material was diluted with DCM (150 mL), treated with loose silica, stirred for 5 minutes, then filtered. The filter cake was washed with DCM (~1 L) and the filtrate was concentrated to give a pale yellow solid.

[00633] The two batches were combined, triturated with Et₂O and the solid was collected by filtration to give the title compound (6.57 g, 30%) as an off-white solid.

Method A: LC-MS (electrospray): m/z = 205.1 (M+H)⁺, RT = 0.79 min

[00634] Step 2: 4-oxopyrido[1,2-a]pyrimidine-2-carboxylic acid

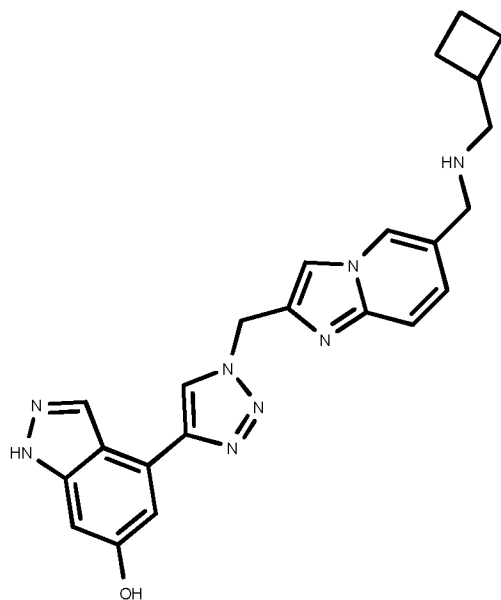


[00635] Methyl 4-oxopyrido[1,2-a]pyrimidine-2-carboxylate (6.57 g, 32.2 mmol) was dissolved in HCl (aq) (~8M, 7.5 mL) at room temperature and the solution was heated at reflux for 2 hours.

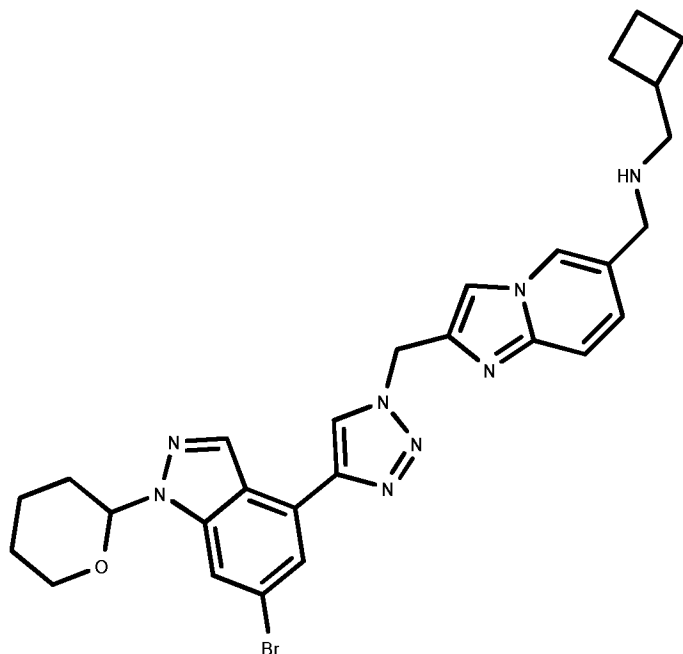
[00636] The mixture was cooled to room temperature and the precipitate was collected by filtration and dried on the filter to give the title compound (5.03 g, 81%) as a white solid.

Method A: LC-MS (electrospray): m/z = 191.1 (M+H)⁺, RT = 0.29 min

[00637] Compound 266: 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazol-6-ol



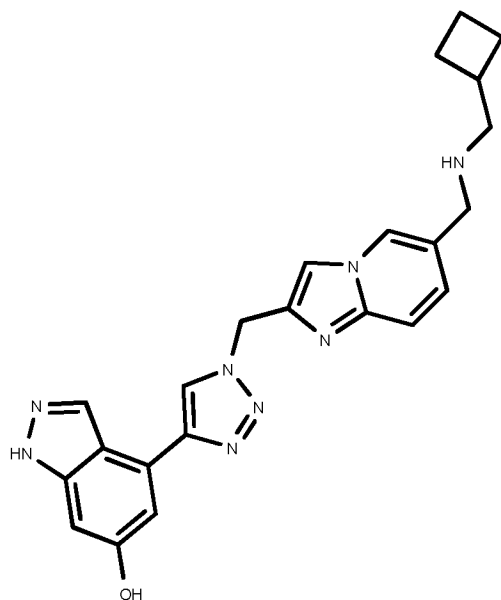
[00638] **Step 1:** {[2-({4-[6-bromo-1-(oxan-2-yl)-1H-indazol-4-yl]-1H-1,2,3-triazol-1-yl}methyl)imidazo[1,2-a]pyridin-6-yl)methyl}(cyclobutylmethyl)amine



[00639] The title compound was prepared from **Intermediate 35** using the method described in **Compound 250** to afford (487 mg, 48%) as a pale yellow solid.

Method B: LC-MS (electrospray): m/z = 508.3/510.3 (M+H)⁺, RT = 1.49 min

[00640] **Step 2:** 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]triazol-4-yl]-1H-indazol-6-ol



[00641] A microwave vial was charged with {[2-({4-[6-bromo-1-(oxan-2-yl)-1H-indazol-4-yl]-1H-1,2,3-triazol-1-yl}methyl)imidazo[1,2-a]pyridin-6-yl)methyl}(cyclobutylmethyl)amine (85 mg, 0.148 mmol), copper(1+) iodide (2.8 mg, 0.0148 mmol) and quinolin-8-ol 1-oxide (10

mg, 0.0591 mmol) in DMSO (1.3 mL) and water (1.3 mL), the mixture was degassed via a stream of N₂ before a solution of caesium hydroxide (66 mg, 0.443 mmol) in water was added, the mixture was further de-oxygenated before the vial was sealed and irradiated in a microwave at 110 °C for 4.5 h.

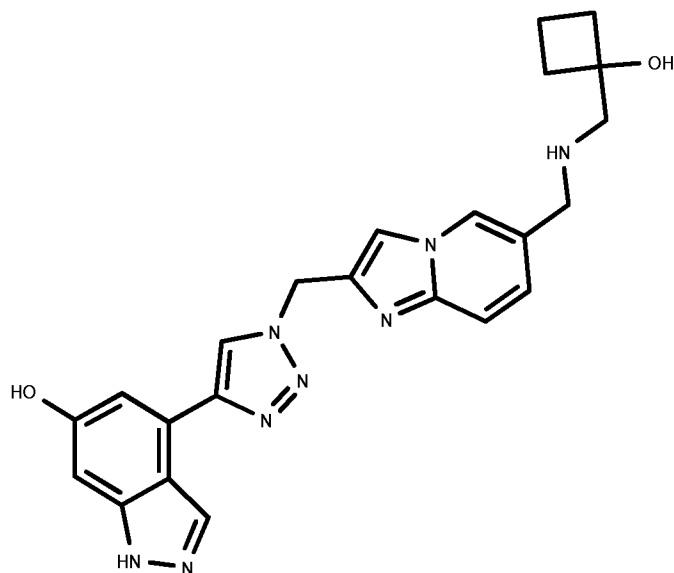
- 5 **[00642]** The mixture was purified by ion exchange (SCX-2 10 g) washed with MeOH and eluted with ammonia solution (3M in MeOH). The eluted fraction was evaporated under vacuum.

1. The residue was diluted with MeOH (0.5 mL) and 4M HCl in dioxane (1.7 mL), and was stirred at RT for 1 h and at 40 °C for 18 hours.

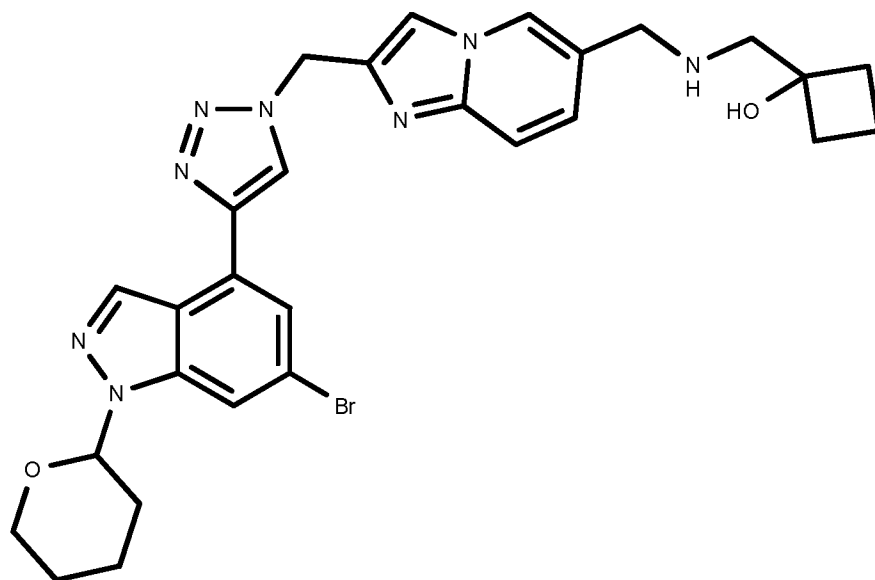
- 10 2. The solvent was removed under vacuum and purified by Basic reverse phase chromatography and the relevant fractions were freeze dried to give the title compound (12 mg, 19%) as a white solid.

Method D: LC-MS (electrospray): m/z = 429.3 (M+H)⁺, RT = 3.02 min

- 15 **[00643]** **Compound 267:** 4-[1-[[6-[(1-hydroxycyclobutyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazol-6-ol



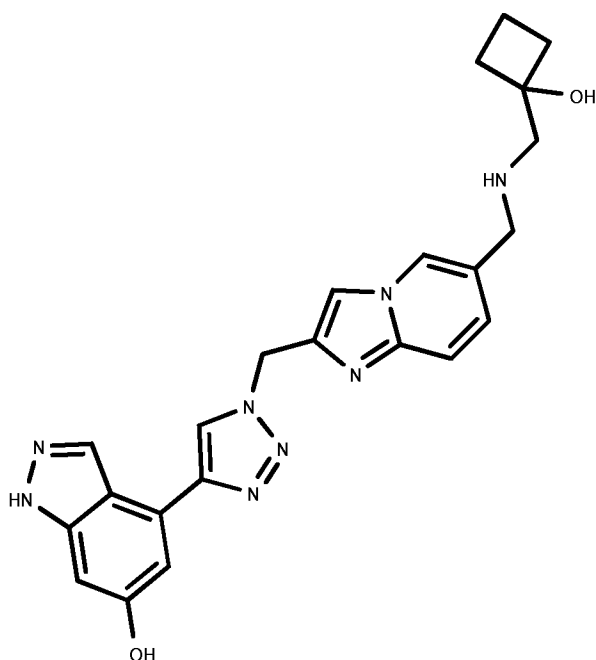
- [00644]** **Step 1:** 1-[[[2-({4-[6-bromo-1-(oxan-2-yl)-1H-indazol-4-yl]-1H-1,2,3-triazol-1-yl}methyl)imidazo[1,2-a]pyridin-6-yl]methyl]amino)methyl]cyclobutan-1-ol



[00645] The title compound was prepared from **Intermediate 35** using the method described in **Compound 250** to afford (357 mg, 66%) as a brown solid.

Method B: LC-MS (electrospray): m/z = 591.3/593.3 ($M+H$)⁺, RT = 1.57 min

- 5 [00646] **Step 2:** 4-[1-[[[6-[[1-(1-hydroxycyclobutyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazol-6-ol



- 10 [00647] 1-[[[2-[[4-(6-bromo-1-tetrahydropyran-2-yl)indazol-4-yl]triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol (150mg, 0.25mmol), tBuBrettPhos Pd G3 (22mg, 0.03mmol) and NaOtBu (29mg, 0.30mmol) were

combined in 1,4-Dioxane-Anhydrous (10ml) and the mixture was sparged with nitrogen for 5 mins. Propan-2-ol (0.4ml, 5.26mmol) was added, the mixture further sparged briefly and the vessel sealed and the mixture was heated at 100°C for 2 hours.

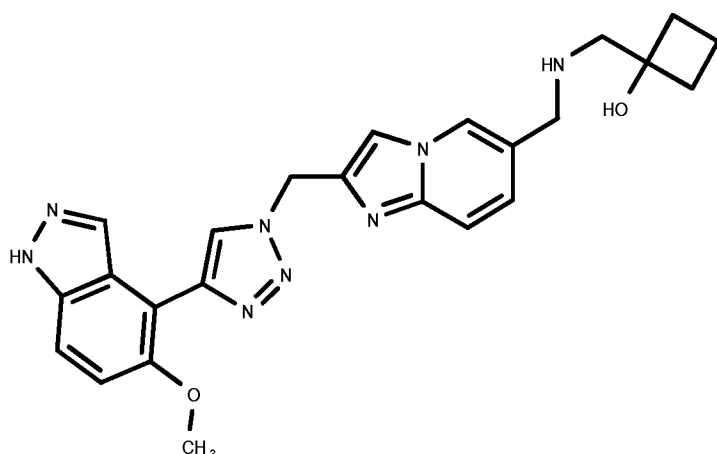
[00648] The reaction mixture was cooled to RT and evaporated under vacuum. The residue was redissolved in MeOH (3ml) and treated with HCl in Dioxane (4M, 3ml) and incubated at room temperature for 18 hours.

[00649] The reaction mixture was evaporated under vacuum and the residue purified by basic reverse phase chromatography. The product-containing fractions combined and evaporated under vacuum to afford crude material.

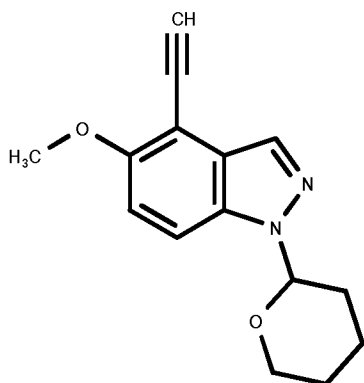
[00650] The residue was further purified by preparative HPLC [method B] to afford the title compound (7mg, 6%) as an off-white solid.

Method C: LC-MS (electrospray): m/z = 445.4 (M+H)⁺, RT = 1.53 min

[00651] **Compound 268:** 1-[[[2-[[4-(5-methoxy-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol



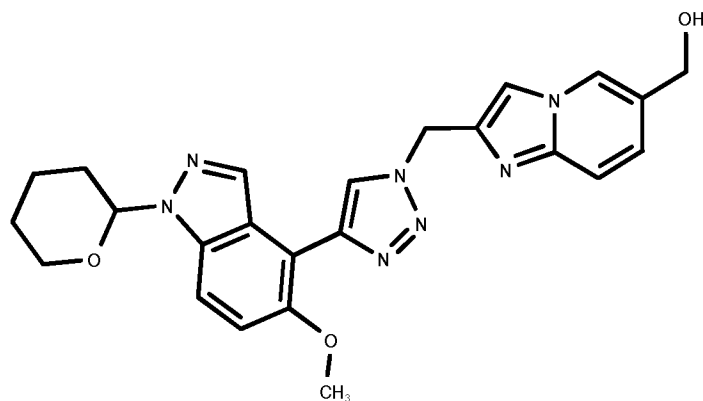
[00652] **Step 1:** 4-ethynyl-5-methoxy-1-(oxan-2-yl)-1H-indazole



[00653] Prepared in a similar manner to **Intermediate 24** from commercial 4-bromo-5-methoxy-1H-indazole to give the title compound (296 mg, 34%) as a brown oil.

Method B: LC-MS (electrospray): m/z = 257.3 (M+H)⁺, RT = 1.62 min

[00654] Step 2: [2-({4-[5-methoxy-1-(oxan-2-yl)-1H-indazol-4-yl]-1H-1,2,3-triazol-1-yl)methyl}imidazo[1,2-a]pyridin-6-yl)methanol



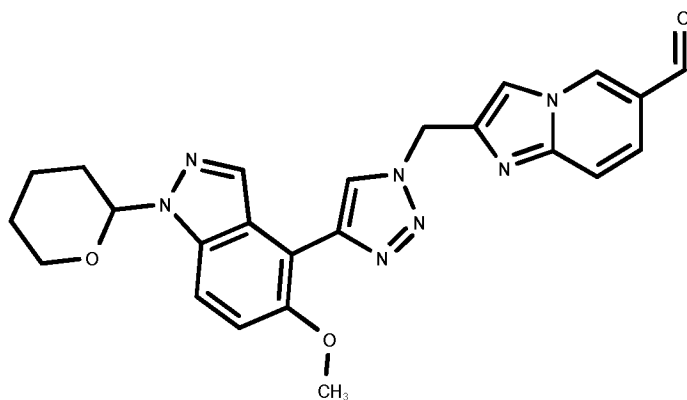
[00655] Prepared using 4-ethynyl-5-methoxy-1-(oxan-2-yl)-1H-indazole and

5 **Intermediate 34 Step 3** using the method described in **Intermediate 34 Step 4** to give the title compound (264 mg, 45%) as an off white solid.

Method F: LC-MS (electrospray): m/z = 460.4 (M+H)⁺, RT = 0.48 min

[00656] Step 3: 2-({4-[5-methoxy-1-(oxan-2-yl)-1H-indazol-4-yl]-1H-1,2,3-triazol-1-yl)methyl}imidazo[1,2-a]pyridine-6-carbaldehyde

10

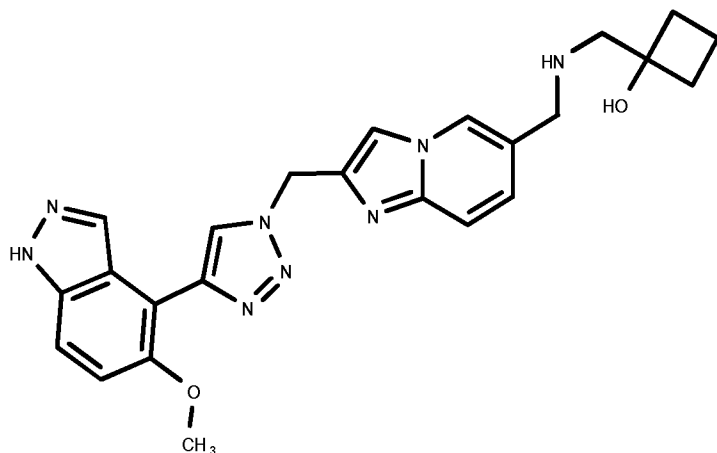


[00657] [2-[[4-(5-methoxy-1-tetrahydropyran-2-yl)indazol-4-yl]triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methanol (264mg, 0.57mmol) and MnO₂ (499mg, 5.75mmol) were combined in DCE (10ml) and the mixture heated at reflux for an hour.

15 **[00658]** The reaction mixture was cooled to RT and filtered through Celite. The residue was rinsed with MeOH and 3:1 chloroform/isopropanol and the combined filtrates were evaporated under vacuum to afford 265mg (80% yield, 79% purity) of the title compound as a grey solid.

[00659] Method F: LC-MS (electrospray): m/z = 458.4 (M+H)⁺, RT = 0.52 min

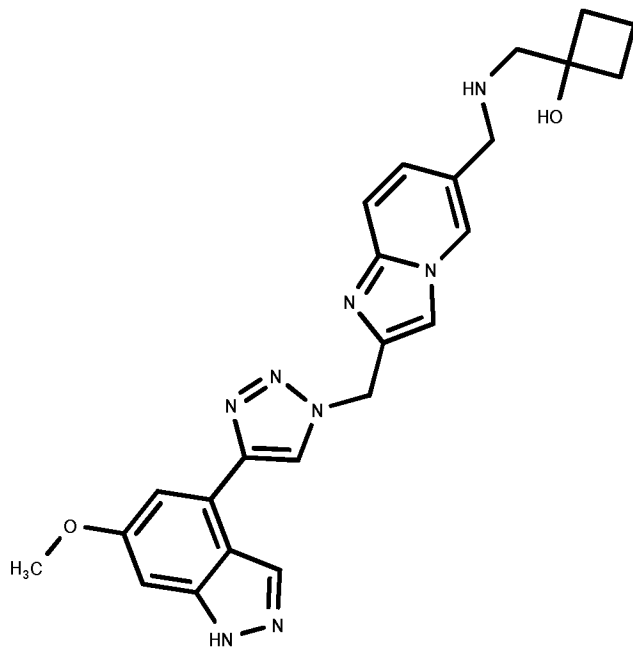
[00660] **Step 4:** 1-[[[2-[[4-(5-methoxy-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol



[00661] The title compound was prepared in a similar fashion to **Compound 252** and purified by phase chromatography (method B) to give (23 mg, 30%) as a white solid.

Method D: LC-MS (electrospray): m/z = 459.3 ($M+H$)⁺, RT = 2.97 min

[00662] **Compound 269:** 1-[[[2-[[4-(6-methoxy-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol



10 [00663] 1-[[[2-[[4-(6-bromo-1-tetrahydropyran-2-yl-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol (**Compound 267 Step 1**) (400mg, 0.68mmol), tBuBrettPhos Pd G3 (58mg, 0.07mmol) and NaOtBu (78mg, 0.81mmol) were combined in 1,4-Dioxane (15ml) and the mixture sparged with nitrogen for

5mins. Anhydrous methanol- (0.3ml, 7.41mmol) was added and the mixture further sparged briefly and the mixture was heated at 100°C for 2 hours.

[00664] The reaction mixture was cooled to room temperature and left standing overnight.

- 5 [00665] The reaction mixture was concentrated under vacuum. The residue was redissolved in methanol (10ml), treated with HCl in Dioxane (4M, 10ml) and heated at 50°C for an hour.

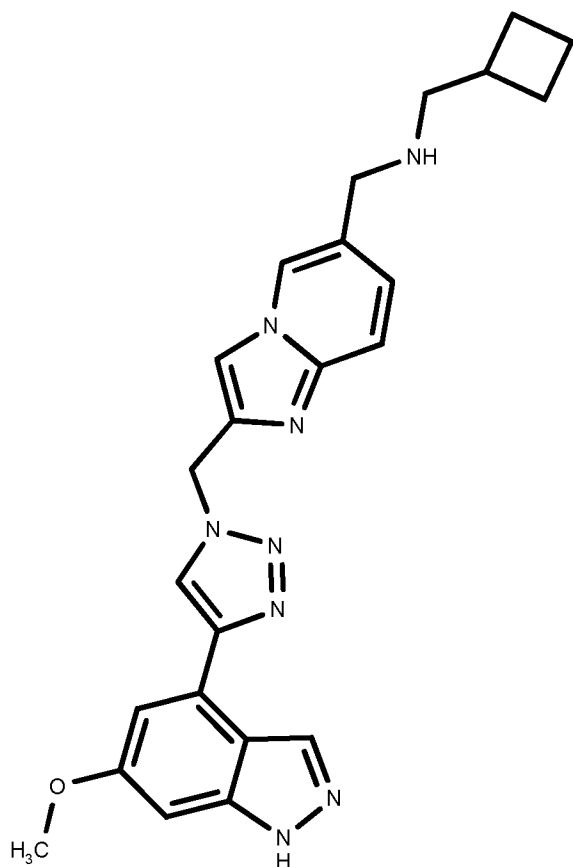
- 10 [00666] The reaction mixture was cooled to RT and evaporated under vacuum. The residue was purified by ion exchange (SCX-2 (10g) washing with DCM and MeOH. The system was eluted with ammonia (7N in MeOH) and the basic eluent evaporated under vacuum.

- 15 [00667] The residue was purified by basic reverse phase chromatography and the product-containing fractions combined and evaporated under vacuum. The residue was triturated with MeOH/Et₂O and the solids collected by filtration to afford the title compound (87mg, 28%) as an off-white solid

Method C: LC-MS (electrospray): m/z = 459.4 (M+H)⁺, RT = 2.10 min

[00668] The filtrates were evaporated under vacuum to afford a second crop of desired product (72mg) as pale yellow solid which was further purified by preparative HPLC (method B) to afford further title compound (50mg, 16%) as an off-white solid.

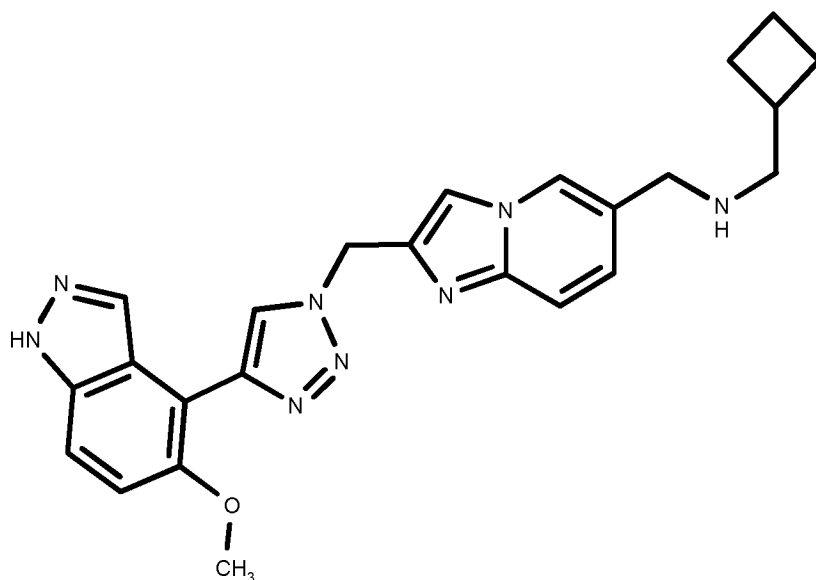
- 20 [00669] **Compound 270:** N-(cyclobutylmethyl)-1-[2-[[4-(6-methoxy-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



[00670] The title compound was prepared in a similar manner to **Compound 269** from
 {[2-({4-[6-bromo-1-(oxan-2-yl)-1H-indazol-4-yl]-1H-1,2,3-triazol-1-yl}methyl)imidazo[1,2-
 a]pyridin-6-yl]methyl}(cyclobutylmethyl)amine (**Compound 266 step 1**) to give (7 mg, 30%)
 5 as a white solid.

Method D: LC-MS (electrospray): m/z = 443.3 (M+H)⁺, RT = 3.55 min

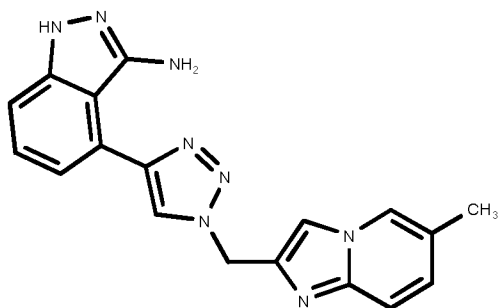
[00671] **Compound 271**: N-(cyclobutylmethyl)-1-[2-[[4-(5-methoxy-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



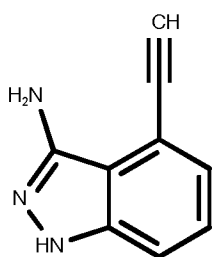
[00672] The title compound was prepared using the intermediate from **Compound 268 Step 3** in a similar manner to **Compound 252** and purified by basic reverse phase chromatography to give (88 mg, 68%) as a pale yellow solid.

5 Method D: LC-MS (electrospray): m/z = 443.3 ($M+H$)⁺, RT = 3.55 min

[00673] **Compound 272**: 4-[1-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]triazol-4-yl]-1H-indazol-3-amine



[00674] **Step 1**: 4-ethynyl-1H-indazol-3-amine

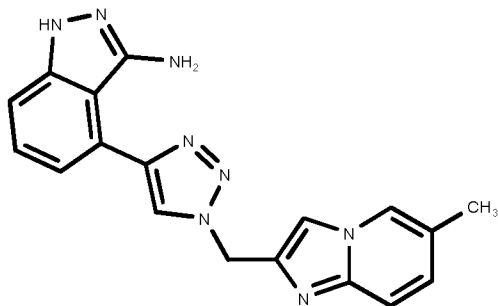


10

[00675] The title compound was prepared in a similar fashion **Intermediate 24** starting from 4-iodo-1H-indazol-3-amine to give (92 mg, 31%) as a pale brown solid.

Method B: LC-MS (electrospray): m/z = 158.2 (M+H)⁺, RT = 1.23 min

[00676] **Step 2:** 4-[1-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]triazol-4-yl]-1H-indazol-3-amine



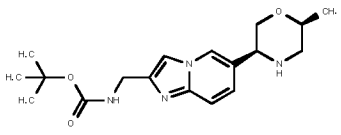
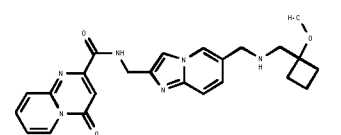
- 5 **[00677]** Prepared using the method described in **Intermediate 34 Step 4** using 4-ethynyl-1H-indazol-3-amine and **Intermediate 23** to give the title compound (38 mg, 41%) as an off white solid.

Method E: LC-MS (electrospray): m/z = 345.2 (M+H)⁺, RT = 1.10 min

- 10 The intermediates in **Table 14** were prepared from commercial reagents and **Intermediate 25 Step 2** in the same manner as **Intermediate 48**.

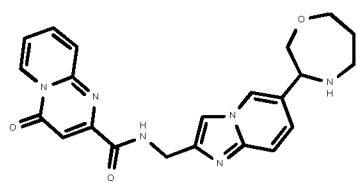
Table 14

Intermediate	Name	Structure	LCMS method	LCMS Retention time	Mass ion
50	tert-butyl N-[[6-(1,4-oxazepan-3-yl)imidazo[1,2-a]pyridin-2-yl]methyl]carbamate		C	2.18	347.3

62	tert-butyl N-[[6-[rac-(3S,6S)-6-methylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate		C	2.23	347.3
63	tert-butyl N-[[6-(7-bromo-9-methoxy-2,3,4,5-tetrahydro-1,4-benzoxazepin-3-yl)imidazo[1,2-a]pyridin-2-yl]methyl]carbamate		C	3.26	503.2/505.2

The Examples in **Table 15** were prepared from **Intermediate 4** and the appropriate intermediate from Table 15 in the same manner as **Compound 233**

Table 15

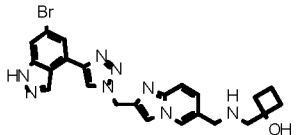
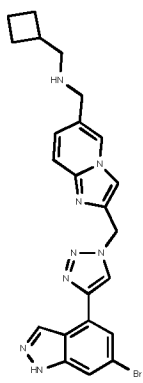
Example	Name	Structure	LCMS method	LCMS Retention time	Mass ion
274	: N-[[6-(1,4-oxazepan-3-yl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.73	429.2

331	N-[[6-(6-methylmorpholin-3-yl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		C	1.77	419.3
332	N-[[6-(7-bromo-9-methoxy-2,3,4,5-tetrahydro-1,4-benzoxazepin-3-yl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide		C	2.78	575.2/ 577.1

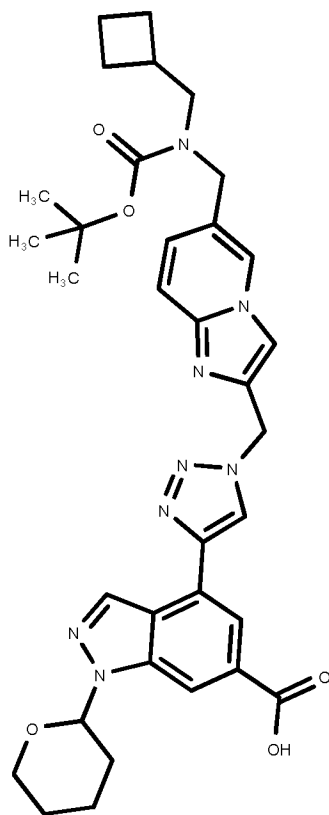
The compounds in Table 16 were prepared from **Intermediate 35** in a similar manner to **Compound 252**.

Table 16

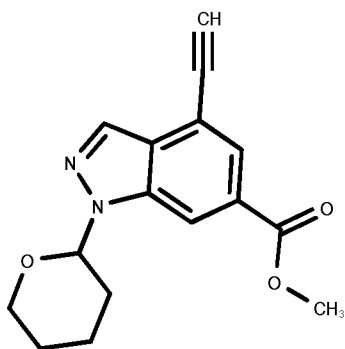
Example No	Name	Structure	LCMS method	LCMS Retention time	Mass ion
294	1-[[[2-[[4-(6-bromo-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclohexanol		C	2.83	535.2/ 537.2

295	1-[[[2-[[4-(6-bromo-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol		C	2.42	507.3/ 509.3
296	1-[2-[[4-(6-bromo-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]-N-(cyclobutylmethyl)methanamine		D	3.82	491.2/ 493.2

[00678] Intermediate 51: 4-[1-[[6-[[tert-butoxycarbonyl(cyclobutylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1-tetrahydropyran-2-yl-indazole-6-carboxylic acid



[00679] Step 1:



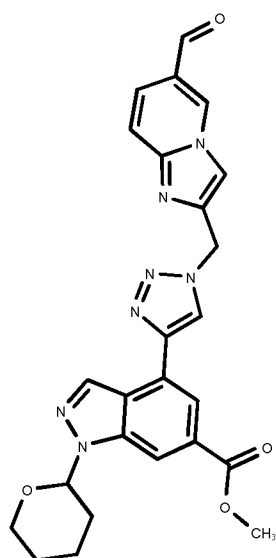
[00680] Step 1: methyl 4-ethynyl-1-(oxan-2-yl)-1H-indazole-6-carboxylate

[00681] The title compound was prepared from methyl 4-bromo-1H-indazole-6-

5 carboxylate in the same manner as **intermediate 24** to give (712 mg, 57%) as a brown solid.

[00682] Method A: LC-MS (electrospray): m/z = 285.05 (M+H)⁺, RT = 1.27 min

[00683] Step 2: methyl 4-[1-({6-formylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-1,2,3-triazol-4-yl]-1-(oxan-2-yl)-1H-indazole-6-carboxylate

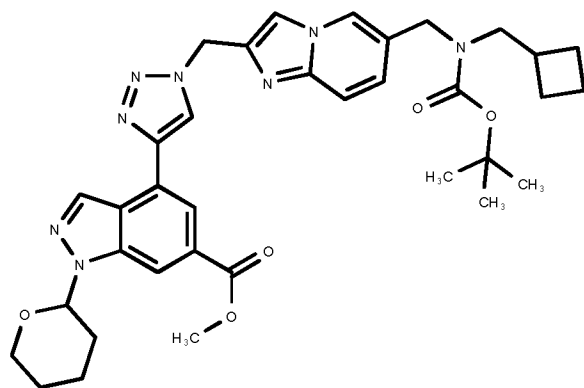


10 [00684] Prepared from **intermediate 51 step 1** using the procedure described in **Intermediate 34** to provide the title compound (867 mg, 62%) as a pale brown solid.

Method B: LC-MS (electrospray): m/z = 486.3 (M+H)⁺, RT = 1.50 min

[00685] Step 3: methyl 4-[1-[[6-[[tert-butoxycarbonyl(cyclobutylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1-tetrahydropyran-2-yl-indazole-6-carboxylate

15



[00686] Methyl 4-[1-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]triazol-4-yl]-1-tetrahydropyran-2-yl-indazole-6-carboxylate (860mg, 1.77mmol) and 1-cyclobutylmethanamine (302mg, 3.54mmol) were combined in 1,1,1,3,3,3-Hexafluoro-2-propanol (8ml) and the mixture stirred at room temperature for 30 minutes before further 1-cyclobutylmethanamine (302mg, 3.54mmol) added and the stir was continued for 1.5 hours.

[00687] Sodium borohydride (536mg, 1.42mmol) was added along with with a few drops MeOH - gas evolution - and the mixture stirred briefly at room temperature.

[00688] The reaction mixture evaporated under vacuum and the residue was suspended in NaHCO₃ (sat, 50ml) and extracted with chloroform/isopropanol (3:1, 3 x 80ml). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum.

[00689] The residue was dissolved in MeOH (20ml) and treated with Boc₂O (773mg, 3.54mmol) and the mixture stirred at room temperature for 30 minutes before further Boc₂O (773mg, 3.54mmol) added and the mixture stirred for 16 hours.

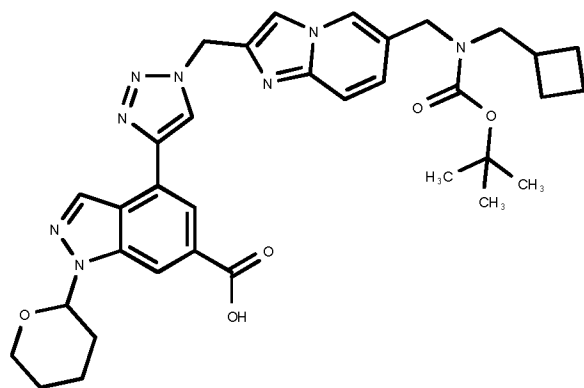
[00690] Further Boc₂O (773mg, 3.54mmol) added and the stir was continued for 2 hours.

[00691] The reaction mixture was evaporated under vacuum and the residue was dissolved in EtOAc (80ml), washed with NaHCO₃ (sat, 2 x 50ml) and brine (50ml), and the organic layer dried over sodium sulfate and evaporated under vacuum.

[00692] The residue was purified by flushing through a short pad of silica, eluting with 0-100% EtOAc/heptane [DP elutes at ~80%] to afford the title compound (360mg, 26%) as a pale brown solid.

Method B: LC-MS (electrospray): m/z = 655.5 (M+H)⁺, RT = 2.02 min

[00693] **Step 4:** 4-[1-[[6-[[tert-butoxycarbonyl(cyclobutylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1-tetrahydropyran-2-yl-indazole-6-carboxylic acid

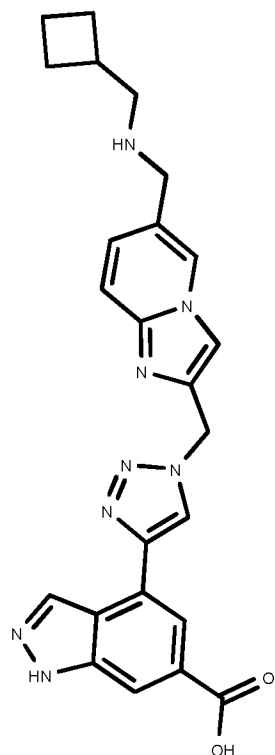


[00694] Methyl 4-[1-[[6-[[tert-butoxycarbonyl(cyclobutylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1-tetrahydropyran-2-yl-indazole-6-carboxylate (360mg, 0.55mmol) and lithium hydroxide (120mg, 5.01mmol) were combined in THF (10ml) and Water (5ml) and the mixture stirred was at room temperature for 18 hours.

[00695] The reaction mixture was concentrated under vacuum, diluted with water (15ml) and acidified with HCl (1M). The mixture was extracted with chloroform/isopropanol (3:13 x 40ml) and the combined organic extracts dried over sodium sulfate and evaporated under vacuum to afford the title compound (279mg, 72%) as a pale brown solid.

[00696] Method B: LC-MS (electrospray): m/z = 641.6 (M+H)⁺, RT = 1.27 min

[00697] **Compound 297:** 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazole-6-carboxylic acid



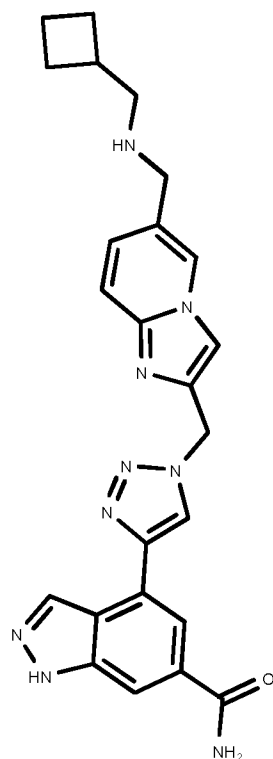
[00698] 4-[1-[[6-[[tert-butoxycarbonyl(cyclobutylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1-tetrahydropyran-2-yl-indazole-6-carboxylic acid

Intermediate 51 (50mg, 0.08mmol) was suspended in methanol (1ml) and HCl (4M in dioxane, 1ml, 4 mmol) was added and the mixture was incubated at room temperature for two hours.

[00699] The reaction mixture was concentrated under vacuum and the residue was purified by basic preparative HPLC (method B) to afford the title compound (18mg, 51%) as a pale yellow solid.

[00700] Method D: LC-MS (electrospray): m/z = 457.3 (M+H)⁺, RT = 2.26 min

[00701] **Compound 298:** 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazole-6-carboxamide



[00702] 4-[1-[[6-[[tert-butoxycarbonyl(cyclobutylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1-tetrahydropyran-2-yl-indazole-6-carboxylic acid

Intermediate 51 (70mg, 0.099mmol) and triethylamine (42μl, 0.298mmol) were combined in THF-Anhydrous (5ml) and isobutyl chloroformate (19μl, 0.149mmol) was added. The resultant solution was stirred at RT for 5mins, then ammonia (28% aqueous, 0.2ml, 1.4mmol) was added, and the mixture further stirred at room temperature for 15mins.

[00703] The reaction mixture was quenched with NaHCO₃ (sat, 30ml) and extracted with chloroform/isopropanol (3:1, 3 x 30ml). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum.

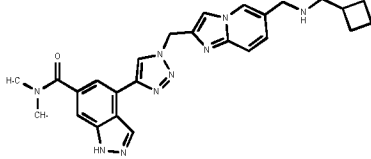
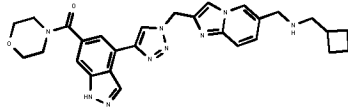
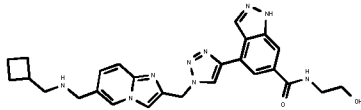
[00704] The residue was suspended in methanol (2ml) and treated with HCl (4M in Dioxane, 2ml). The mixture was incubated at room temperature for two hours.

[00705] The reaction mixture was evaporated under vacuum. The residue was purified by preparative HPLC (method B) to afford the title compound (19mg, 42%) as a pale brown solid.

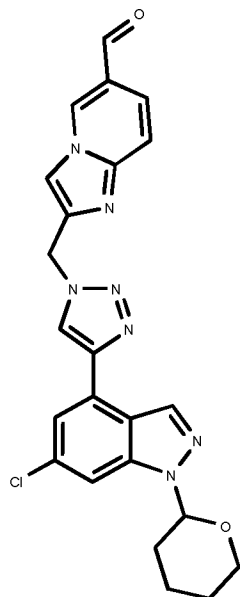
[00706] Method D: LC-MS (electrospray): m/z = 456.3 (M+H)⁺, RT = 3.09 min

[00707] The Examples in Table 17 were prepared in a similar manner **Compound 298** using the appropriate amine.

Table 17

Example No	Name	Structure	LCMS method	LCMS Retention time	Mass ion
299	4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-N,N-dimethyl-1H-indazole-6-carboxamide		C	2.42	484.4
300	[4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazol-6-yl]-morpholinomethanone		C	2.41	526.5
301	4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-N-(2-hydroxyethyl)-1H-indazole-6-carboxamide		C	2.24	500.6

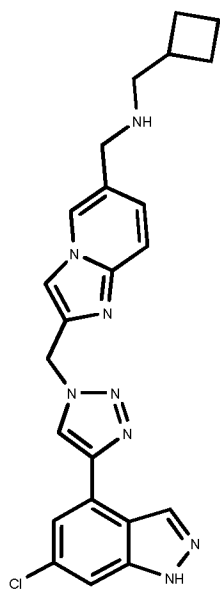
[00708] Intermediate 52: 2-[[4-(6-chloro-1-tetrahydropyran-2-yl-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carbaldehyde



[00709] The title compound was prepared from 6-chloro-4-iodo-1H-indazole in a similar fashion to **Intermediate 34** giving (370 mg, 36%) as a beige solid.

[00710] Method B: LC-MS (electrospray): m/z = 462.3 (M+H)⁺, RT = 1.58 min

- 5 **[00711]** **Example 302:** 1-[2-[[4-(6-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]-N-(cyclobutylmethyl)methanamine



[00712] The title compound was prepared from **intermediate 52** using the procedure described for **Compound 250** to give (41 mg, 34%) as an off-white solid.

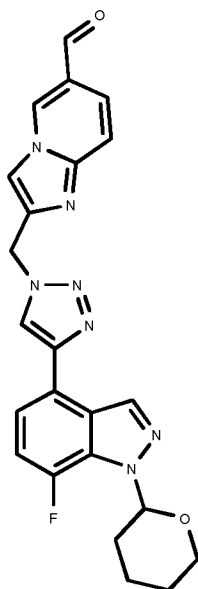
- 10 **[00713]** Method D: LC-MS (electrospray): m/z = 447.3 (M+H)⁺, RT = 3.86 min

The compounds in **Table 18** were prepared from **Intermediate 52** using the procedure described for **Example 302**.

Table 18

Example No	Name	Structure	LCMS method	LCMS Retention time	Mass ion
303	1-[[[2-[[4-(6-chloro-1H-indazol-4-yl)triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methylamino]methyl]cyclobutanol		C	2.40	463.3
304	N-[[2-[[4-(6-chloro-1H-indazol-4-yl)triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]-2,2-dimethylpropan-1-amine		C	3.24	449.4

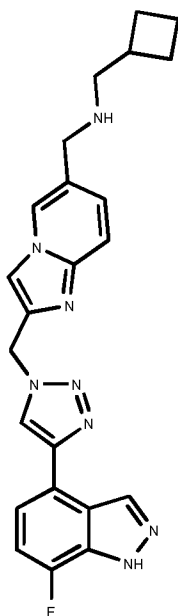
- 5 **[00714]** **Intermediate 53:** 2-({4-[6-chloro-1-(oxan-2-yl)-1H-indazol-4-yl]-1H-1,2,3-triazol-1-yl)methyl)imidazo[1,2-a]pyridine-6-carbaldehyde



[00715] The title compound was prepared from 4-bromo-7-fluoro-1H-indazole in a similar fashion to **Intermediate 34** giving (739 mg, 95%) as a pale brown solid.

[00716] Method B: LC-MS (electrospray): m/z = 446.2 (M+H)⁺, RT = 1.50 min

- 5 **[00717]** **Example 305:** N-(cyclobutylmethyl)-1-[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



[00718] The title compound was prepared from **intermediate 53** using the procedure described for **Compound 250** to give (15 mg, 23%) as a white solid.

- 10 **[00719]** Method D: LC-MS (electrospray): m/z = 431.3 (M+H)⁺, RT = 3.55 min

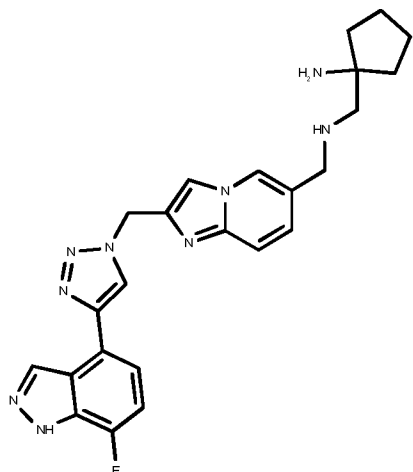
[00720] The compounds in **Table 19** were prepared from **Intermediate 53** using the procedure described for **Example 305**.

Table 19

Exempl e No	Name	Structure	LCMS metho d	LCMS Retentio n time	Mass ion
306	1-[[[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclohexanol		D	3.32	475. 3
307	N-(cyclohexylmethyl)-1-[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine		D	4.03	459. 3
308	1-[[[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol		D	3.00	447. 2

5

[00721] **Example 309:** 1-[[[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclopentanamine



[00722] 2-[[4-(7-fluoro-1-tetrahydropyran-2-yl)indazol-4-yl]triazol-1-yl)methyl]imidazo[1,2-a]pyridine-6-carbaldehyde **Intermediate 53** (90mg, 0.19mmol) and tert-butyl [1-(aminomethyl)cyclopentyl]carbamate (81mg, 0.38mmol) were combined in 1,1,1,3,3,3-Hexafluoro-2-propanol (3ml) and the mixture stirred at room temperature for an hour.

[00723] NaBH₄ (50mg, 1.32mmol) was added along with a few drop MeOH - gas evolution - and the mixture stirred briefly at room temperature

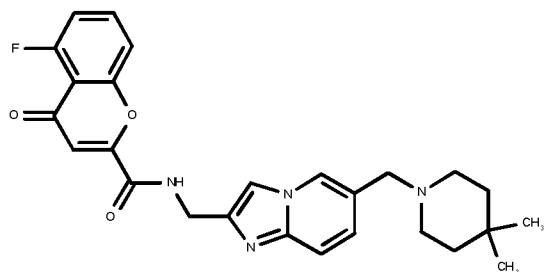
[00724] The reaction mixture was quenched with MeOH (30ml) - gas evolution - and evaporated under vacuum. The residue was suspended in NaHCO₃ (sat, 30ml) and extracted with chloroform/isopropanol (3:1, 3 x 30ml). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum.

[00725] The residue was purified by chromatography on SiO₂ (28 g kp-NH, eluting with EtOAc/heptane 0-100% followed by MeOH/EtOAc 0-20%) to afford the title compound (70mg (54%) as a colourless residue which was dissolved in methanol (3ml) and treated with HCl (4M in dioxane, 2ml) and incubated at room temperature for 16 hours.

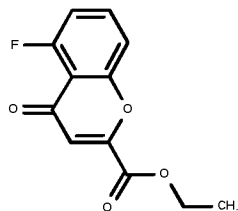
[00726] The reaction mixture was evaporated under vacuum. The residue was purified by ion exchange (SCX-2 5g) washed with DCM and MeOH and eluted with NH₃/MeOH (7N). The eluent was evaporated under vacuum and the residue dried to afford the title compound (25mg, 50%) as a pale yellow solid.

Method E: LC-MS (electrospray): m/z = 460.2 (M+H)⁺, RT = 0.96 min

[00727] **Example 310:** N-[[6-[(4,4-dimethyl-1-piperidyl)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-5-fluoro-4-oxo-chromene-2-carboxamide



[00728] Step 1: ethyl 5-fluoro-4-oxo-chromene-2-carboxylate



[00729] A solution of 1-(2-fluoro-6-hydroxyphenyl)ethanone (700 mg, 4.54

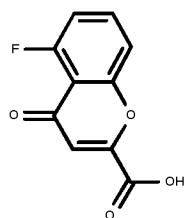
5 mmol) and diethyl oxalate (1.4 mL, 10.4 mmol) in ethanol (23 ml) was treated with NaOEt (21% wt solution, 7.3 mL, 19.5 mmol) which gave a dark brown solution. The mixture was heated at reflux for 30 minutes during which time a Yellow precipitate formed.

[00730] The mixture was cooled in ice and acidified (c.HCl) during which the yellow precipitate dissolved and a white precipitate formed. The solids were removed by filtration
10 and washed with a little EtOH and the filtrate was evaporated under vacuum.

[00731] The residue was dissolved in EtOAc (20 mL), washed with brine/water (1:1, 20ml). The aqueous phase was extracted with EtOAc (2 x 20ml). The combined organics were dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on SiO₂ (Biotage, 50 g kp-Sil, eluting with EtOAc/heptane 0-50%) to afford
15 a title compound (600 mg, 56%) as an off white solid.

Method B: LC-MS (electrospray): m/z = 237.1 (M+H)⁺, RT = 1.42 min

[00732] Step 2: 5-fluoro-4-oxo-chromene-2-carboxylic acid



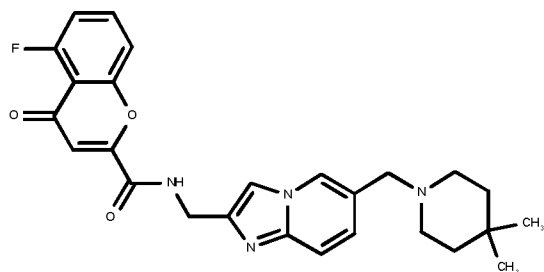
[00733] To a solution of ethyl 5-fluoro-4-oxo-chromene-2-carboxylate (600 mg, 2.54 mmol) in acetic acid (8 mL) was added hydrogen chloride (6M, 4.0 mL, 24.0 mmol) at room temperature and the reaction was stirred at 90 °C for 16 hours.

[00734] The mixture was cooled to room temperature and evaporated under vacuum.

- 5 The residue was suspended in CH₃CN-water (1:1, 5 mL) and the solid was collected by filtration, washed with a little water and CH₃CN, and dried under vacuum to provide the title compound (520 mg, 98%) as a beige solid.

Method E: LC-MS (electrospray): m/z = 209.0 (M+H)⁺, RT = 1.50 min

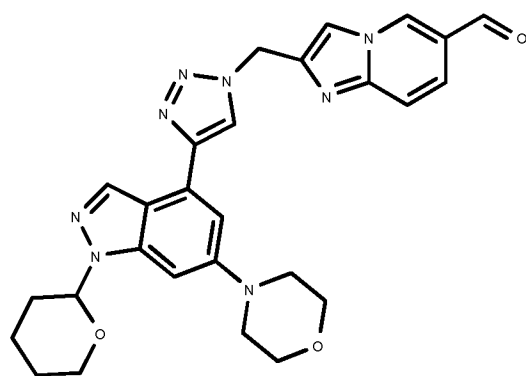
- [00735] **Step 3:** N-[[6-[(4,4-dimethyl-1-piperidyl)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-5-fluoro-4-oxo-chromene-2-carboxamide
- 10



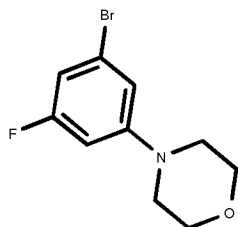
- [00736] The title compound was prepared by coupling 5-fluoro-4-oxo-chromene-2-carboxylic acid with **Intermediate 43** using the procedure described in **Example 1** with DMF as solvent to give (4.6 mg, 2%) as an off-white solid.
- 15

Method D: LC-MS (electrospray): m/z = 463.3 (M+H)⁺, RT = 4.03 min

- [00737] **Intermediate 54:** 2-({4-[6-chloro-1-(oxan-2-yl)-1H-indazol-4-yl]-1H-1,2,3-triazol-1-yl}methyl)imidazo[1,2-a]pyridine-6-carbaldehyde



- 20 [00738] **Step 1:** 4-(3-bromo-5-fluoro-phenyl)morpholine



[00739] A solution of 3-bromo-5-fluoroaniline (1.00 g, 5.26 mmol), 1-bromo-2-(2-bromoethoxy)ethane (0.79 mL, 6.32 mmol) and N-ethyl-N-isopropyl-propan-2-amine (2.8 mL, 15.8 mmol) in DMF (20 mL) were stirred at 90 °C deg C for 16 hours.

5 **[00740]** More 1-bromo-2-(2-bromoethoxy)ethane (0.40 mL, 3.16 mmol) was added and mixture was heated at 110 °C for 4 hours.

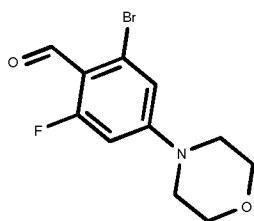
[00741] The reaction was cooled to room temperature, diluted with ethyl acetate (100 mL) and washed with water (1 x 50 mL) followed by brine (5 x 50 mL). The organic layer was dried over sodium sulfate, concentrated *in vacuo* to give the crude material as a black oil.

[00742] The residue was purified by chromatography on SiO₂ (Biotage KP-NH 30 g, eluting with EtOAc:Heptane 5 to 50 %) gave a mixture of desired product and starting material as an orange oil which crystallised upon standing. Further chromatography on SiO₂ (Biotage KP-Sil 25 g eluting with EtOAc:Heptane, 0 to 30 %) which gave the title product

15 (740 mg, 50%) as a pale yellow solid.

Method B: LC-MS (electrospray): m/z = 260.4/262.4 (M+H)⁺, RT = 1.74 min

[00743] **Step 2:** 2-bromo-6-fluoro-4-morpholino-benzaldehyde

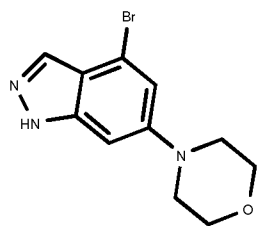


[00744] A cold (0 °C) solution of 4-(3-bromo-5-fluoro-phenyl)morpholine (300 mg, 1.15 mmol) in DMF (anhydrous, 5 mL) was treated dropwise with phosphoryl trichloride (0.13 mL, 1.27 mmol). Once the addition was complete the mixture was warmed 60 °C and stirred for 16 hours.

[00745] The reaction was quenched via dropwise addition of the reaction mixture into an ice cold saturated solution of sodium bicarbonate (10 mL). The aqueous was extracted

25 with ethyl acetate (3 x 10 mL) and the combined organics were washed with brine (3 x 10 mL) dried over sodium sulfate and concentrated *in vacuo* to give the title compound (268 mg, 65%) as a pale yellow solid.

Method A: LC-MS (electrospray): m/z = 287.9/289.9 (M+H)⁺, RT = 1.10 min

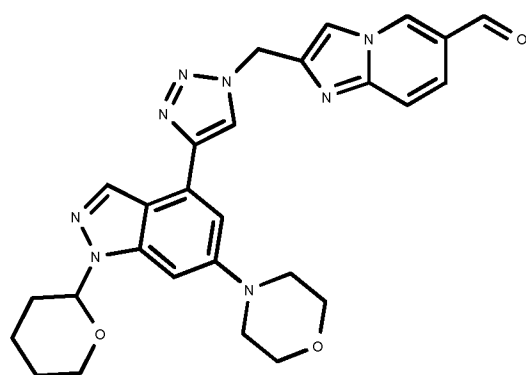
[00746] Step 3: 4-(4-bromo-1H-indazol-6-yl)morpholine

[00747] Hydrazine (55%, 10 mL, 0.132 mol) was added to a solution of 2-bromo-6-fluoro-4-morpholino-benzaldehyde (4.30 g, 12.1 mmol) in 1,4-Dioxane (50 mL) and the reaction was stirred at 100 °C for 16 hours.

[00748] The reaction was cooled to room temperature and evaporated under vacuum. The residue was dissolved in EtOAc (100 mL), washed with water (100 mL) followed by brine (100 mL), dried (Na₂SO₄) and evaporated under reduced pressure to give a pale yellow solid, which was purified by chromatography on SiO₂ (Biotage 25 g eluting by 10-90 % EtOAc in Heptane) to give the title compound (2.90 g, 76%) as a pale yellow solid.

Method B: LC-MS (electrospray): m/z = 282.1/284.1 (M+H)⁺, RT = 1.41 min

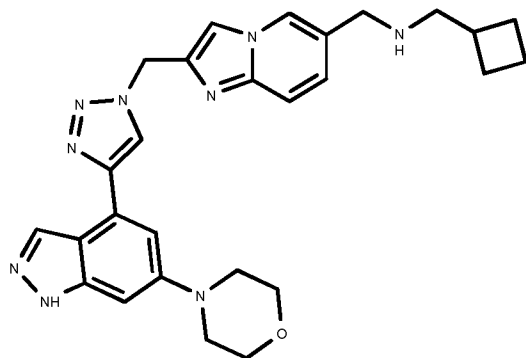
[00749] Step 4: 2-({4-[6-chloro-1-(oxan-2-yl)-1H-indazol-4-yl]-1H-1,2,3-triazol-1-yl}methyl)imidazo[1,2-a]pyridine-6-carbaldehyde



[00750] The title compound was prepared from 4-(4-bromo-1H-indazol-6-yl)morpholine using the procedures described in **Intermediate 24 steps 1, 2 and 3** and **intermediate 34 steps 4 and 5** to give (1.0 g, 83%) as a beige solid.

Method B: LC-MS (electrospray): m/z = 513.3 (M+H)⁺, RT = 1.41 min

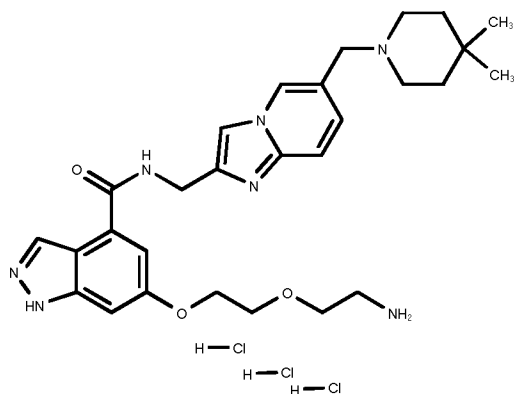
[00751] Example 311: N-(cyclobutylmethyl)-1-[2-[[4-(6-morpholino-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



[00752] The title compound was prepared from **intermediate 53** using the method described for **Compound 250** giving (104 mg, 26%) as a white powder.

5 **Method C:** LC-MS (electrospray): $m/z = 498.4$ ($M+H$)⁺, $RT = 2.56$ min

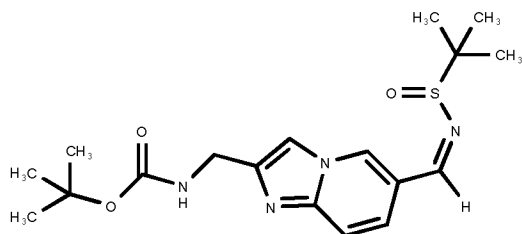
[00753] **Example 312:** 6-[2-(2-aminoethoxy)ethoxy]-N-[[6-[(4,4-dimethyl-1-piperidyl)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-1H-indazole-4-carboxamide trihydrochloride.



10 **[00754]** HCl (4M in dioxane, 3.1mL, 12.4 mmol) was added to tert-butyl N-[2-[2-[4-[[6-[(4,4-dimethyl-1-piperidyl)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamoyl]-1-tetrahydropyran-2-yl-indazol-6-yl]oxyethoxy]ethyl]carbamate (30 mg, 0.0426 mmol) and the mixture was stirred at room temperature for 1 hour and at 50 °C for 1 hour. The solvent was removed under vacuum to give the title compound (20 mg, 72%) as a tan solid.

15 **[00755]** **Method D:** LC-MS (electrospray): $m/z = 520.3$ ($M+H$)⁺, $RT = 4.11$ min

[00756] **Intermediate 55:** tert-butyl N-[[6-[(Z)-tert-butylsulfinyliminomethyl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate

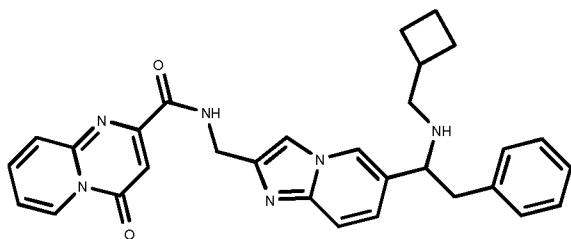


[00757] A solution of tert-butyl N-[(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]carbamate **Intermediate 25 Step 2** (1.00 g, 3.63 mmol) and 2-methylpropane-2-sulfonamide (533 mg, 4.40 mmol) in DCE (Anhydrous, 97 mL), under a nitrogen atmosphere, was treated with CuSO₄ (1.76 g, 10.9 mmol) and the resultant blue solution was heated at reflux for 44 hours and left standing at room temperature for a further 5 days.

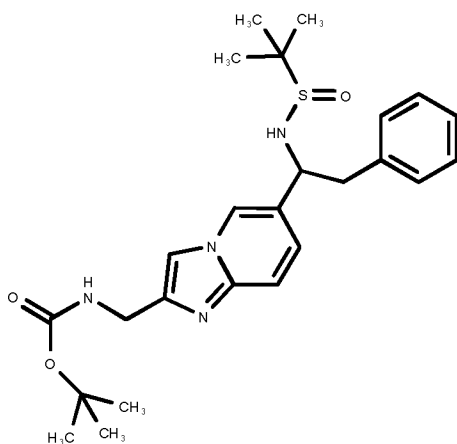
[00758] The dark green suspension was filtered through Celite washing with DCM and the filtrate was concentrated under vacuum and purified by chromatography on SiO₂ [Biotage KPNH 28 g eluting with 50-100% EtOAc/heptane] to give the title compound (725 mg, 53%) as a pale yellow solid.

Method B: LC-MS (electrospray): m/z = 379.3 (M+H)⁺, RT = 1.49 min

[00759] **Example 313:** N-[[6-[1-(cyclobutylmethylamino)-2-phenyl-ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide



[00760] **Step 1:** tert-butyl N-[[6-[1-(tert-butylsulfinylamino)-2-phenyl-ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate

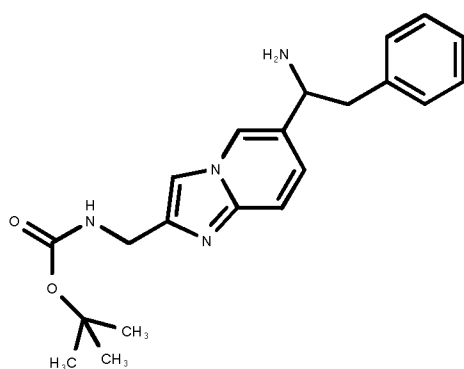


[00761] A solution of benzylmagnesium chloride (1.5M in THF, 969 μ L, 1.45 mmol) was added dropwise over 1 min to a solution of tert-butyl N-[[6-[(E)-tert-butylsulfinyliminomethyl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate **Intermediate 54** (110 mg, 0.291 mmol) in dry DCM (14mL) at room temperature and the solution was stirred for 16 hours. The reaction mixture became turbid upon the addition of the first few drops but became clear after the addition was complete.

[00762] The reaction was quenched by the addition of NH_4Cl (sat) and extracted with DCM (phase sep cartridge). The organics were evaporated under vacuum to a pale gum which was purified by chromatography on SiO_2 [Biotage KPNH 11 g eluting with EtOAc] to give the title compound (2:1 mixture of diastereoisomers, 102 mg, 75%) as a beige foam.

Method B: LC-MS (electrospray): m/z = 471.3 ($\text{M}+\text{H}$)⁺, RT = 1.54 & 1.59 min

[00763] **Step 2:** tert-butyl N-[[6-(1-amino-2-phenyl-ethyl)imidazo[1,2-a]pyridin-2-yl]methyl]carbamate



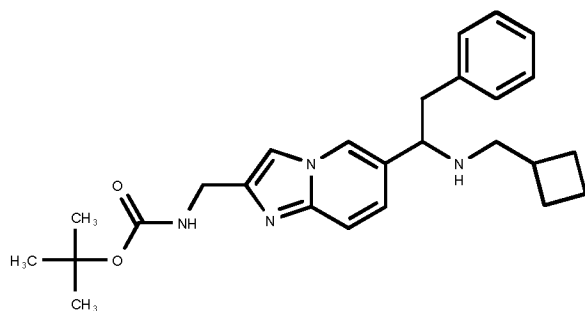
[00764] A solution of tert-butyl N-[[6-[1-(tert-butylsulfinylamino)-2-phenylethyl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate (185 mg, 0.39 mmol) in THF (9.25 mL) and Water (1.85 mL) was treated with molecular iodine (20 mg, 0.08 mmol) and the mixture was warmed at 60 °C for 16 hours.

[00765] The mixture was cooled to room temperature, quenched by the addition of sodium thiosulfate (sat 10 ml) and extracted with DCM (phase sep cartridge). The organics were evaporated under vacuum and purified by chromatography on SiO_2 [Biotage KPNH 11 g eluting with 50 to 100% EtOAc in heptane followed by 0 to 20 % MeOH in DCM]. To give the title compound (30 mg, 7% Yield) as a white powder.

[00766] During the separation a white solid was seen between the layers. The solid was collected by filtration, washed with ether and dried to give the title compound (40 mg, 28%) as a white powder.

Method B: LC-MS (electrospray): $m/z = 367.3$ ($M+H$)⁺, RT = 1.46 min

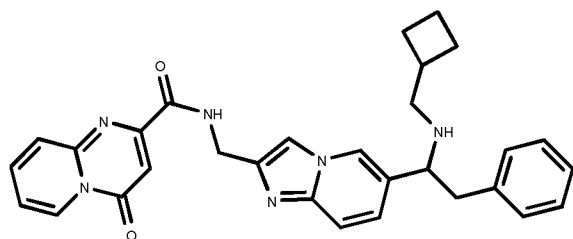
[00767] **Step 3:** tert-butyl N-[[6-[1-(cyclobutylmethylamino)-2-phenyl-ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate



- 5 **[00768]** The title compound was prepared from tert-butyl N-[[6-(1-amino-2-phenyl-ethyl)imidazo[1,2-a]pyridin-2-yl]methyl]carbamate using the procedure described in **Compound 250** to give (21 mg, 22%) as a white powder along with the doubly alkylated product (30 mg, 31%).

Method B: LC-MS (electrospray): $m/z = 435.4$ ($M+H$)⁺, RT = 1.78 min

- 10 **[00769]** **Step 4:** N-[[6-[1-(cyclobutylmethylamino)-2-phenyl-ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide



- 15 **[00770]** tert-butyl N-[[6-[1-(cyclobutylmethylamino)-2-phenyl-ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate (30 mg, 0.07 mmol) was dissolved in hydrogen chloride (4M in dioxane, 0.17 mL, 0.7 mmol) and stirred at room temperature for 1 hour.

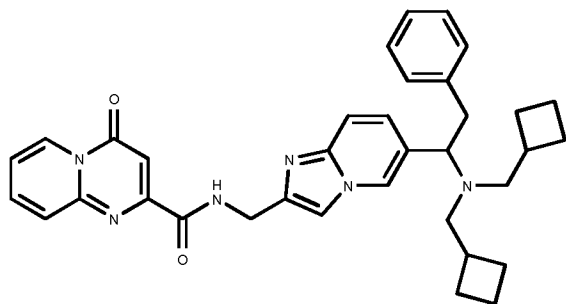
[00771] The solvent was removed in vacuo and the resulting crude material dissolved in DMF (1 mL), N-ethyl-N-isopropyl-propan-2-amine (0.06 mL, 0.35 mmol) was added and the mixture was stirred at room temperature for 10 minutes.

- 20 **[00772]** In a separate flask tert-butyl N-[[6-[1-(cyclobutylmethylamino)-2-phenyl-ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate (30 mg, 0.07 mmol), HATU (39 mg, 0.1 mmol) and N-ethyl-N-isopropyl-propan-2-amine (0.06 mL, 0.35 mmol) in DMF (1 mL) were combined at room temperature and stirred for 5 minutes before the amine solution was added and the mixture was stirred at room temperature for 2 hours.

[00773] Water (2 mL) and IPA/CHCl₃ (1/4, 5 mL) were added and the layers separated (phase sep cartridge). The organic filtrate was concentrated in vacuo to give a brown oil. Purification by reverse phase chromatography (Biotage 12 g, water/MeCN + 0.1% NH₃, 10 to 90 %) and subsequent freeze-drying overnight gave the title compound (8.0 mg, 23%) a pale yellow solid.

Method D: LC-MS (electrospray): m/z = 507.3 (M+H)⁺, RT = 4.13 min

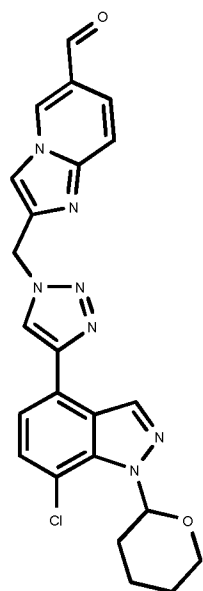
[00774] **Example 314:**



[00775] The title compound was prepared from the bis alkylated product isolated in **Example 313 Step 3** in the same manner as **Example 313 Step 4** to give (10 mg, 25%) as a white powder.

Method C: LC-MS (electrospray): m/z = 575.4 (M+H)⁺, RT = 4.86 min

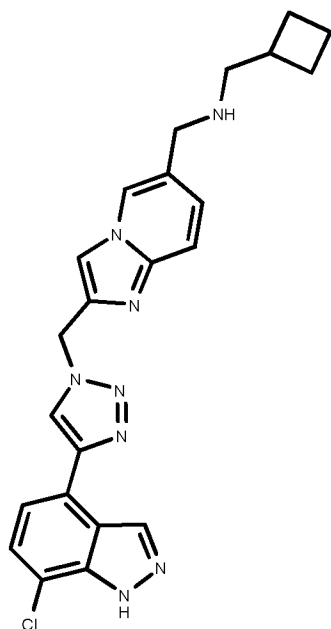
[00776] **Intermediate 56:** 2-({4-[7-chloro-1-(oxan-2-yl)-1H-indazol-4-yl]-1H-1,2,3-triazol-1-yl}methyl)imidazo[1,2-a]pyridine-6-carbaldehyde



[00778] The title compound was prepared from 4-bromo-7-chloro-1H-indazole in a similar fashion to **Intermediate 34** using the oxidation described in **Compound 268 Step 3** for the final step giving (388 mg, 75%) as a grey solid.

Method B: LC-MS (electrospray): m/z = 462.2 (M+H)⁺, RT = 1.54 min

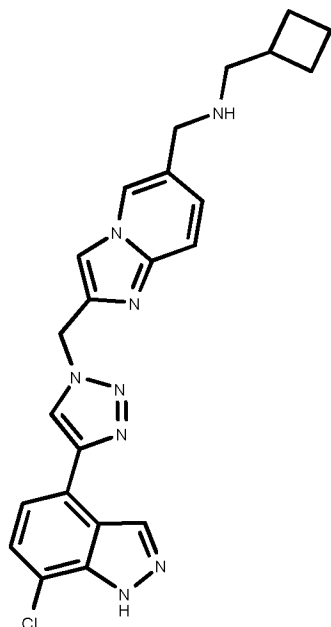
- 5 [00779] **Example 315:** 1-[2-[[4-(7-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]-N-(cyclobutylmethyl)methanamine



- 10 [00780] The title compound was prepared from **Intermediate 56** in a similar manner to **Example 305** to give (58 mg, 40%) as a white solid.

Method E: LC-MS (electrospray): m/z = 447.2 (M+H)⁺, RT = 1.37 min

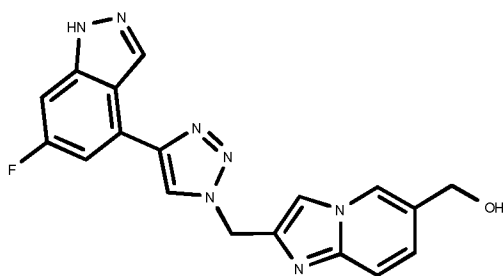
- [00781] **Example 316:** 1-[[[2-[[4-(7-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol



[00782] The title compound was prepared in the same manner as **Example 315** to give (20 mg, 14%) as a white solid.

Method D: LC-MS (electrospray): m/z = 463.2 ($M+H$)⁺, RT = 3.09 min

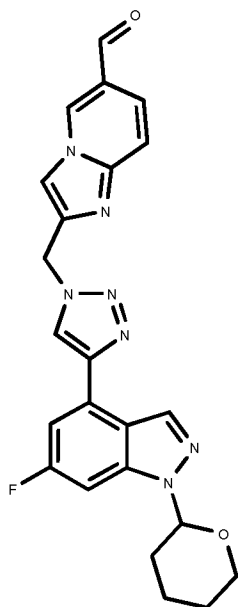
- 5 **[00783]** **Example 317:** [2-[[4-(6-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanol



[00784] The title compound was prepared from 4-bromo-6-fluoro-1H-indazole in a similar fashion to **Compound 253** giving (20 mg, 6%) as a white solid.

- 10 Method D: LC-MS (electrospray): m/z = 364.6 ($M+H$)⁺, RT = 2.71 min

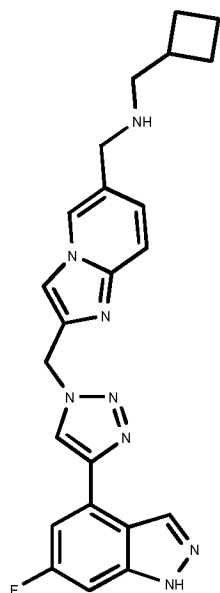
[00785] **Intermediate 57:** 2-({4-[6-fluoro-1-(oxan-2-yl)-1H-indazol-4-yl]-1H-1,2,3-triazol-1-yl}methyl)imidazo[1,2-a]pyridine-6-carbaldehyde



[00786] The title compound was prepared from 4-bromo-6-fluoro-1H-indazole in a similar fashion to **Intermediate 34** giving (472 mg, 96%) as a sandy solid.

Method B: LC-MS (electrospray): $m/z = 446.7$ ($M+H$)⁺, RT = 1.49 min

- 5 **[00787]** **Example 318:** N-(cyclobutylmethyl)-1-[2-[[4-(6-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



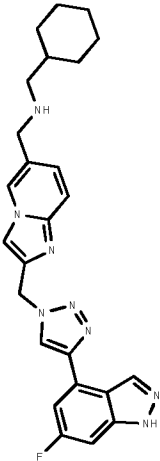
[00788] The title compound was prepared from **Intermediate 57** in a similar fashion to **Compound 250** giving (30 mg, 29%) as an off white solid.

Method C: LC-MS (electrospray): m/z = 431.4 ($M+H$)⁺, RT = 2.79 min

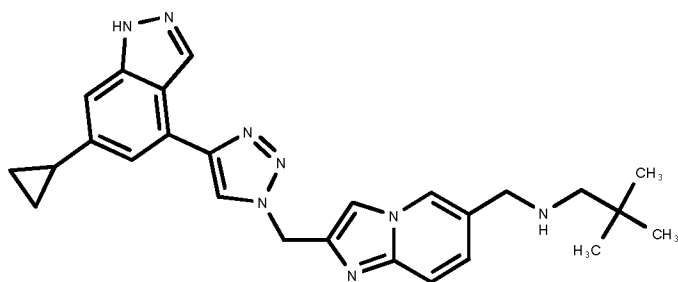
- 5 **[00789]** The compounds in **Table 20** were prepared from **Intermediate 57** using the procedure described for **Example 318**.

[00790] Table 20

Exempl e No	Name	Structure	LCMS metho d	LCMS Retentio n time	Mass ion
319	1-[[[2-[[4-(6-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol		C	2.21	447. 3

320	N-(cyclohexylmethyl)-1-[2-[[4-(6-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine		C	3.23	459.5

[00791] Example 321: N-[[2-[[4-(6-cyclopropyl-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methyl]-2,2-dimethyl-propan-1-amine



[00792] A pressure vial charged with bromo(cyclopropyl)zinc (0.5M in THF, 0.38 mL, 0.188 mmol), THF (0.3 mL) and N-[[2-[[4-(6-bromo-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methyl]-2,2-dimethyl-propan-1-amine (31 mg, 0.0628 mmol) **Compound 229** was degassed with

nitrogen. Tetrakis(triphenylphosphine)palladium(0) (3.6 mg, 3.14 μ mol) was added and the reaction degassed with nitrogen for 2 minutes before the reaction was heated to 50 °C.

[00793] Further . Tetrakis(triphenylphosphine)palladium(0) (3.6 mg, 3.14 μ mol) and bromo(cyclopropyl)zinc (0.5M in THF, 0.38 mL, 0.188 mmol) were added and the reaction degassed for 5 minutes before heating to 65 °C for 2 hours.

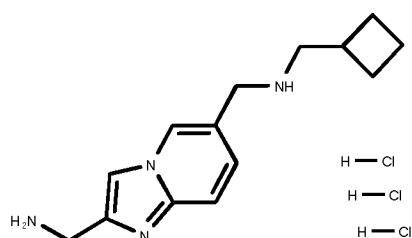
[00794] [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (2.6 mg, 3.14 μ mol) was added and the reaction heated to 70 °C for 18 hours.

[00795] The reaction was cooled to room temperature, filtered through a pad of Celite washing with MeOH (10 mL). The solvent was removed *in vacuo* to give a red/brown oil. The crude mixture was purified by reverse phase chromatography [water/MeCN + 0.1% NH₃, 0 to 100 %] gave partially clean fractions containing product. Concentration of these fractions *in vacuo* gave a yellow residue (5 mg)

[00796] Repurification by reverse phase chromatography [water/MeCN + 0.1% NH₃, 0 to 100 %] followed by freeze drying overnight gave the title compound (1.2 mg, 3.8% Yield) as a white solid.

Method C: LC-MS (electrospray): *m/z* = 455.4 (M+H)⁺, RT = 3.15 min

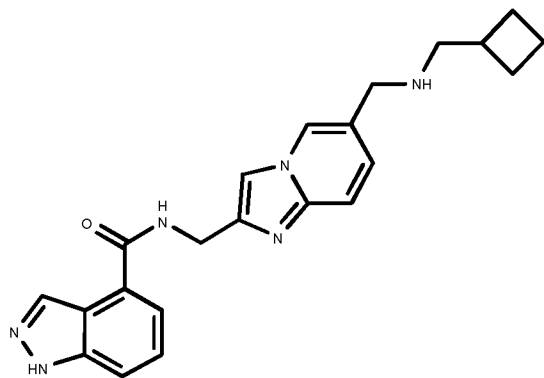
10 [00797] **Intermediate 58:** [6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methanamine trihydrochloride



[00798] The title compound was prepared in a similar fashion to **Intermediate 25** to give (953 mg, 95%) as a pale yellow solid.

15 Method C: LC-MS (electrospray): *m/z* = 245.1 (M+H)⁺, RT = 2.02 min

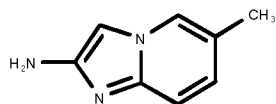
[00799] **Example 322:** N-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-1H-indazole-4-carboxamide



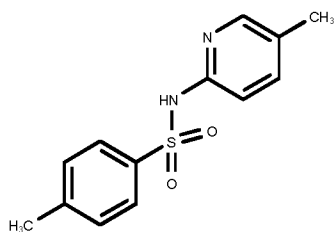
[00800] The title compound was prepared in the same manner as **Example 1** by coupling of 1-tetrahydropyran-2-ylindazole-4-carboxylic acid and **Intermediate 58** followed by deprotection to give (7.8 mg, 10%) as a white powder.

Method C: LC-MS (electrospray): *m/z* = 389.4 (M+H)⁺, RT = 2.38 min

[00801] **Intermediate 59:** 6-methylimidazo[1,2-a]pyridin-2-amine



[00802] **Step 1:** 4-methyl-N-(5-methyl-2-pyridyl)benzenesulfonamide

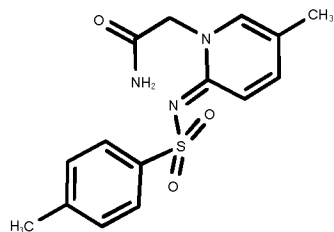


[00803] A solution of 5-methylpyridin-2-amine (5.00 g, 46.2 mmol) in Pyridine (50 mL) was treated with (p-toluenesulfonyl chloride (11.47 g, 55.5 mmol) and the mixture was stirred at room temperature for 20 hours. The addition caused an orange colouration and a slight exotherm.

[00804] The solvent was removed under vacuum and the residue was triturated with MeOH, the solids were collected by filtration, washed with MeOH and dried under vacuum to provide the title compound (10.9 g, 90%) as a white solid.

Method A: LC-MS (electrospray): m/z = 263.2 ($M+H$)⁺, RT = 0.96 min

[00805] **Step 2:** 2-[5-methyl-2-(4-methylbenzenesulfonamido)-1,2-dihydropyridin-1-yl]acetamide

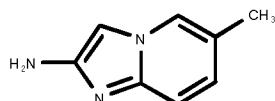


[00806] A suspension of 4-methyl-N-(5-methyl-2-pyridyl)benzenesulfonamide (3.00 g, 11.4 mmol) and N-ethyl-N-isopropyl-propan-2-amine (2.2 mL, 12.6 mmol) in DMF-Anhydrous (36 mL), under a nitrogen atmosphere, was treated with idoacetamide (2.33 g, 12.6 mmol) and the mixture was stirred at room temperature for 20 hours.

[00807] The solvent was removed under vacuum and the residue was triturated with DCM/EtOAc (30 mL) but the product was too soluble. EtOAc was added until cloud point and the mixture was aged. The solids were collected by filtration and dried on the sinter to give the title compound (5.3 g, >100%) as a white solid. The material was used without further purification.

Method A: LC-MS (electrospray): m/z = 320.0 (M+H)⁺, RT = 0.88 min

[00808] **Step 3:** 6-methylimidazo[1,2-a]pyridin-2-amine

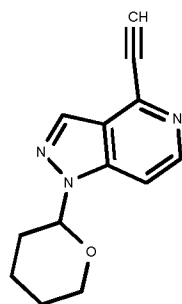


[00809] A suspension of 2-[5-methyl-2-(4-methylbenzenesulfonamido)-1,2-dihydropyridin-1-yl]acetamide (3.60 g, 11.3 mmol) in DCM (40 mL), under a nitrogen atmosphere, was slowly treated with (2,2,2-trifluoroacetyl) 2,2,2-trifluoroacetate (7.9 mL, 56.4 mmol) and the mixture was stirred at room temperature for 16 hours. During the addition, the solids dissolved and the solution darkened to nearly black.

[00810] The dark solution was cautiously quenched by the addition of NaHCO₃ (sat). The solvent was removed under vacuum and the residue was extracted with EtOAc (x2). The organics were washed with brine, dried (MgSO₄) and evaporated under vacuum to a dark gum which was purified by ion exchange [SCX-2 (5 g) washing with methanol and eluting with ammonia in MeOH) to give the title compound (476 mg, 29%) as a dark gum.

Method A: LC-MS (electrospray): m/z = 147.9 (M+H)⁺, RT = 0.17 min

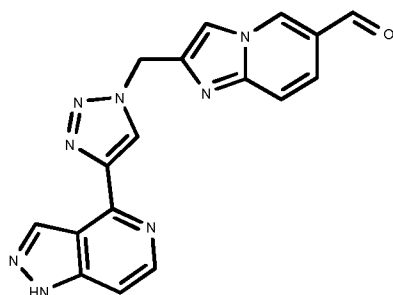
[00811] **Intermediate 60:** 4-ethynyl-1-tetrahydropyran-2-yl-pyrazolo[4,3-c]pyridine



[00812] The title compound was prepared from 4-chloro-1H-pyrazolo[4,3-c]pyridine using the procedures described for **Intermediate 24** to give the title compound (243 mg, 33%) as a brown oil.

Method B: LC-MS (electrospray): m/z = 228.3 (M+H)⁺, RT = 1.40 min

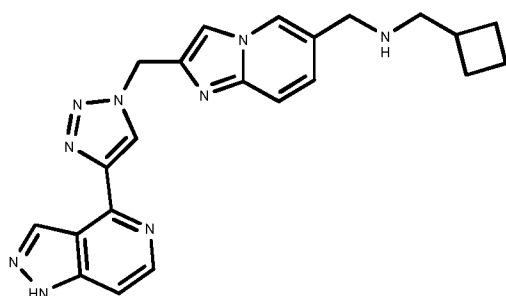
[00813] Intermediate 61: 2-[[4-(1-tetrahydropyran-2-yl)pyrazolo[4,3-c]pyridin-4-yl]triazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carbaldehyde



- 5 **[00814]** The title compound was prepared from **Intermediate 60** using the procedures described for **Intermediate 34** to give the title compound (290 mg, 95%) as a very pale yellow solid.

Method B: LC-MS (electrospray): m/z = 429.3 (M+H)⁺, RT = 1.39 min

- 10 **[00815] Example 324:** N-(cyclobutylmethyl)-1-[2-[[4-(1H-pyrazolo[4,3-c]pyridin-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



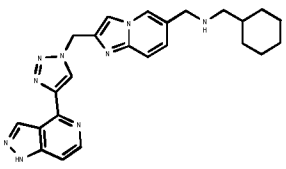
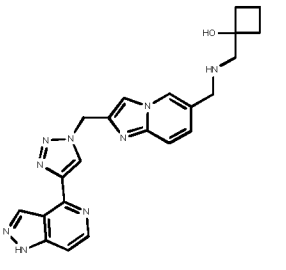
[00816] The title compound was prepared from **Intermediate 61** in a similar manner to **Compound 250** to give (45 mg, 47%) as a white solid.

Method D: LC-MS (electrospray): m/z = 414.3 (M+H)⁺, RT = 3.20 min

- 15 **[00817]** The compounds in Table 21 were prepared in a similar manner to **Example 324**.

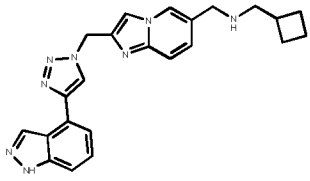
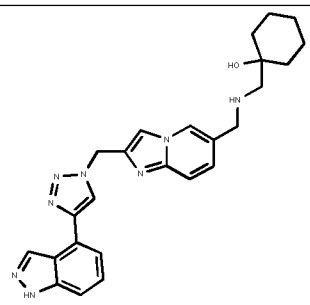
Table 21

Example No	Name	Structure	LCMS method	LCMS Retention time	Mass ion

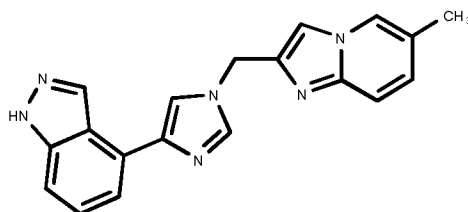
325	N-(cyclohexylmethyl)-1-[2-[[4-(1H-pyrazolo[4,3-c]pyridin-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine		D	3.66	442.3
326	1-[[[2-[[4-(1H-pyrazolo[4,3-c]pyridin-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol		D	2.66	430.3

[00818] The Compounds in Table 22 were prepared from **Intermediate 34** in a similar fashion to **Compound 250**.

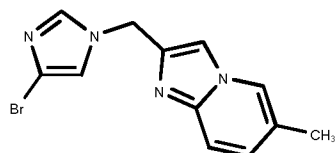
Table 22

Exempl e No	Name	Structure	LCMS Retention time	Mass ion
327	N-(cyclobutylmethyl)-1-[2-[[4-(1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine		2.62	413.4
328	1-[[[2-[[4-(1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclohexanol		2.42	457.4

[00819] Example 329: 2-[[4-(1H-indazol-4-yl)imidazol-1-yl]methyl]-6-methyl-imidazo[1,2-a]pyridine formate



[00820] Step 1: 4-bromo-1-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-imidazole



5

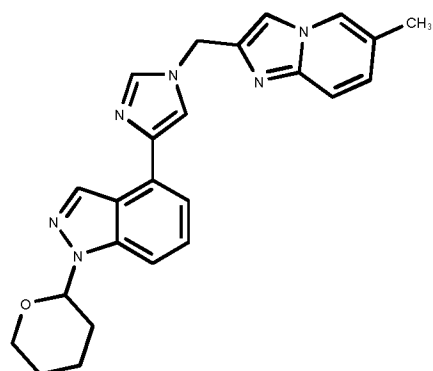
[00821] A mixture of 4-bromo-1H-imidazole (500mg, 3.40 mmol), K_2CO_3 (1.41g, 10.2 mmol) and 2-(chloromethyl)-6-methyl-imidazo[1,2-a]pyridine hydrochloride (886mg, 4.08 mmol) were combined in DMF (8ml) and stirred at room temperature for 1.5 hours before NaI (30mg, 0.20 mmol) was added and the stir was continued for 19 hours.

10 **[00822]** The reaction mixture was diluted with $NaHCO_3$ (sat, 50ml) and extracted with chloroform/isopropanol (3:1, 3 x 50ml). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum.

[00823] The residue was purified by chromatography on SiO_2 (Biotage 28 g kp-NH, eluting with EtOAc/heptane 0-100% followed by MeOH/EtOAc 0-20%) to afford the title
15 compound (836 mg, 84%) as a white solid which contained a small amount of the regioisomeric product.

Method B: LC-MS (electrospray): m/z = 291.1/293.1 ($M+H$)⁺, RT = 1.31 min

[00824] Step 2: 4-[1-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-imidazol-4-yl]-1-(oxan-2-yl)-1H-indazole



20

[00825] 1-tetrahydropyran-2-yl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole (300mg, 0.91mmol), 2-[(4-bromoimidazol-1-yl)methyl]-6-methyl-imidazo[1,2-a]pyridine (319mg, 1.10mmol) and K₂CO₃ (1.2M aqueous, 2.28 ml, 2.74 mmol) were combined in 1,4-Dioxane (6ml) and the mixture sparged with nitrogen for 5mins. PdCl₂dppf (67mg, 0.09 mmol) was added and the mixture further sparged briefly and the vessel sealed. The mixture was heated at 90°C for 2 hours.

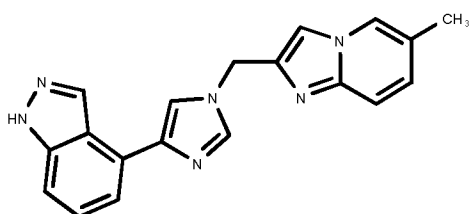
[00826] Further PdCl₂dppf (67mg, 0.09 mmol) was added, mixture briefly sparged with nitrogen and further heated at 100°C for 4 hours. The reaction mixture was cooled to room temperature and stood over the weekend.

[00827] The reaction mixture was diluted with NaHCO₃ (sat, 50ml) and extracted with chloroform/isopropanol (3:1, 3 x 50ml). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum.

[00828] The residue was purified by chromatography on SiO₂ (Biotage 28 g kp-NH, eluting with EtOAc/heptane 0-100% followed by MeOH/EtOAc 0-20%) to afford the crude title compound (229mg, 27% yield, 45% purity) as a brown oil. No further purification attempted; carried direct to next step.

Method A: LC-MS (electrospray): m/z = 413.2 (M+H)⁺, RT = 0.87 min

[00829] **Step 3:** 2-[[4-(1H-indazol-4-yl)imidazol-1-yl]methyl]-6-methyl-imidazo[1,2-a]pyridine formate



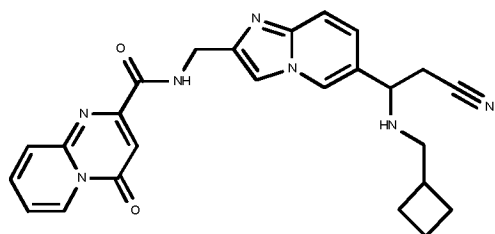
[00830] A solution of 4-[1-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]imidazol-4-yl]-1-tetrahydropyran-2-yl-indazole (229mg, 0.56 mmol) in methanol (5ml) was treated with HCl (4M in dioxane, 5ml) and the mixture was incubated at room temperature for 18 hours.

[00831] The reaction mixture was evaporated under vacuum and the residue was purified by reverse phase chromatography on SiO₂ (12 g C18-Ultra, eluting with Acetonitrile+0.1%NH₃/Water+0.1%NH₃ 10-100%) the relevant fractions were combined to afford crude material which was triturated with MeOH/EtOAc/heptane. The solids were collected by filtration to give a grey solid 100 mg.

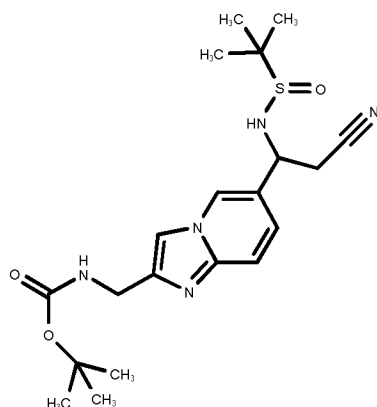
[00832] The material was purified by preparative HPLC [Acidic method A] to give the title compound (20 mg, 9%) as a white solid.

Method E: LC-MS (electrospray): m/z = 329.1 (M+H)⁺, RT = 1.00 min

[00833] **Example 330:** N-[[6-[2-cyano-1-(cyclobutylmethylamino)ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide



[00834] **Step 1:** tert-butyl N-[(6-{2-cyano-1-[(2-methylpropane-2-sulfinyl)amino]ethyl}imidazo[1,2-a]pyridin-2-yl)methyl]carbamate



[00835] An oven dried flask containing N-(propan-2-yl)propan-2-amine (0.28 mL, 2.00 mmol) in THF (2.5 mL) was cooled to -78 °C and a solution of n-butyllithium (1.6 M in hexanes, 1.3 mL, 2.00 mmol) was added whilst maintaining the temperature at -78 °C. Once the addition was complete, the mixture was stirred at ambient temperature for 20 minutes.

[00836] The mixture was cooled to -78 °C and a solution of acetonitrile (0.10 mL, 2.00 mmol) in THF (1 mL) was added and the mixture was stirred at -78 °C for 10 minutes before a quarter of the mixture was syringed into a separate oven dried flask and cooled to -78 °C and stirred for 20 minutes before a solution of tert-butyl N-[[6-[(E)-tert-butylsulfinyliminomethyl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate **Intermediate 55** (190 mg, 0.502 mmol) in THF (0.5 mL) was added dropwise. The reaction was stirred at -78 °C for 20 minutes.

[00837] A further quarter of the LDA mixture was added dropwise and the reaction was stirred for at -78 °C for 15 minutes.

[00838] A further quarter of the LDA mixture was added dropwise and the reaction was stirred for at -78 °C for 15 minutes.

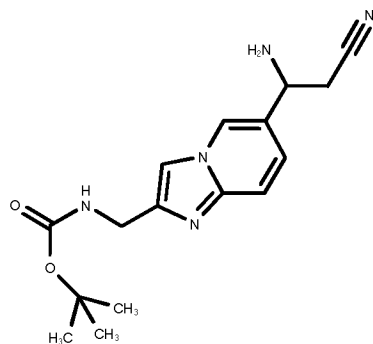
5 [00839] The remaining LDA mixture was added dropwise and the reaction was stirred for at -78 °C for 15 minutes.

[00840] The reaction was quenched *via* dropwise addition of NH₄Cl (sat) and the reaction was warmed to room temperature. The mixture was diluted with EtOAc (5 mL) and the layers separated. The aqueous layer was extracted with ethyl acetate (5 mL). The
10 organic layers were washed with brine (5 mL), dried over magnesium sulfate and concentrated *in vacuo* to give a red viscous oil.

[00841] The crude product was purified by reverse phase chromatography on SiO₂ (Biotage 12 g, water/MeCN (+0.1 % NH₃) at a gradient of 90:10 to 20:80) concentration of product fractions *in vacuo* and subsequent freeze drying overnight gave the desired product
15 (110 mg, 52%) as an off-white solid.

[00842] Method B: LC-MS (electrospray): *m/z* = 420.3 (M+H)⁺, RT = 1.35 min

[00843] Step 2: tert-butyl N-[[6-(1-amino-2-cyanoethyl)imidazo[1,2-a]pyridin-2-yl]methyl]carbamate



20 [00844] A solution of tert-butyl N-[[6-[1-(tert-butylsulfinylamino)-2-cyano-ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate (110 mg, 0.26 mmol) in THF (2 mL) and Water (0.2 mL) was treated with iodine (13 mg, 0.052 mmol) and the mixture was warmed at 60 °C for 18 hours.

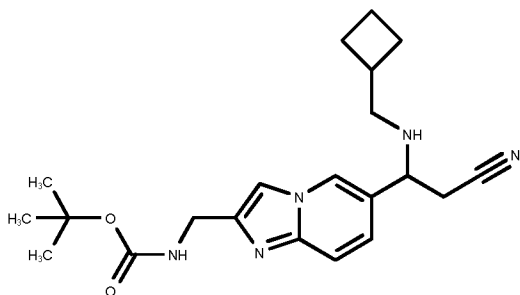
[00845] Further iodine (13 mg, 0.052 mmol) was added and the heating was
25 continued for a further 4 hours.

[00846] The mixture was cooled to room temperature, quenched by the addition of sodium thiosulfate (sat 10 ml) and extracted with EtOAc, dried over sodium sulfate and concentrated *in vacuo*

[00847] Purification by reverse phase chromatography on SiO₂ (12g C18 cartridge, water/MeCN + 0.1% NH₃ gradient) gave the desired product (20 mg, 23%) as a yellow oil.

[00848] Method B: LC-MS (electrospray): *m/z* = 316.3 (M+H)⁺, RT = 1.23 min

[00849] **Step 3:** tert-butyl N-[(6-{2-cyano-1-[(cyclobutylmethyl)amino]ethyl}imidazo[1,2-a]pyridin-2-yl)methyl]carbamate

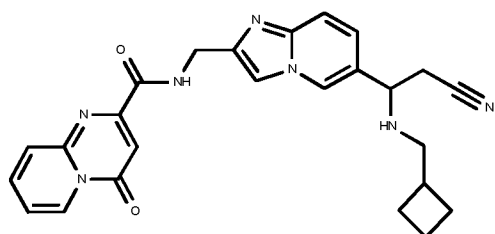


[00850] tert-butyl N-[[6-(1-amino-2-cyano-ethyl)imidazo[1,2-a]pyridin-2-yl)methyl]carbamate (20 mg, 0.06 mmol) and N-ethyl-N-isopropyl-propan-2-amine (0.055 mL, 0.32 mmol) were combined in DCM (0.3 mL) and methanol (0.06 mL). To the yellow suspension was added cyclobutanecarbaldehyde (6.4 mg, 0.0761 mmol) and the reaction was stirred at room temperature for an hour.

[00851] The reaction was concentrated *in vacuo* to remove any excess aldehyde and the resulting crude yellow oil was dissolved in DCM (0.5 mL). sodium borohydride (22 mg, 0.57 mmol) was added followed by a drop of methanol and the reaction was stirred at room temperature for 30 minutes. The reaction was quenched with dropwise addition of water (3 mL). IPA/CHCl₃ (1:4, 5 mL) was added and the separated (phase sep cartridge). The organic filtrate was concentrated *in vacuo* to give the title compound (21 mg, 75%) as a pale yellow residue, which was used without further purification.

[00852] Method B: LC-MS (electrospray): *m/z* = 384.4 (M+H)⁺, RT = 1.53 min

[00853] **Step 4:** N-[[6-[2-cyano-1-(cyclobutylmethylamino)ethyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide



[00854] tert-butyl N-[[6-[2-cyano-1-(cyclobutylmethylamino)ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]carbamate (21 mg, 0.06 mmol) was dissolved in hydrogen chloride solution (4 M in dioxane, 0.14 mL, 0.55 mmol) and stirred at room temperature for an hour.

5 [00855] The solvent was removed *in vacuo* and the resulting crude material was dissolved in DMF (1 mL) and treated with N-ethyl-N-isopropyl-propan-2-amine (0.048 mL, 0.274 mmol) and stirred at RT for 10 minutes.

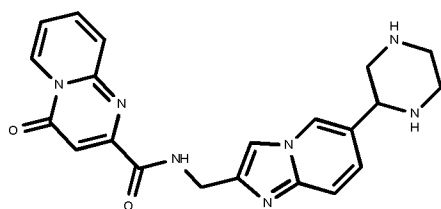
[00856] In a separate flask were combined (4-oxopyrido[1,2-a]pyrimidine-2-carbonyl)oxylithium (11 mg, 0.0548 mmol), HATU (31 mg, 0.0821 mmol) and N-ethyl-N-isopropyl-propan-2-amine (0.048 mL, 0.274 mmol) in DMF (1 mL) at room temperature. The mixture was stirred for 5 minutes before the amine solution was added and resultant mixture was stirred at RT for 2 hours.

[00857] Water (2 mL) and IPA/CHCl₃ (1:4, 5 mL) were added and the layers separated (phase sep cartridge). The organic filtrate was concentrated *in vacuo* to give a green oil. Purification over silica (Reversed phase, 12 g cartridge, water/MeCN + 0.1% formic acid, 10 to 90 %) and concentration of the fractions containing product *in vacuo* gave impure material.

[00858] The compound was further purified over silica (reversed phase 12 g cartridge, water/MeCN + 0.1% NH₃, 10 to 90 %). And freeze dried to give the title compound (4.5 mg, 18%) as a white solid.

Method C: LC-MS (electrospray): m/z = 456.4 (M+H)⁺, RT = 2.53 min

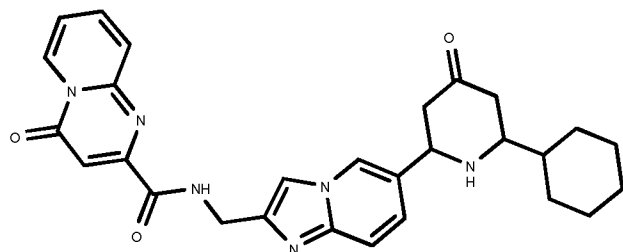
[00859] **Example 333:** 4-oxo-N-[(6-piperazin-2-ylimidazo[1,2-a]pyridin-2-yl)methyl]pyrido[1,2-a]pyrimidine-2-carboxamide



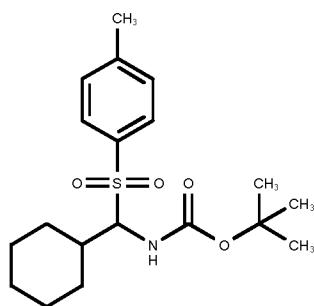
25 [00860] The title compound was prepared from **Example 49** using the procedure described for **Compound 231** to give (12 mg, 15%) as a white solid.

Method C: LC-MS (electrospray): m/z = 404.2 (M+H)⁺, RT = 1.39 min

[00861] Example 334: N-[[6-(6-cyclohexyl-4-oxo-2-piperidyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide



[00862] Step 1: tert-butyl N-[cyclohexyl(p-tolylsulfonyl)methyl]carbamate



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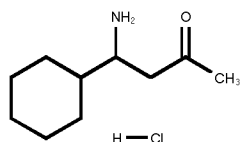
[00863] A mixture of cyclohexanecarbaldehyde (2.24 g, 20.0 mmol), tert-butyl carbamate (2.34 g, 20.0 mmol), sodium;4-methylbenzenesulfinate (3.56 g, 20.0 mmol), water (40 mL), methanol (20 mL) and formic acid (5 mL) was stirred for 15 minutes (until it became homogenous) and then left standing for 18 hours at RT. The crystalline product was filtered off with suction, washed successively with water (30 mL) and diethyl ether (30 mL) and dried in the vacuum oven at 45°C for 4 hours to afford The title compound (4.81 g, 65%) as a white solid.

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[00864] ¹HNMR(500 MHz, Chloroform-d) δ 1.03 – 1.45 (m, 14H), 1.58 – 1.72 (m, 2H), 1.74 – 1.80 (m, 2H), 2.06 – 2.20 (m, 1H), 2.35 – 2.49 (m, 4H), 4.44 – 4.70 (m, 1H), 4.87 – 5.21 (m, 1H), 7.28 – 7.36 (m, 2H), 7.73 – 7.80 (m, 2H).

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[00865] Step 2: 4-amino-4-cyclohexyl-butan-2-one hydrochloride



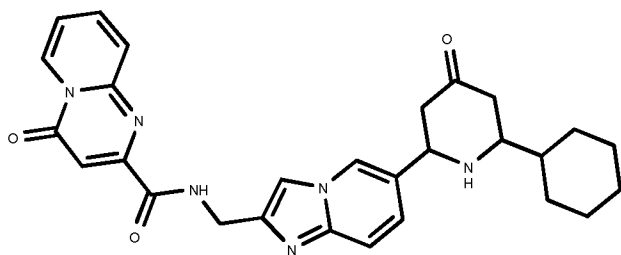
[00866] To a solution tert-butyl N-[cyclohexyl(p-tolylsulfonyl)methyl]carbamate (1.84 g, 5.00 mmol) in THF-Anhydrous (30 mL) was added potassium;2-methylpropan-2-olate (95%, 1.18 g, 10.0 mmol) at 0°C. The mixture was stirred for 10 minutes before a solution of tert-

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butyl 3-oxobutanoate (0.79 g, 5.00 mmol) in THF-Anhydrous (10 mL) was added dropwise via syringe. The reaction was allowed to warm slowly to room temperature and was stirred for 2 hours. The reaction was then cooled to 0°C (ice-bath) and quenched with NH₄Cl (sat, 12.5 mL). Diethyl ether (50 mL) was added and the organic layer was separated. The aqueous layer was extracted with diethyl ether (25 mL). The combined organic layers were washed with brine (30 mL), dried (MgSO₄) and concentrated at reduced pressure to give a clear colourless oil. The oil was treated with HCl (3M, 15 mL) and the mixture was heated at reflux with efficient stirring for 2 hours. Water and the excess HCl were removed at reduced pressure to afford the title compound (0.86 g, 79%) as a brown oil that was used without further purification.

[00867] ¹HNMR(500 MHz, Methanol-d₄) δ 1.05 – 1.90 (m, 11H), 2.23 (s, 3H), 2.80 (dd, J = 19.0, 9.1 Hz, 1H), 3.01 (dd, J = 19.0, 3.2 Hz, 1H), 3.38 – 3.48 (m, 1H).

[00868] **Step 3:** N-[[6-(6-cyclohexyl-4-oxo-2-piperidyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide



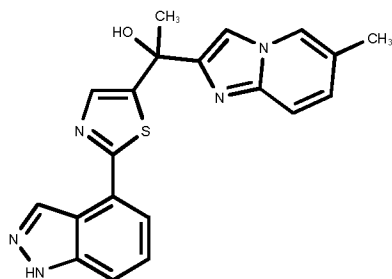
[00869] To a solution of 4-amino-4-cyclohexyl-butan-2-one hydrochloride (54 mg, 0.24 mmol) in ethanol (2 mL) was added DL-Proline (5.5 mg, 0.0477 mmol), magnesium sulfate (29 mg, 0.24 mmol), triethylamine (0.033 mL, 0.24 mmol) and N-[[6-(6-formylimidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide **Example 49** (92 mg, 0.24 mmol) and the mixture was stirred at room temperature for 6 hours. NaHCO₃ (sat, 10 mL) was added and the mixture was extracted with EtOAc (3 x 15 mL). The combined extracts were washed with brine (10 mL), dried (Na₂SO₄), and concentrated at reduced pressure.

[00870] The residue was purified by open access preparative HPLC (Method B) The product containing fractions were combined and concentrated to dryness under reduced pressure.

[00871] The residue was dissolved acetonitrile and water (1:1, 4 mL) and lyophilised to afford the title compound (24 mg, 19%) as an off-white solid as a 7:3 mixture of cis and trans diastereoisomers.

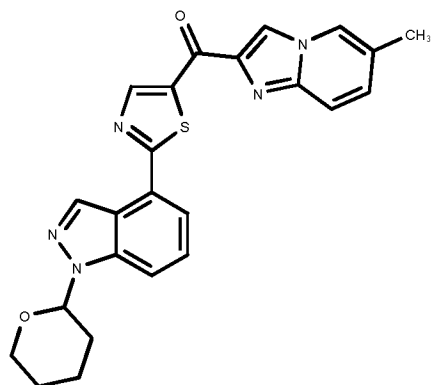
Method C: LC-MS (electrospray): $m/z = 499.4$ ($M+H$)⁺, $RT = 2.99$ min

[00872] Example 335: 1-[2-(1H-indazol-4-yl)thiazol-5-yl]-1-(6-methylimidazo[1,2-a]pyridin-2-yl)ethanol



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[00873] Step 1: (6-methylimidazo[1,2-a]pyridin-2-yl)-[2-(1-tetrahydropyran-2-ylindazol-4-yl)thiazol-5-yl]methanone



[00874] A solution of (6-methylimidazo[1,2-a]pyridin-2-yl)-[2-(1-tetrahydropyran-2-ylindazol-4-yl)thiazol-5-yl]methanol **Compound 258 Step 1** (190mg, 0.43mmol) was dissolved in DCM (5ml) was treated with Dess-Martin periodinane (271mg, 0.64mmol) and the mixture was stirred at room temperature for 2 hours.

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[00875] The reaction was quenched with NaHCO_3 (sat, 20ml) and extracted with chloroform/isopropanol (3:1, 3 x 20ml). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum.

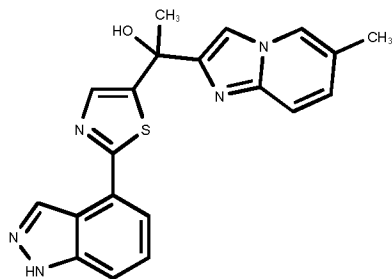
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[00876] The residue was purified by chromatography on SiO_2 (Biotage 25 g kp-Sil, eluting with EtOAc/heptane 0-100%) to afford the title compound (117mg 53%) as a yellow solid

Method A: LC-MS (electrospray): $m/z = 444.2$ ($M+H$)⁺, $RT = 1.35$ min

[00877] Step 2: 1-[2-(1H-indazol-4-yl)thiazol-5-yl]-1-(6-methylimidazo[1,2-a]pyridin-2-yl)ethanol

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[00878] A suspension of (6-methylimidazo[1,2-a]pyridin-2-yl)-[2-(1-tetrahydropyran-2-ylindazol-4-yl)thiazol-5-yl]methanone (110mg, 0.25mmol) in THF (Anhydrous, 10ml) was cooled in an ice/water bath. MeMgBr (3M in Et₂O, 165μl, 0.496 mmol) was added dropwise and the dark red mixture was stirred under cooling for 45 minutes.

[00879] The reaction mixture was quenched with NH₄Cl (sat, 20ml), warmed to room temperature and extracted with chloroform/isopropanol (3:1, 3 x 20ml). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum.

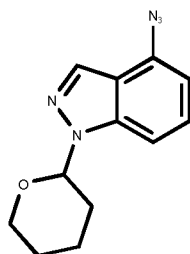
[00880] The residue was dissolved in methanol (3ml), treated with HCl (4M in Dioxane, 3ml) and incubated at room temperature for 3 hours.

[00881] The reaction mixture was evaporated under vacuum. The residue was purified by ion exchange (SCX-2 cartridge (5g) washed with DCM and MeOH and eluted with NH₃/MeOH (7M) and the basic eluent evaporated under vacuum.

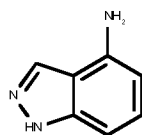
[00882] The residue was purified by Preparative HPLC (method B) and the clean product-containing fractions combined and evaporated under vacuum. The residue was triturated with EtOAc/heptane to afford the title compound (32mg, 34%) as an off-white solid.

[00883] Method D: LC-MS (electrospray): m/z = 376.3 (M+H)⁺, RT = 3.24 min

[00884] **Intermediate 62:** 4-azido-1H-indazole



[00885] **Step-1:** 1H-indazol-4-amine

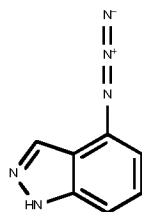


[00886] To a solution of 4-nitro-1H-indazole (50.0 g, 153.33 mmol) in MeOH (500 ml) was added Pd/C (50% wet) (10%, 5.00 g) at room temperature. The reaction mixture was placed under a an atmosphere of hydrogen and stirred at room temperature for 5 hours. The

reaction mixture was filtered through celite pad and washed with additional methanol (3 x 200 ml). The combined filtrate was concentrated under vacuum to afford the title compound (14.0 g, 34%).

Method G: LC-MS (electrospray): m/z = 134.0 ($M+H$)⁺, RT = 0.49 min

5 **[00887] Step-2: 4-azido-1H-indazole**

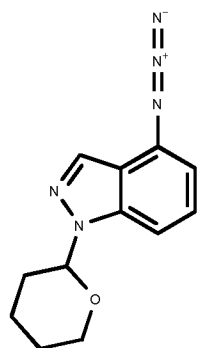


[00888] To a solution of 1H-indazol-4-amine (0.50 g, 3.14 mmol) in acetonitrile (5 ml) was added tert butyl nitrite (1.16 g, 12.57 mmol) followed by addition of sodium azide (0.97 g, 15.7 mmol) at 0 °C. The resulting reaction mixture was stirred at 60 °C for 16 h. The reaction mixture was cooled to room temperature. This procedure was repeated five times and the combined reactions were poured into water (250ml). The mixture was extracted with ethyl acetate (3 X 100 mL). The combined organic layer were dried (Na₂SO₄) and concentrated under vacuum. The crude material was purified by chromatography on SiO₂ (60-120) eluting with 15% EtOAc in hexane to afford the title compound (0.90 g, 25%).

LCMS: 1.504 min, MS: ES+ 160.1 ($M+1$);

Method G: LC-MS (electrospray): m/z = 160.1 ($M+H$)⁺, RT = 1.50 min

[00889] Step-3: 4-azido-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole

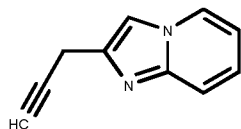


[00890] To a solution of 4-azido-1H-indazole (1.0 g, 6.3 mmol) in EtOAc (10 ml) was added dihydropyran (1.30 g, 15.5 mmol) followed by TFA (0.07 g, 0.63 mmol) at 0° C and the resulting reaction mixture was stirred at 70°C temperature for 4 hours.

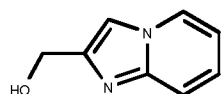
[00891] The reaction mixture was allowed to cool to room temperature, poured into saturated NaHCO₃ (sat, 100ml) and extracted with ethyl acetate (2 X 50 ml). The organic layer was dried (Na₂SO₄) and concentrated under vacuum. The crude material was purified by chromatography on SiO₂ (60-120) eluting with 8% EtOAc in hexane to afford the title compound (0.9 g, 59%).

[00892] Method G: LC-MS (electrospray): $m/z = 244.1$ ($M+H$)⁺, $RT = 2.07$ min

[00893] **Intermediate 63:** 2-(prop-2-yn-1-yl)imidazo[1,2-a]pyridine



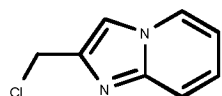
[00894] **Step-1:** imidazo[1,2-a]pyridin-2-ylmethanol



[00895] A solution of ethyl imidazo[1,2-a]pyridine-2-carboxylate (10.00 g, 52.5 mmol) in THF (40 ml) was added dropwise to a cold (0 °C) solution of LiAlH₄ (2M in THF, 34.2 ml, 68.3 mmol) in THF (60 ml) and the resulting reaction mixture was stirred at 0° C for 1 hour. The reaction mixture was quenched with NaOH (10%, 50 ml) and the slurry was filtered through Celite. The filtrate was extracted with methanol in DCM (10% 7 x 50 ml). The combined organic layers were dried (Na₂SO₄) and concentrated under reduced pressure to afford the title compound (7.5 g, 96%).

Method H: LC-MS (electrospray): $m/z = 149.3$ ($M+H$)⁺, $RT = 1.22$ min

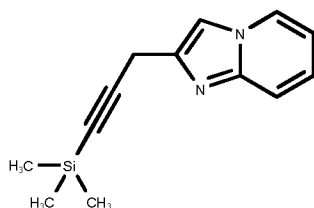
[00896] **Step-2:** 2-(chloromethyl)imidazo[1,2-a]pyridine



[00897] To a solution of imidazo[1,2-a]pyridin-2-ylmethanol (7.50 g, 50.7 mmol) in DCM (100 ml) was added SOCl₂ (4.4 ml, 60.7 mmol) at 0° C dropwise and the mixture was stirred at 0° C for 1 hour. The mixture was diluted with NaHCO₃ (sat, 200 ml) and extracted with DCM (4 x 50 ml). The combined organics were dried (Na₂SO₄) and concentrated under reduced pressure to afford the title compound (6.5 g, 39.14 mmol).

Method G: LC-MS (electrospray): $m/z = 166.9$ ($M+H$)⁺, $RT = 1.10$ min

[00898] **Step-3:** 2-(3-(trimethylsilyl)prop-2-yn-1-yl)imidazo[1,2-a]pyridine

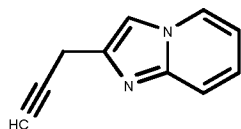


[00899] A mixture of 2-(chloromethyl)imidazo[1,2-a]pyridine (1.50 g, 9.0 mmol), potassium carbonate (3.72 g, 27.0 mmol) and Cu-I (0.17 g, 0.9 mmol) in DMF (15 ml) was de-oxygenated via a stream of N₂ for 15 minutes. TMS acetylene (6.3 ml, 45.0 mmol) was added and the resulting mixture was heated at 70 °C temperature for 10 hours. The mixture

was diluted with ice cold water (300 ml) and extracted with EtOAc (3 x 150 ml). The combined organic layers were dried (Na_2SO_4) filtered and concentrated under reduced pressure. The crude was purified by column chromatography on SiO_2 eluting with 5 % EtOAc in hexane to afford the title compound (0.13 g, 6.3%).

5 Method G: LC-MS (electrospray): m/z = 229.1 ($\text{M}+\text{H}$)⁺, RT = 1.31 min

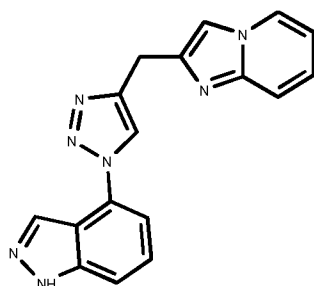
[00900] Step-4: 2-(prop-2-yn-1-yl)imidazo[1,2-a]pyridine



[00901] To a solution of 2-(3-(trimethylsilyl)prop-2-yn-1-yl)imidazo[1,2-a]pyridine (0.23 g, 1.0 mmol) in THF (3 ml) was added TBAF (1M in THF, 0.10 ml, 1.0 mmol) at -20°C
 10 temperature dropwise and the mixture was stirred at -10° C for 15 minutes before it was diluted with NaHCO_3 (sat, 50 ml) and extracted with EtOAc (4 x 30 ml). The extracts were dried (Na_2SO_4) and concentrated under reduced pressure to afford the title compound (0.15 g, 96%).

Method I: LC-MS (electrospray): m/z = 157.28 ($\text{M}+\text{H}$)⁺, RT = 1.62 min

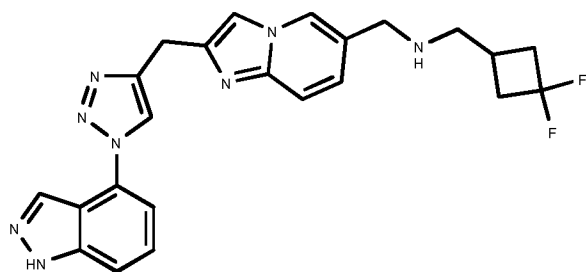
15 [00902] **Example 336:** 4-(4-(imidazo[1,2-a]pyridin-2-ylmethyl)-1H-1,2,3-triazol-1-yl)-1H-indazole



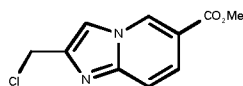
[00903] A mixture of 2-(prop-2-yn-1-yl)imidazo[1,2-a]pyridine **Intermediate 63** (0.10 g, 0.64 mmol), 4-azido-1H-indazole **Intermediate 62** (0.1 g, 0.64 mmol), sodium ascorbate (0.013 g, 0.064 mmol) and CuSO_4 (0.037 g, 0.230 mmol) in tert-butanol: water (1:1, 3 ml)
 20 was heated in a microwave reactor at 100°C for 30 minutes. The resultant mixture was concentrated under reduced pressure and the residue was purified by reverse phase column chromatography using C18 silica gel and product (eluted at 30 % MeCN in water) to afford the title product (32 mg, 16%).

25 Method D: LC-MS (electrospray): m/z = 316.3 ($\text{M}+\text{H}$)⁺, RT = 2.94 min

[00904] **Example 337:** [(3,3-difluorocyclobutyl)methyl][(2-{[1-(1H-indazol-4-yl)-1H-1,2,3-triazol-4-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methyl]amine



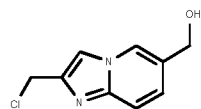
[00905] Step 1: methyl 2-(chloromethyl)imidazo[1,2-a]pyridine-6-carboxylate



5 **[00906]** To a stirred Solution of methyl 6-aminonicotinate (40.0 g, 262.8 mmol) in acetonitrile (400ml) was added 1, 3-dichloropropan-2-one (66.73 g, 525.6 mmol) at room temperature under a nitrogen atmosphere and the resulting reaction mixture was heated at 80°C temperature for 16 hours. The mixture was cooled to room temperature, diluted with NaHCO₃ (sat, 500ml) and extracted with DCM (3 x 500ml). The combined organics were
10 dried (Na₂SO₄), concentrated under reduced pressure and purified by column chromatography on SiO₂ (60-120) eluting with 5% acetone/DCM to afford the title compound (28.0 g, 64%).

Method G: LC-MS (electrospray): m/z = 225.2 (M+H)⁺, RT = 0.95 min

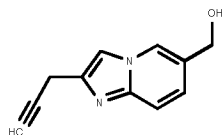
[00907] Step 2: (2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl)methanol



15 **[00908]** To a stirred Solution of methyl 2-(chloromethyl)imidazo[1,2-a]pyridine-6-carboxylate (9.50 g, 42.3 mmol) in THF (dry, 200ml) was added DIBAL-H (1M in THF, 168.8ml, 168.8 mmol) at 0 °C, under a nitrogen atmosphere, and the resulting mixture was stirred at room temperature for 2 hours. The mixture was cooled at 0 °C, quenched with
20 MeOH (70ml) and diluted with DCM (500ml). The resulting slurry was filtered through a Celite bed washing with DCM (3 x 250ml). The filtrate was washed with NaHCO₃ (sat, 2 X 100ml), dried (Na₂SO₄), concentrated under reduced pressure and purified by column chromatography on SiO₂ (60-120) eluting with 5 % MeOH in DCM to give the title compound (4.0 g, 42%).

25 Method H: LC-MS (electrospray): m/z = 197.4 (M+H)⁺, RT = 1.42 min

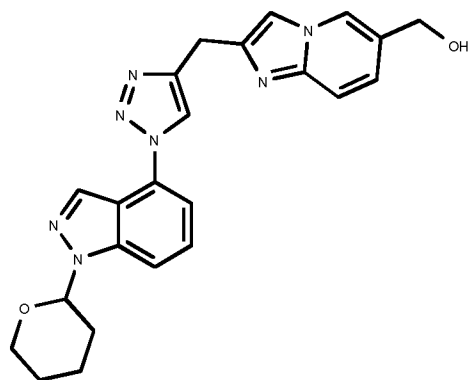
[00909] Step 3: (2-(prop-2-yn-1-yl)imidazo[1,2-a]pyridin-6-yl)methanol



[00910] To a stirred Solution of (2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl)methanol (0.50 g, 2.5 mmol) in THF (dry, 10ml) in a sealed tube was added ethynylmagnesium bromide (0.5 M in THF, 40ml, 20 mmol) at room temperature, under a nitrogen atmosphere and the mixture was heated at 70 °C for 16 hours. The resulting reaction mixture was cooled at room temperature, diluted with ammonium bicarbonate (sat, 25 ml) and extracted with DCM (3 x 30 ml). The extracts were dried (Na₂SO₄), concentrated under reduced pressure and purified by column chromatography on (neutral alumina) eluting with 5% MeOH in DCM to give the title compound (0.197 g, 42%).

Method G: LC-MS (electrospray): m/z = 187.1 (M+H)⁺, RT = 0.63 min

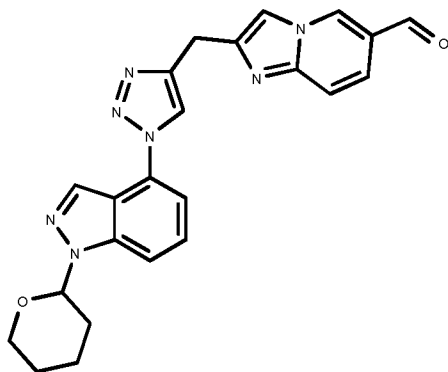
[00911] Step 4: (2-((1-(1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-4-yl)-1H-1,2,3-triazol-4-yl)methyl) imidazo[1,2-a]pyridin-6-yl)methanol



[00912] To a stirred solution of (2-(prop-2-yn-1-yl)imidazo[1,2-a]pyridin-6-yl)methanol (0.19 g, 1.0 mmol) in tert-BuOH : water (1:1, 10 ml) was added 4-azido-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole **Intermediate 62** (0.24 g, 1.0 mmol), sodium ascorbate (0.019 g, 0.10 mmol) and CuSO₄ (0.063 g, 0.4 mmol) at room temperature under nitrogen atmosphere and the resulting mixture was heated at 100 °C for 16 hours. The mixture was cooled to room temperature, diluted with water (25 ml) and extracted with MeOH:DCM (10%, 3 x 30 ml). The extracts were dried (Na₂SO₄), concentrated under reduced pressure and purified by column chromatography (neutral alumina) eluting with 5% MeOH in DCM to give the title compound (0.25 g, 67%).

Method G: LC-MS (electrospray): m/z = 430.2 (M+H)⁺, RT = 1.20 min

[00913] Step 5: 2-((1-(1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-4-yl)-1H-1,2,3-triazol-4-yl)methyl) imidazo[1,2-a]pyridine-6-carbaldehyde

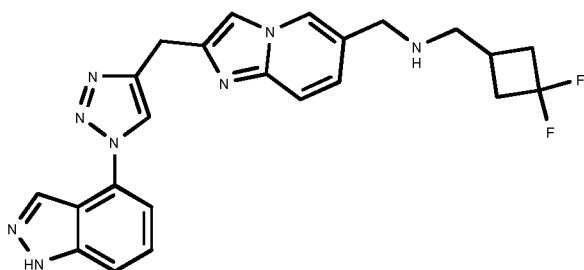


[00914] To a stirred solution of 2-((1-(1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-4-yl)-1H-1,2,3-triazol-4-yl)methyl)imidazo[1,2-a]pyridin-6-yl)methanol (0.25 g, 0.58 mmol) in DCM (10 ml) was added Dess–Martin periodinane (0.424 g, 1.164 mmol) at 0°C under a nitrogen atmosphere and the reaction mixture was stirred at room temperature for an hour.

[00915] The mixture was diluted with NaHCO₃ (sat, 25 ml) and extracted with DCM (3 x 30 ml). The extracts were dried (Na₂SO₄) and concentrated under reduced pressure to give the title compound (0.25 g, 100%).

Method G: LC-MS (electrospray): m/z = 428.2 (M+H)⁺, RT = 1.34 min

[00916] Step 6: 1-(2-((1-(1H-indazol-4-yl)-1H-1,2,3-triazol-4-yl)methyl)imidazo[1,2-a]pyridin-6-yl)-N-((3,3-difluorocyclobutyl)methyl)methan amine



[00917] To a stirred solution of 3,3-difluorocyclobutyl)methanamine hydrochloride (0.118 g, 0.878 mmol) in DCE (10ml) was added Et₃N (0.140 ml, 1.170 mmol) at room temperature. 2-((1-(1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-4-yl)-1H-1,2,3-triazol-4-yl)methyl)imidazo[1,2-a]pyridine-6-carbaldehyde (0.250 g, 0.585 mmol) was added followed by AcOH (0.003g, 0.058mmol) at room temperature and the mixture was stirred for 10-15min before the mixture was cooled to 0°C, Na(OAc)₃BH (0.42 g, 2.340 mmol) was added and the mixture was stirred at room temperature for 15 hours.

[00918] The mixture was cooled to 0 °C, NaBH₄ (0.018 g, 0.585 mmol) was added and the mixture was stirred at room temperature for an hour. The mixture was diluted with water

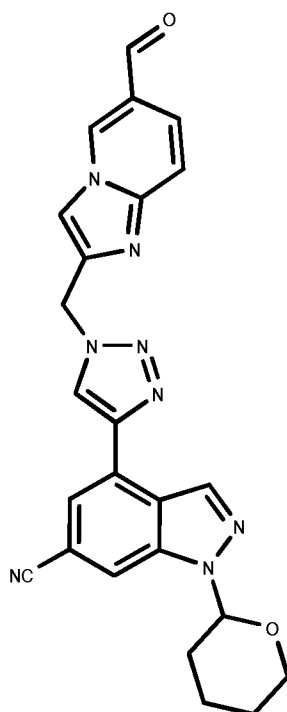
(25 ml) and extracted with DCM (3 x 30 ml). The extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give the intermediate product.

[00919] The intermediate product was dissolved in 1,4-dioxane (5.0 ml), cooled to 0 °C and HCl (4M in dioxane, 0.400 ml, 1.652 mmol) was added dropwise and the resulting mixture was stirred at room temperature for 1 hour.

[00920] The mixture was diluted with DCM (15 ml) quenched with NaHCO_3 (sat, 50 ml) and extracted with DCM (3 x 50 ml). The extracts were dried (Na_2SO_4), concentrated under reduced pressure and purified by reverse phase flash chromatography using C18 silica eluting with 30% acetonitrile in water to give the title compound (37 mg, 14%) as a white solid.

Method C: LC-MS (electrospray): m/z = 449.4 ($\text{M}+\text{H}$)⁺, RT = 2.48 min

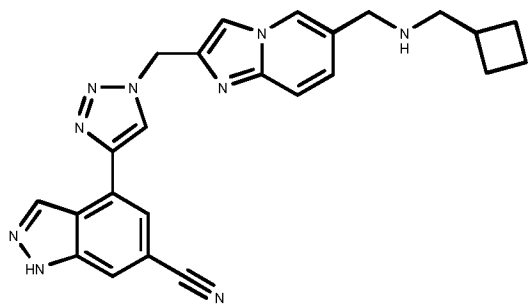
[00921] **Intermediate 64:** 4-[1-({6-formylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-1,2,3-triazol-4-yl]-1-(oxan-2-yl)-1H-indazole-6-carbonitrile



[00922] The title compound was prepared from 4-bromo-1H-indazole-6-carbonitrile in a similar fashion to **Intermediate 34** giving (313 mg, 78%) as a beige powder.

Method C: LC-MS (electrospray): m/z = 453.3 ($\text{M}+\text{H}$)⁺, RT = 2.96 min

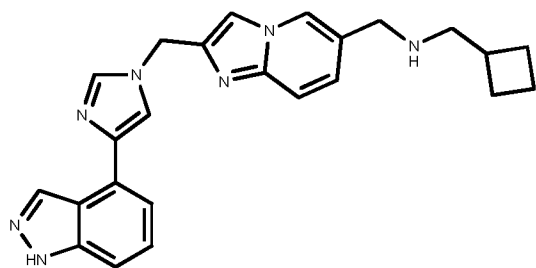
[00923] **Example 338:** 4-{1-[(6-{[(cyclobutylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-1H-1,2,3-triazol-4-yl}-1H-indazole-6-carbonitrile



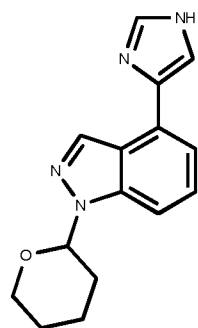
[00924] The title compound was prepared from **intermediate 64** using the procedure described for **Compound 250** to give (42 mg, 38%) as an off-white solid.

5 Method C: LC-MS (electrospray): m/z = 438.4 ($M+H$)⁺, RT = 2.73 min

[00925] **Example 339:** N-(cyclobutylmethyl)-1-[2-[[4-(1H-indazol-4-yl)imidazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



[00926] Step 1: 4-(1H-imidazol-4-yl)-1-tetrahydropyran-2-yl-indazole



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[00927] 1-tetrahydropyran-2-yl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indazole (700mg, 1.75mmol), 4-bromo-1H-imidazole (397mg, 2.62mmol), Pd(OAc)₂ (39mg, 0.17mmol), A-ta-Phos (111mg, 0.42mmol) and K₂CO₃ (1.2M aqueous, 4.4ml, 5.25mmol) were combined in 1,4-Dioxane (10 ml) and the mixture was sparged with nitrogen for 5 minutes. The vessel was sealed and the mixture was heated at 115°C for 3 hours. The mixture was cooled to room temperature and more K₂CO₃ (1.2M aqueous, 1 ml, 1.2 mmol), Pd(OAc)₂ 39 mg, 0.17 mmol) and A-ta-Phos (111 mg, 0.42 mmol) were added the mixture was sparged with nitrogen for 5 minutes and heated at 115°C for 3 hours. The mixture was

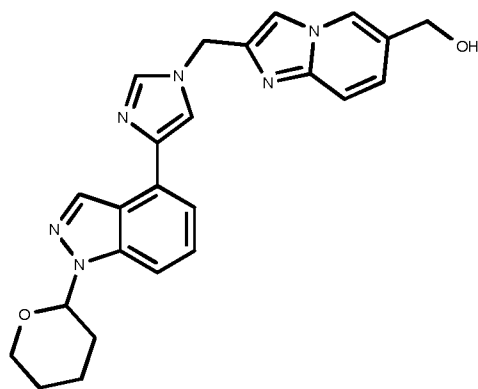
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cooled to room temperature and more K_2CO_3 (1.2M aqueous, 1 ml, 1.2 mmol), $Pd(OAc)_2$ 39 mg, 0.17 mmol) and A-ta-Phos (111 mg, 0.42 mmol) were added the mixture was sparged with nitrogen for 5 minutes and heated at 115°C for 17 hours.

[00928] The reaction mixture was cooled to room temperature, diluted with water (40ml) and extracted with chloroform/isopropanol (3:1, 3 x 40ml). The organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified chromatography on SiO_2 (Biotage kp-NH 28 g, eluting with EtOAc/heptane 0-100% followed by MeOH/EtOAc 0-20%) to afford the title compound 405 mg, 73%) as a white solid.

Method B: LC-MS (electrospray): m/z = 269.2 (M+H)⁺, RT = 1.35 min

[00929] **Step 2:** [2-[[4-(1-tetrahydropyran-2-yl)indazol-4-yl]imidazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanol

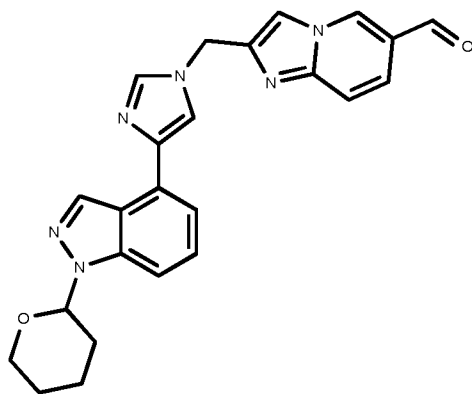


[00930] 4-(1H-imidazol-4-yl)-1-tetrahydropyran-2-yl-indazole (400mg, 1.27mmol), [2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl]methanol **Intermediate 34 Step 2** (274 mg, 1.39 mmol), Cs_2CO_3 (1.24g, 3.80mmol) and NaI (19 mg, 0.13 mmol) were combined in DMF (10 ml) and the mixture was at heated at 80 °C for an hour. The mixture was cooled to room temperature, further [2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl]methanol (274 mg, 1.39 mmol) was added the mixture was at heated at 80 °C for 16 hours.

[00931] The reaction mixture was cooled to room temperature, diluted with water (80ml) and extracted with chloroform/isopropanol (3:1, 3 x 50ml) and the combined organic extracts dried over sodium sulfate and evaporated under vacuum. The residue was purified by chromatography on SiO_2 (Biotage, 28 g kp-NH, eluting with EtOAc/heptane 0-100% followed by MeOH/EtOAc 0-20%) to afford the title compound (259mg, 31%) as a pale pink solid.

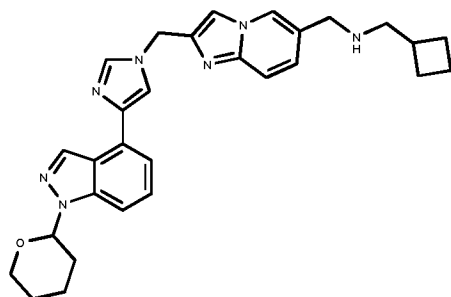
Method B: LC-MS (electrospray): m/z = 429.3 (M+H)⁺, RT = 1.33 min

[00932] **Step 3:** 2-[[4-(1-tetrahydropyran-2-yl)indazol-4-yl]imidazol-1-yl]methyl]imidazo[1,2-a]pyridine-6-carbaldehyde



5

[00934] Step 4: N-(cyclobutylmethyl)-1-[2-[[4-(1-tetrahydropyran-2-yl)indazol-4-yl]imidazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



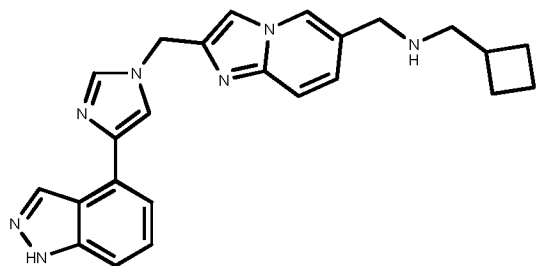
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Method B: LC-MS (electrospray): $m/z = 496.3$ ($M+H$)⁺, $RT = 1.59$ min

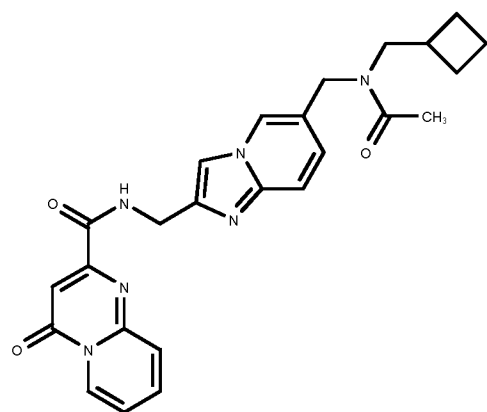
[00936] Step 5: N-(cyclobutylmethyl)-1-[2-[[4-(1H-indazol-4-yl)imidazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



[00937] N-(cyclobutylmethyl)-1-[2-[[4-(1-tetrahydropyran-2-yl)indazol-4-yl]imidazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine (83 mg, 0.17 mmol) was dissolved in MeOH (3ml) and treated with HCl (4M in dioxane, 3 ml, 12 mmol) and the mixture was incubated at room temperature for 2 hours. The reaction mixture was filtered and the residue was purified by preparative HPLC (method B) to afford the title compound (16 mg, 27%) as a white solid.

Method D: LC-MS (electrospray): $m/z = 412.3$ ($M+H$)⁺, $RT = 3.30$ min

[00938] Example 340: N-[(6-{[N-(cyclobutylmethyl)acetamido]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide



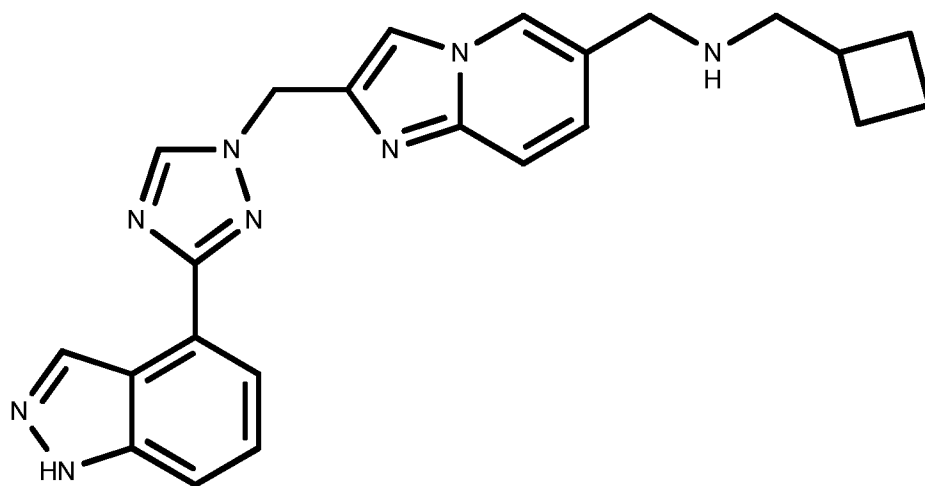
[00939] A solution of N-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide **Compound 212** (72 mg, 0.17 mmol) in DCE (5 ml) was treated with acetic anhydride (162 μ l, 1.71 mmol) and the mixture was stirred at room temperature for an hour.

[00940] The reaction was quenched with NaHCO_3 (sat, 20ml) and extracted with chloroform/isopropanol (3:1, 3 x 10ml). The combined organic extracts were dried over sodium sulfate and evaporated under vacuum. The residue was purified by ion exchange (SCX-2, 2g) washing with DCM and MeOH, and eluted with NH_3 (7M in MeOH). The basic eluent was evaporated under a stream of nitrogen.

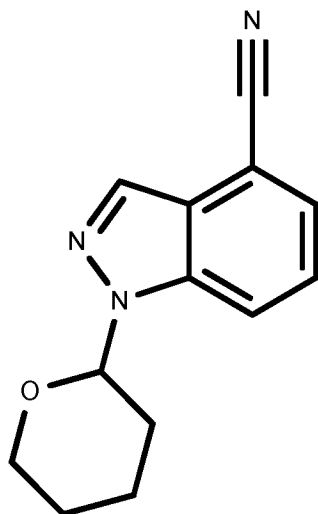
[00941] The residue was purified by preparative HPLC (Method B) and evaporated under vacuum to afford the title compound (59mg, 75%) as a pale yellow solid.

[00942] Method D: LC-MS (electrospray): $m/z = 459.3$ ($\text{M}+\text{H}^+$), $\text{RT} = 3.18$ min

[00943] **Example 341:** N-(cyclobutylmethyl)-1-[2-[[3-(1H-indazol-4-yl)-1,2,4-triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



[00944] **Step 1:** 1-tetrahydropyran-2-ylindazole-4-carbonitrile

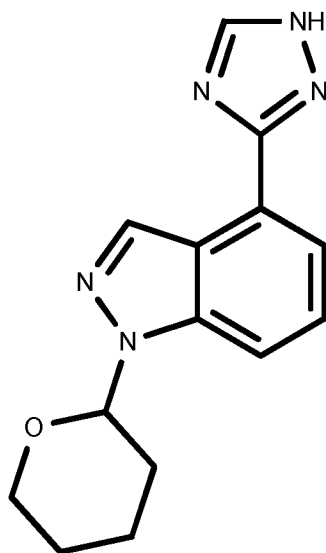


[00945] An oven-dried three-neck 25 mL RBF was charged with zinc cyanide (459 mg, 3.91 mmol), 4-bromo-1-tetrahydropyran-2-yl-indazole (1.00 g, 3.56 mmol), $\text{Pd}(\text{PPh}_3)_4$ (206 mg, 0.178 mmol) and anhydrous DMF (9 mL). The flask was equipped with a reflux condensor, the assembly flushed with nitrogen and then the reaction mixture was de-

oxygenated by passing a stream of nitrogen gas for 5 min. The reaction was placed in a pre-heated heating block at 100 °C and stirred at this temperature for 3 hours. The reaction was cooled to room temperature and diluted with EtOAc (30 mL) and water (20 mL). The aqueous phase was extracted with EtOAc (2 x 30 mL). The combined organics were washed with brine (10 mL), dried over magnesium sulfate and concentrated to give a reddish oily solid which was purified by chromatography on SiO₂ (Biotage 25 g) eluting with EtOAc/heptane (0-100%) to give the title compound (697 mg, 86%) as a white solid.

Method B: LC-MS (electrospray): m/z = 228.3, (M+H)⁺, RT = 1.6 min.

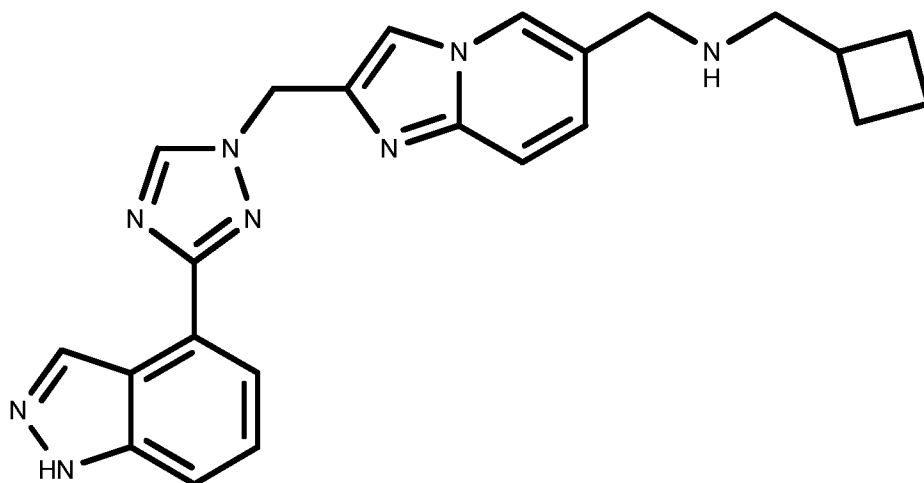
[00946] Step 2: 1-tetrahydropyran-2-yl-4-(1H-1,2,4-triazol-3-yl)indazole



[00947] A flask was charged with 1-tetrahydropyran-2-ylindazole-4-carbonitrile (627 mg, 2.76 mmol), sodium methoxide (1.34 g, 24.8 mmol) and anhydrous methanol (10 mL) and the resulting suspension was stirred at room temperature for an hour before formic hydrazide (4.81 g, 80.0 mmol) was added and the reaction was heated at 65 °C for 16 hours. The mixture was cooled to room temperature and concentrated. The residue was partitioned between water (50 mL) and EtOAc (50 mL), the phases were separated and the aqueous was extracted with EtOAc (20 mL). The combined organic phases were washed with water (20 mL) and brine (20 mL), dried (MgSO₄) and concentrated under vacuum. The residue was purified by chromatography on SiO₂ (Biotage 25 g) eluting with EtOAc/heptane 0-100 % followed by MeOH/DCM (0-50%) to give the title compound (113 mg, 12%) as a yellow solid.

Method B: LC-MS (electrospray): m/z = 270.2, (M+H)⁺, RT = 1.22 min.

[00948] Step 3: N-(cyclobutylmethyl)-1-[2-[[3-(1H-indazol-4-yl)-1,2,4-triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine

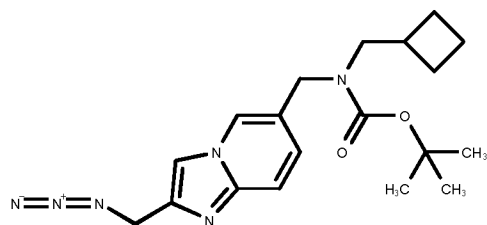


[00949] A suspension of 1-tetrahydropyran-2-yl-4-(1H-1,2,4-triazol-3-yl)indazole 113 mg, 0.344 mmol), sodium hydride (60%, 14 mg, 0.344 mmol) and DMF (anhydrous 2 mL) was stirred at room temperature for 20 minutes during which time it developed a deep red-brown colouration. A solution containing tert-butyl N-[[2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl]methyl]-N-(cyclobutylmethyl)carbamate (138 mg, 0.378 mmol) in DMF (anhydrous 2 mL) was added, the flask was equipped with a reflux condensor and the reaction was stirred at 90 °C for 2 hours.

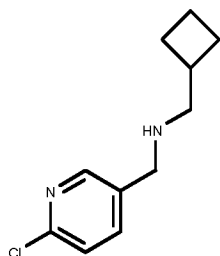
[00950] The mixture was cooled to room temperature, diluted with water (1 mL) and concentrated to a brown oil which was diluted with water (5 mL) and extracted with DCM (20 mL and 2 x 5 mL). The combined organics were washed with brine (5 mL) dried (MgSO₄) and concentrated to give a brown oil (303 mg). The residue was dissolved in ethanol (5 mL) treated with HCl (4M in dioxane 6 mL) and the resulting solution was stirred at room temperature for 16 hours. The mixture was concentrated and the resulting residue was suspended in HCl (4M in 1,4-dioxane 4 mL) and stirred at room temperature for 45 minutes. The mixture was concentrated under vacuum to give a brown solid which was dissolved in methanol (~50 mL) and the resulting solution was diluted with NaHCO₃ (sat, 10 mL), DCM (20 mL) and IPA/CHCl₃ (1:3, 20 mL). The organic phase was separated and the aqueous was extracted with IPA/CHCl₃ (1:3, 20 + 10 mL). The combined organics were washed with brine (5 mL), dried (MgSO₄) and concentrated to give the crude product as a brown oil (240 mg) which was purified by preparative HPLC (method B). The product containing fractions were combined and diluted with brine (10 mL) and extracted with DCM (3 x 10 mL). The combined organics were washed with brine (2 x 5 mL), dried (MgSO₄) and concentrated to give the title compound (60 mg, 42%) as a yellow solid.

Method C: LC-MS (electrospray): m/z = 413.4, (M+H)⁺, RT = 2.57 min.

[00951] **Intermediate 65:** tert-butyl N-[[2-(azidomethyl)imidazo[1,2-a]pyridin-6-yl]methyl]-N-(cyclobutylmethyl)carbamate



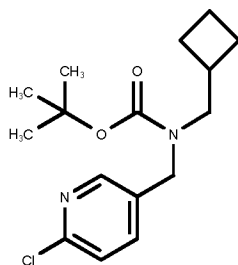
[00952] Step 1: [(6-chloropyridin-3-yl)methyl](cyclobutylmethyl)amine



[00953] A solution of 1-cyclobutylmethanamine (1.80 g, 21.2 mmol) in DCE (30 mL) was treated with 6-chloropyridine-3-carbaldehyde (2.50 g, 17.7 mmol) followed by magnesium sulfate (1.06 g, 8.83 mmol) and the reaction was stirred at room temperature for 1.5 hours. Sodium borohydride (0.67 g, 17.7 mmol) and MeOH (0.5 mL) were added and the mixture was stirred at room temperature for 17 hours. More Sodium borohydride (1.54 g, 40.7 mmol) and methanol (1.5 mL) were added and the mixture was stirred at room temperature for 5 hours and at 40 °C, for 1.5 hours. The mixture was poured into NaHCO₃ (sat, 50 mL) and stirred for 20 minutes. The phases were separated and the aqueous phase extracted with DCM (2x25 mL). The combined organics were washed with brine (25 mL). The combined aqueous phases were extracted with DCM (25 mL). All the organic phases were combined, dried MgSO₄ and concentrated. to give a yellow oil which was purified by chromatography on SiO₂ (Biotage Kp-Sil 50g) eluting with EtOAc. to give the title compound (1.89 g, 46%) as a pale yellow oil.

Method C: LC-MS (electrospray): m/z = 210.9, (M+H)⁺, RT = 2.95 min.

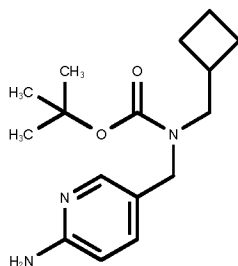
[00954] Step 2: tert-butyl N-[(6-chloro-3-pyridyl)methyl]-N-(cyclobutylmethyl) carbamate



[00955] A solution of Di-tert-butyl dicarbonate (3.76 g, 17.2 mmol) in MeCN (30 mL) was added to a flask containing 1-(6-chloro-3-pyridyl)-N-(cyclobutylmethyl)methanamine (3.44 g, 14.4 mmol) and the mixture was refluxed at 80 °C for 2 hours. The mixture was cooled to room temperature and concentrated to a yellow oil which was purified by chromatography on SiO₂ (Biotage Kp-Sil 100g) eluting with EtOAc in heptane (0-15%) to give the title compound (4.47 g, 100%) as a colourless oil.

Method C: LC-MS (electrospray): m/z = 311.2, (M+H)⁺, RT = 4.32 min.

[00956] **Step 3:** tert-butyl N-[(6-amino-3-pyridyl)methyl]-N-(cyclobutylmethyl)carbamate



[00957] An oven-dried 100 mL two-neck RBF was charged with tert-butyl N-[(6-chloro-3-pyridyl)methyl]-N-(cyclobutylmethyl)carbamate (4.40 g, 14.2 mmol), XPhos (1350 mg, 2.83 mmol) and Pd₂dba₃ (648 mg, 0.708 mmol). The flask was equipped with a reflux condensor and the assembly was flushed with nitrogen. THF (anhydrous, 47 mL) was added and the resulting solution was de-oxygenated by bubbling nitrogen for 30 minutes.

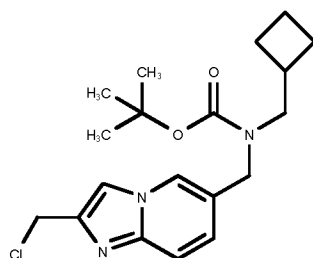
[Bis(trimethylsilyl)amino]lithium (1M in THF, 21 mL, 21.2 mmol) was added with vigorous stirring dropwise over 5 minutes and the mixture was placed in a pre-heated heating block at 70 °C and stirred for 2 hours.

[00958] The mixture was cooled to room temperature, poured into NaHCO₃ (sat, 50 mL) and stirred for 5 minutes before the mixture was extracted with DCM (2x50 mL). The aqueous phase was diluted with brine (30 mL) and extracted with DCM (2x50 mL). The combined organics were washed with brine (30 mL). The brine washings were extracted with DCM (50 mL). All the organics were combined, dried (MgSO₄) and concentrated to give the crude product as a viscous brown oil which was purified by chromatography on SiO₂

(Biotage, Amino Duo D 55 g) eluting with EtOAc in heptane (0-100%) to give the title compound (3.25 g, 75%) as a light orange solid.

Method D: LC-MS (electrospray): m/z = 292.3, (M+H)⁺, RT = 4.24 min.

[00959] **Step 4:** tert-butyl N-[[2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl]methyl]-N-(cyclobutylmethyl)carbamate

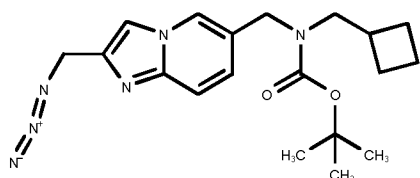


[00960] A mixture of tert-butyl N-[(6-amino-3-pyridyl)methyl]-N-

(cyclobutylmethyl)carbamate (3.16 g, 10.3 mmol) in DME (anhydrous, 45 mL) was treated with 1,3-dichloropropan-2-one (1.44 g, 11.3 mmol) and the mixture was heated, with stirring, at 80 °C for 1.5 hours. More 1,3-dichloropropan-2-one (260 mg, 2 mmol) was added and the mixture was heated at 80 °C for 30 minutes. The mixture was cooled to room temperature and washed with NaHCO₃ (sat, 2x15 mL). The aqueous was extracted with EtOAc (2x20 mL) and the combined organics were dried (MgSO₄) and concentrated to give the crude product as an orange-brown semi-solid. The product was purified by chromatography on neutral alumina (~250 g) eluting in a step gradient of EtOAc/heptane: 1:3 (500 mL), 1:2 (500 mL), 1:1 (1.5 L) to give the title compound (1.90 g, 49%) as a light yellow solid.

Method C: LC-MS (electrospray): m/z = 364.2, (M+H)⁺, RT = 3.89 min.

[00961] **Step 5:** tert-butyl N-[[2-(azidomethyl)imidazo[1,2-a]pyridin-6-yl]methyl]-N-(cyclobutylmethyl)carbamate



[00962] A vial was charged with sodium azide (300 mg, 4.62 mmol), sodium iodide (28 mg, 0.185 mmol), tert-butyl N-[[2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl]methyl]-N-(cyclobutylmethyl)carbamate (700 mg, 1.85 mmol) and DMF (3.7 mL). The resulting

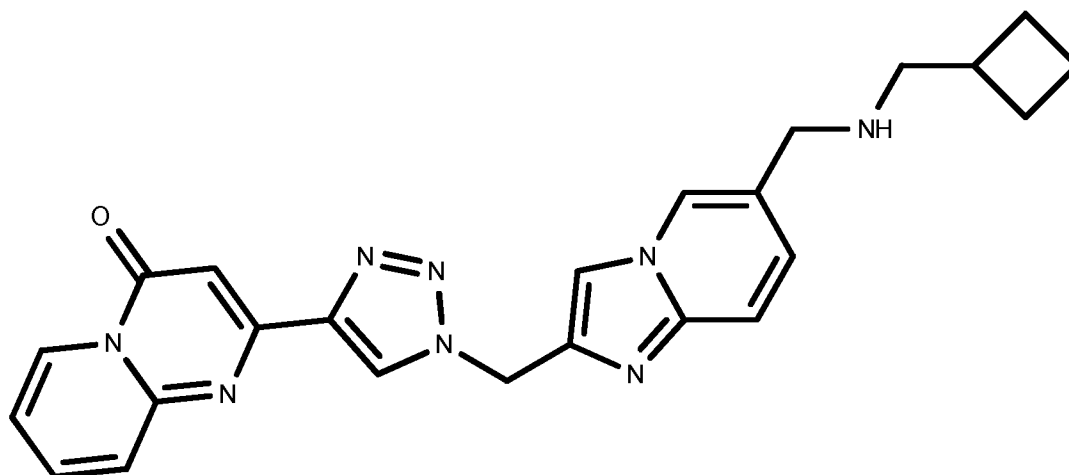
suspension was stirred at room temperature for 2 hours. The mixture was diluted with water (3 mL) and extracted with EtOAc (3x10 mL). The combined organics were washed with brine (5 mL), dried (MgSO₄) and concentrated to give the crude product as a yellow oil which partially solidifies on standing. The material was purified by chromatography on SiO₂

(Biotage 25g) eluting with EtOAc/heptane (0-50%). The product to give the title compound (719 mg, 99%) as a yellow oil.

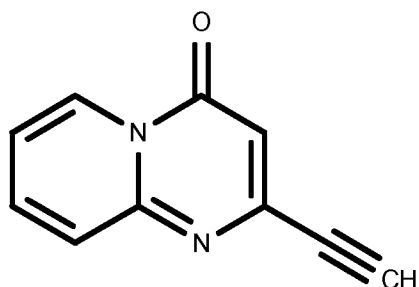
Method C: LC-MS (electrospray): m/z = 371.4, (M+H)⁺, RT = 3.91 min.

[00963] Example 342: 2-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-

5 2-yl]methyl]triazol-4-yl]pyrido[1,2-a]pyrimidin-4-one



[00964] Step 1: 2-ethynylpyrido[1,2-a]pyrimidin-4-one

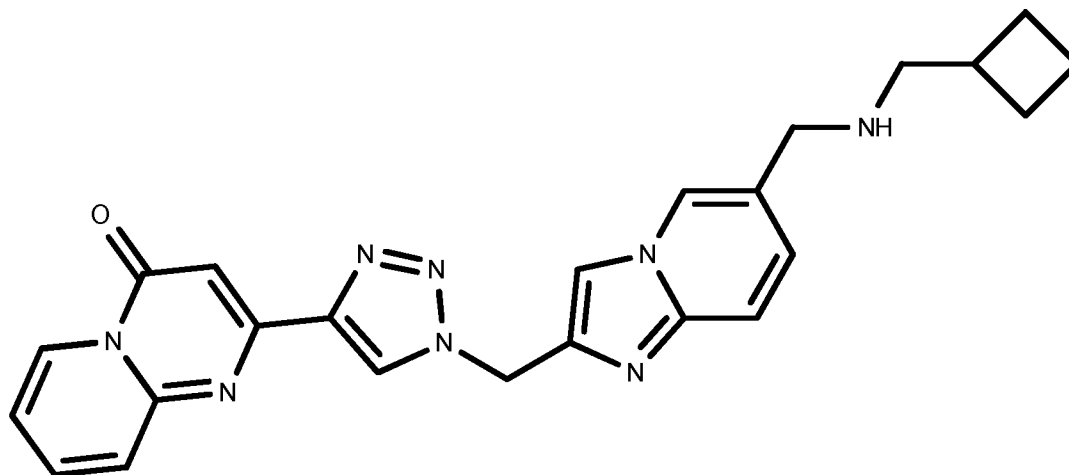


10 **[00965]** A mixture of 2-chloropyrido[1,2-a]pyrimidin-4-one (700 mg, 3.88 mmol), PdCl₂dppf (284 mg, 0.39 mmol), copper iodide (74 mg, 0.39 mmol) and trimethylamine (2.6 mL, 18.5 mmol) were combined in DMF (anhydrous, 4 mL) and sparged with nitrogen. Ethynyl(trimethyl)silane (1.6 mL, 11.6 mmol) was added and the mixture was briefly sparged with nitrogen and stirred at 100 °C for 16 hours.

15 **[00966]** The reaction mixture was cooled to room temperature diluted with NaHCO₃ (sat, 50 mL) and extracted with DCM (3 x 50 mL). The combined organic extracts were washed with NaHCO₃ (sat, 50 mL), dried over Na₂SO₄, and concentrated under vacuum. The residue was purified by chromatography on SiO₂ (Biotage 28 g SNAP NH, eluting with 0-50% EtOAc in heptane) to afford the title compound (302 mg, 46%) as a brown solid.

20 Method B: LC-MS (electrospray): m/z = 171.2 (M+H)⁺, RT = 1.14 min

[00967] Step 2: 2-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]pyrido[1,2-a]pyrimidin-4-one



[00968] 2-ethynylpyrido[1,2-a]pyrimidin-4-one (86 mg, 0.505 mmol), tert-butyl N-[[2-(azidomethyl)imidazo[1,2-a]pyridin-6-yl]methyl]-N-(cyclobutylmethyl)carbamate **Intermediate 65** (170 mg, 0.459 mmol) and CuSO₄ (4.6 mg, 0.0282 mmol) were combined in DMF (2 mL) and water (0.5 mL). Sodium ascorbate (137 mg, 0.688 mmol) was added and the mixture was stirred at room temperature for one and a half hours.

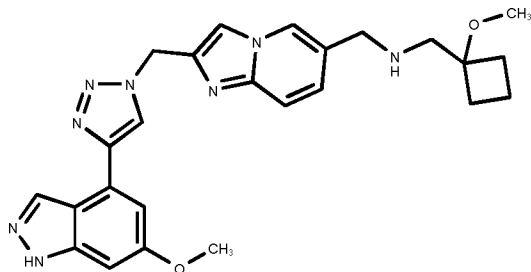
[00969] The mixture was diluted with chloroform/isopropanol (3:1, 40ml) and water (30ml) the phases were separated and the aqueous was extracted with CHCl₃/IPA (3:1, 3x20 mL). The combined organics were washed with water (50 mL), dried (Na₂SO₄) and concentrated under vacuum to a residue.

[00970] The material was dissolved in methanol (0.5 mL), HCl (4M in dioxane, 5 mL) was added and the mixture was stirred for an hour before the solvent was removed under vacuum.

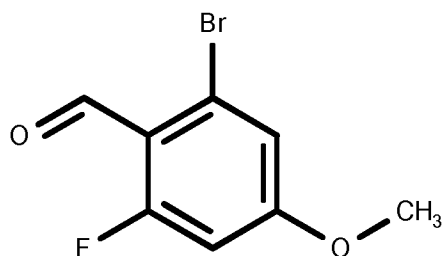
[00971] The residue was purified by preparative HPLC (method B) to give the title compound (92 mg, 46%) as an off-white solid.

Method C: LC-MS (electrospray): m/z = 441.4 (M+H)⁺, RT = 2.49 min.

[00972] **Example 343:** N-[(1-methoxycyclobutyl)methyl]-1-[2-[[4-(6-methoxy-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



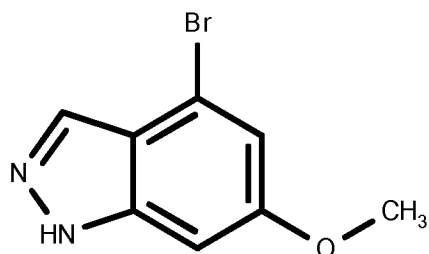
[00973] **Step 1:** 2-bromo-6-fluoro-4-methoxy-benzaldehyde



[00974] To a solution of N-isopropylpropan-2-amine (3.4 mL, 24.4 mmol) in THF (80 mL) at -78°C was added n-butyllithium (2.5M in hexanes, 10 mL, 24.4 mmol) dropwise and the mixture was stirred for 15 minutes before a solution of 1-bromo-3-fluoro-5-methoxybenzene (5.00 g, 24.4 mmol) in THF (10 mL) was added dropwise, and the mixture was stirred at -78°C for 20 minutes. DMF (1.1 mL, 12.2 mmol) was added dropwise and the mixture was stirred at -78°C for an hour, then quenched with HCl (1M, 50 mL) and allowed to warm to room temperature. The mixture was extracted with EtOAc (3 x 50 mL) and the combined organic layers were washed with brine, dried (Na₂SO₄) and evaporated under reduced pressure. The residue was purified by chromatography on SiO₂ (Biotage, 340 g) eluting with EtOAc/heptane 0-30% to afford the title compound (3.20 g, 56%) as a yellow solid.

Method A: LC-MS (electrospray): m/z = 232.9/234.9 (M+H)⁺, RT = 1.13 min.

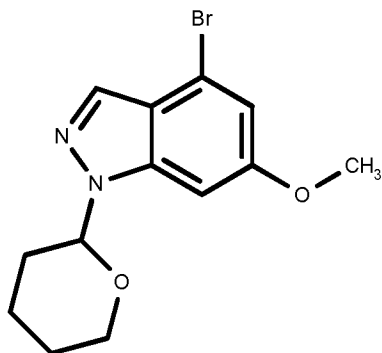
[00975] Step 2: 4-bromo-6-methoxy-1H-indazole



[00976] Hydrazine (55%, 2.6 mL, 34.8 mmol) was added to a solution of 2-bromo-6-fluoro-4-methoxybenzaldehyde (2.70 g, 11.6 mmol) in 1,4-dioxane (55 mL) and the mixture was stirred at 100 °C for 42 hours. The mixture was cooled to room temperature, and the solvent was removed under vacuum. The residue was dissolved in EtOAc (60 mL) and washed with water and brine, dried (Na₂SO₄) and evaporated under reduced pressure. The residue was purified by chromatography on SiO₂ (Biotage 100 g) eluting with EtOAc/heptane 10-50% to afford the title compound (750 mg, 26%) as an off-white solid.

Method A: LC-MS (electrospray): m/z = 226.9/228.9 (M+H)⁺, RT = 1.08 min.

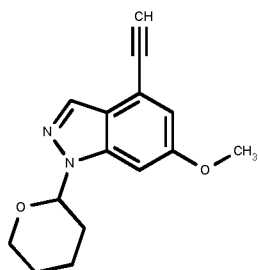
[00977] Step 3: 4-bromo-6-methoxy-1-tetrahydropyran-2-yl-indazole



[00978] To a mixture of 4-bromo-6-methoxy-1H-indazole (620 mg, 2.65 mmol) and tosic acid monohydrate (50mg, 0.26mmol) in DCM (20 mL) was added 3,4-dihydro-2H-pyran (0.75 mL, 7.95 mmol) and the reaction mixture was stirred at room temperature for 2 days
 5 then concentrated under vacuum. The residue was dissolved in EtOAc (60ml) and washed with water and NaHCO₃ (sat) . The organic layer was dried (Na₂SO₄) and evaporated under reduced pressure. The residue was purified by chromatography on SiO₂ (Biotage 100 g kp-Sil) eluting with EtOAc/heptane 0-25% to afford the title comound (720 mg, 81%) as a white gum.

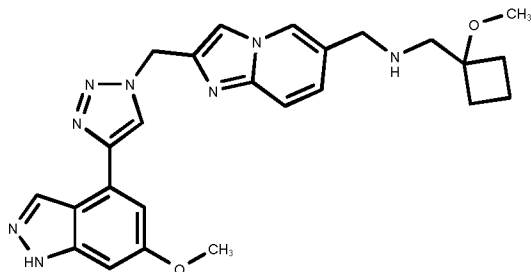
10 Method A: LC-MS (electrospray): m/z = 310.95/313.00 (M+H)⁺, RT = 1.43 min.

[00979] Step 4: 4-ethynyl-6-methoxy-1-tetrahydropyran-2-yl-indazole



[00980] The title compound was prepared from 4-bromo-6-methoxy-1-tetrahydropyran-2-yl-indazole using the chemistry described in **Intermediate 24 Steps 2 and 3** to give (210 mg, 34%) as a colourless oil which solidified on standing to a white solid.
 15 Method A: LC-MS (electrospray): m/z = 257.1 (M+H)⁺, RT = 1.22 min.

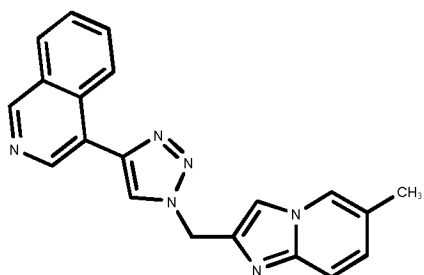
[00981] Step 5: N-[(1-methoxycyclobutyl)methyl]-1-[2-[[4-(6-methoxy-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



[00982] The title compound was prepared from 4-ethynyl-6-methoxy-1-tetrahydropyran-2-yl-indazole and [2-(azidomethyl)imidazo[1,2-a]pyridin-6-yl]methanol using the chemistry described in **Compound 268 Steps 2, 3 and 4** to give (95 mg, 65%) as a white solid.

5 Method C: LC-MS (electrospray): m/z = 473.5 (M+H)⁺, RT = 2.43 min.

[00983] **Example 344:** 4-[1-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]triazol-4-yl]isoquinoline



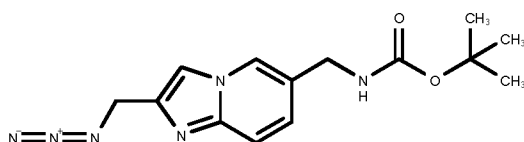
[00984] 2-(azidomethyl)-6-methyl-imidazo[1,2-a]pyridine **Intermediate 23** (50mg, 0.27mmol), 4-ethynylisoquinoline (49mg, 0.32mmol) and sodium ascorbate (80mg, 0.40mmol) were combined in DMF (2ml) and Water (0.5ml), CuSO₄ (4mg, 0.03mmol) was added and the mixture was stirred at room temperature for 30 minutes during which time a precipitate formed.

[00985] The mixture was diluted with water (15 ml) and the solids were collected by filtration. The residue was purified by reverse phase chromatography (method B) to afford the title compound (24mg (26%)) as an off-white solid.

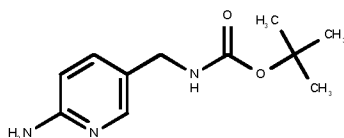
Method D: LC-MS (electrospray): m/z = 341.3 (M+H)⁺, RT = 3.33 min.

[00986] **Intermediate 66:** tert-butyl N-[(2-(azidomethyl)imidazo[1,2-a]pyridin-6-yl)methyl]carbamate

20



[00987] Step 1: tert-butyl N-[(6-aminopyridin-3-yl)methyl]carbamate

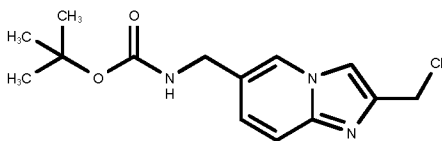


[00988] A solution of 6-aminopyridine-3-carbonitrile (1.00 g, 8.39 mmol) and tert-butoxycarbonyl tert-butyl carbonate (3.66 g, 16.8 mmol) in MeOH (32 mL) was cooled to 0 °C and treated with nickel (II) chloride (1.10 g, 8.39 mmol) followed by the addition of sodium borohydride (2.86 g, 75.6 mmol) in small portions. The mixture was stirred and allowed to warm to room temperature overnight.

[00989] The stir was continued for 24 hours before the black suspension was evaporated under vacuum, quenched by the addition of NaHCO₃ (sat) and EtOAc was added. The solids were removed by filtration through Celite (washing with EtOAc). The phases were separated and the aqueous extracted with EtOAc. The organics were washed with brine, dried (MgSO₄) and evaporated under vacuum to a brown foam which was purified by chromatography on SiO₂ (Biotage KPNH 28 g) eluting with 0-100% EtOAc in heptane to give the title compound (734 mg, 28%) as a beige foam along with an earlier eluting product (178 mg).

Method B: LC-MS (electrospray): m/z = 224.3 (M+H)⁺, RT = 1.24 min.

[00990] Step 2: tert-butyl N-[[2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl]methyl]carbamate

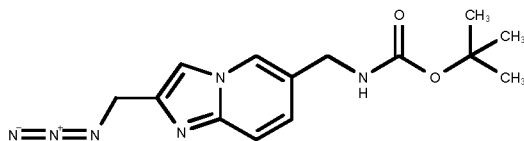


[00991] A solution of tert-butyl N-[(6-amino-3-pyridyl)methyl]carbamate (730 mg, 3.27 mmol) and 1,3-dichloropropan-2-one (450 µL, 4.90 mmol) in MeCN (20 mL) was stirred at 80 °C for 20 hours.

[00992] The mixture was cooled to room temperature, evaporated to dryness and purified by chromatography on SiO₂ (Biotage; 28 g KP-NH) eluting with EtOAc in heptane 50-100% to afford the title compound (581 mg, 52%) as a beige solid.

Method B: LC-MS (electrospray): m/z = 296.2 (M+H)⁺, RT = 1.53 min.

[00993] Step 3: : tert-butyl N-[[2-(azidomethyl)imidazo[1,2-a]pyridin-6-yl]methyl]carbamate



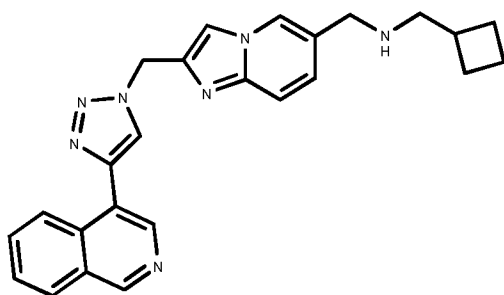
[00994] A solution of tert-butyl N-[[2-(chloromethyl)imidazo[1,2-a]pyridin-6-yl]methyl]carbamate (581 mg, 1.96 mmol) and NaI (30 mg, 0.196 mmol) in DMF (4 mL) was treated with NaN₃ (255 mg, 3.93 mmol) and the mixture was stirred at room temperature 17 hours.

[00995] The brown suspension was quenched with NaHCO_3 (sat, 10 ml) and extracted with chloroform/isopropanol (3:1, 3 x 80ml). The combined organic extracts were dried (Na_2SO_4) and evaporated under vacuum. The residue was triturated with EtOAc/heptane and the solids were collected by filtration to afford the title compound

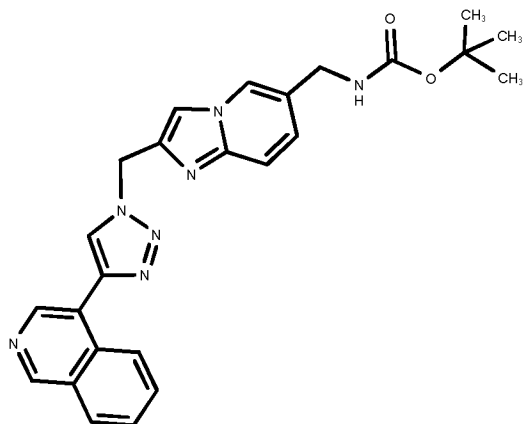
(400mg, 67%) as a beige solid.

Method B: LC-MS (electrospray): $m/z = 303.2$ ($\text{M}+\text{H}^+$), $\text{RT} = 1.42$ min.

[00996] **Example 345:** N-(cyclobutylmethyl)-1-[2-[[4-(4-isoquinolyl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



[00997] **Step 1:** tert-butyl N-[[2-[[4-(4-isoquinolyl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methyl]carbamate



[00998] Under nitrogen atmosphere, isoquinoline-4-carbaldehyde (100 mg, 0.636 mmol) was suspended in MeOH (anhydrous, 1 mL) and THF (anhydrous, 1 mL), dimethyl (1-diazo-2-oxopropyl)phosphonate (245 mg, 1.28 mmol) and K_2CO_3 (264 mg, 1.91 mmol) were added to the reaction mixture and stirred for 5 hours.

[00999] Tert-butyl N-[[2-[[4-(4-isoquinolyl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methyl]carbamate

[001000] **Intermediate 66** (193 mg, 0.636 mmol) and copper(I) iodide (25 mg, 0.131 mmol) were added and the mixture was stirred at room temperature for 2 hours.

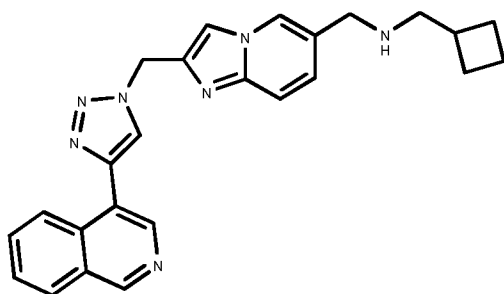
[001001] Water was added and the mixture was extracted with CHCl_3/IPA x 3. The organic extracts were combined, dried (MgSO_4) and evaporated under vacuum to give the crude material which was

[001002] Purified by chromatography on SiO_2 (Botage, KP-NH) eluting with

5 Heptane/EtOAc 50 to 100% followed by 5% MeOH in EtOAc) to give the title compound (84 mg, 29%) as an off-white solid.

Method B: LC-MS (electrospray): m/z = 456.4 ($\text{M}+\text{H}$)⁺, RT = 1.42 min.

[001003] Step 2: N-(cyclobutylmethyl)-1-[2-[[4-(4-isoquinolyl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine



[001004] To a solution of [2-[[4-(4-isoquinolyl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine (13 mg, 0.0368 mmol) in DCE (1.0 ml) was added cyclobutanecarbaldehyde (3.1 mg, 0.0368 mmol) and the reaction was stirred at room temperature for 30 minutes, before sodium triacetoxyborohydride (16 mg, 0.0737 mmol) was added and the reaction was stirred at 40 °C for 2 hours.

[001005] The reaction was cooled to room temperature and the solvent was removed in vacuo. Water (5 ml) and NaOH (1M, 2.0 ml) were added and the aqueous was extracted with IPA- CHCl_3 (1:4, 3 x 3 ml). The organics dried (Na_2SO_4) and evaporated under reduced pressure to give a yellow gum, which was purified by preparative HPLC (method B) to give the title compound (2.1 mg, 13%) as an off white solid along with the bis alkylated by-product.

Method C: LC-MS (electrospray): m/z = 424.4 ($\text{M}+\text{H}$)⁺, RT = 2.87 min.

[001006] **Intermediate 67:** [rel-(1S,2R,4S)-7-oxabicyclo[2.2.1]hept-5-en-2-yl]methanamine and [rel-(1S,2S,4S)-7-oxabicyclo[2.2.1]hept-5-en-2-yl]methanamine



[001007] Prepared according to Tetrahedron, 49 (8), 1649-1664, 1993.

Abbreviations:

HATU - [dimethylamino(triazolo[4,5-b]pyridin-3-yloxy)methylene]-dimethyl-ammonium-hexafluorophosphate

5 DCM - Dichloromethane

DIPEA - N-ethyl-N-isopropyl-propan-2-amine

DEAD - Diethylazodicarboxylate

DMF - Dimethylformamide

EtOAc - Ethyl acetate

10 EtOH - Ethanol

MeCN - Acetonitrile

RT - Retention Time

Phase separation cartridge - Telos phase separator 6 mL

STAB – Sodium triacetoxymethylborohydride

15 THF – Tetrahydrofuran

XPHOS - dicyclohexyl-[2-(2,4,6-triisopropylphenyl)phenyl]phosphane

Example 3: METTL3/14 methyltransferase assay**[001008] Biochemical assay - METTL3_14 RFMS**

20 **[001009]** The enzymatic assay was established to determine IC₅₀ values for inhibition of RNA methyltransferase activity. The enzyme used was full-length his-tagged METTL3 co-expressed with full length FLAG-tagged METTL14 in a baculovirus expression system. Enzymatic reactions were performed at room temperature in 384-well plates using a final reaction volume of 20 µL containing 20 mM TrisCl pH 7.6, 1 mM DTT, 0.01% Tween-20. 5

25 nM final concentration of METTL3/14 was pre-incubated with various compound concentrations for 10 minutes, followed by addition of 0.2 µM final concentration synthetic RNA substrate (5'-uacacucgaucuggacuaaagcugcuc-3') and 0.5 µM final concentration S-adenosyl-methionine (SAM). The reaction was incubated for further 60 minutes at room temperature, and then quenched by the addition of 40 µL 7.5% TCA with two internal

30 product standards (D₄-SAH and ¹³C₁₀-SAH). After termination, plates were sealed, centrifuged and stored at 4°C until analysis. Note: the lower limit of the assay is IC₅₀ = 5nM.

[001010] Mass spectrometry analysis

[001011] RNA methyltransferase activity was measured label free using the RapidFire™ mass spectrometry (RF/MS) platform. Stopped and stable assay plates were

35 analyzed on the Agilent RF300 integrated autosampler/solid-phase extraction (SPE) system coupled to an ABSciex 4000 mass spectrometer for the generation of the product S-

adenosyl homocysteine (SAH) and normalized to the ratio of signal of the two internal product standards, respectively. Solvent A was water containing 0.1% (v/v) TCA. Solvent B was acetonitrile/0.1% ammonium acetate (8:2, v/v). More specifically, plates were centrifuged at 4350 rpm for 10 min, samples were aspirated under vacuum for 600 ms, then loaded onto a C18 solid-phase extraction cartridge and washed for 3 s with solvent A at a flow rate of 1.5 mL/min. Retained product and internal standards were eluted with solvent B at a flow rate of 1 mL/min for 3 s and finally the cartridge was reequilibrated with solvent A for 500 ms. The mass transition for the product (SAH) was 384.9/135.9 Da. Transitions of the two internal product standards (IS1: D₄-SAH and IS2: ¹³C₁₀-SAH) were 389.1/135.8 Da and 395.0/134.2 Da, respectively. Ratios of SAH/IS1 and SAH/IS2 were used for normalization of matrix effects. IC₅₀ values were calculated based on dilution series of individual compounds. Potency of a compound was measured at varied inhibitor concentrations and normalized to control wells without RNA substrate and without inhibition (DMSO only).

Results:

Compound No	METTL3_14 RFMS IC ₅₀ nM
1	5600
2	9840
3	4660
4	6070
5	9450
6	9120
7	2670
8	4560
9	2710
10	1610
11	4100
12	1410
13	4180
14	5900
15	536
16	8010
17	2240
18	1859
19	2600
20	8410
21	3060
22	2210
23	1790

24	6770
25	543
26	2060
27	6610
28	5340
29	2780
30	8520
31	9350
32	7340
33	5870
34	5350
35	15820
36	3910
37	4740
38	5440
39	1470
40	7390
41	1340
42	6260
43	1290
44	5050
45	2580
46	2210
47	3980
48	2040
49	1040
50	272
51	1220
52	267
53	38
54	16
55	87
56	945
57	702
58	299
59	939
60	700
61	695
62	8760

Compound No	METTL3_14 RFMS IC50 nM
63	299

64	7326
65	6600
66	1350
67	8140
68	5090
69	1340
70	143
71	206
72	18.52
73	64.9
74	122
75	48.1
76	30
77	84
78	163
79	62.5
80	16.5
81	27.67
82	354
83	10.64
84	36.5
85	25.5
86	23.1
87	48.5
88	114
89	1860
90	79.2
91	57.6
92	112
93	13
94	131
95	74.4
96	947
97	1020
98	45.6

99	318
100	1380
101	18.1
102	429
103	13.7
104	69.07
105	1200
106	15
107	143
108	241
109	350
110	102
111	109
112	755
113	16.42
114	244
115	43.5
116	280
117	83.7
118	87.2
119	578
120	24.7
121	16.8
122	110
123	332
124	119
125	221
126	79.8
127	429
128	333
129	84.3
130	206
131	87.7
132	917
133	480

134	440
135	18.3
136	99
137	17.8
138	31.4
139	32.6
140	18.7
141	14.5
142	48.8
143	136
144	59.7
145	276
146	25.1
147	224
148	28.5
149	40.21
150	29.9
151	16.3
152	104
153	1580
154	1180
155	177
156	61.7
157	42.9
158	3810
159	19.5
160	93.2
161	99.1
162	225
163	80.1
166	10500
167	8070
168	114
169	391
170	29.4

171	293
172	309
175	214
176	909
177	1890
178	209
180	889
181	179
182	179
185	1070
187	44.1
188	1190
189	132
190	56.1
191	4790
193	12.4
194	305
195	32.4
196	597
197	84.8
198	44.1
199	1860
200	1260
202	61.1
203	32
204	61.5
205	197
206	15.6
207	37.9
208	5730
209	10
210	20.3
211	19.3
212	6.25
213	41.8

214	15.8
215	54.3
216	14.9
217	7.58
218	26.4
219	247
220	168
221	46.7
222	33.9
223	2170
224	1870
225	6.69
226	8.145
227	7.898
228	239
229	100
230	81.26
231	1220
232	8370
233	1390
234	3440
235	111
236	28.7
237	742
238	850
239	513
240	260
241	2110
242	68
243	1450
245	735
247	1080
248	12.7
249	229
250	11.34

251	5.76
252	8.02
253	207
254	10100
255	25.8
256	246
257	4440
263	2730
264	195
265	50.6

Compound	METTL3_14 RFMS IC50 nM
266	4.23
267	6.95
268	10.6
269	8.05
270	3.63
271	6.1
272	9020
273	27.7
274	1510
275	1240
276	6.1
277	76.3
278	27.6
279	6.19
280	13.14
281	98.7
282	10.6
283	29.3
284	11.53
285	15.01
286	19.3
287	69.5
288	13.89
289	103
290	17.98
291	62.2
292	19.96
293	12.77
294	5.8
295	6.1
296	4.44
297	737
298	42.1
299	112

300	511
301	233
302	4.35
303	5.92
304	6.1
305	6.009
306	9.46
307	6.721
308	11.4
309	120
310	186
311	19
312	52.1
313	37.6
314	7110
315	19.3
316	38.4
317	462
318	5.67
319	7.838
320	6.156
321	13.2
322	32.5
324	8.857
325	14.49
326	76.6
327	5.776
328	8.837
329	1640
330	202
331	3440
332	1700
333	1230
334	122
335	7290
336	4160
337	16.3
338	7.49
339	10.1
340	6810
341	64.4
342	18.4
343	6.1
346	7.68
347	7.5
348	9.02
349	303
350	56.2
351	24.1

Example 4: Cell assay protocols

[001012] MOLM-13 and MOLM-14 cell culture

[001013] MOLM-13 and MOLM-14 cells (Purchased from Leibniz-Institut DSMZ-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH) were established from the blood of a 20 year old man with acute myeloid leukaemia (AML) in 1995 and are of a round morphology which grow in suspension. These are regularly maintained in aseptic tissue culture conditions, and grown in RPMI 1640 media containing 10% FBS at a density of $0.4-2 \times 10^6/\text{ml}$.

[001014] Treatment of MOLM-13 and MOLM-14 cells with METTL3 inhibitors

[001015] MOLM-13 or MOLM-14 cells were plated, in suspension, in 24 well tissue culture plates at final concentration of 200,000/ml, with or without 50ng/ml IFN γ . METTL3 inhibitors (Compound 15, Compound 54, Compound 55, and Compound 53) were dissolved in DMSO, titration curve generated at 200x final concentration, compounds were then diluted in tissue culture media (RPMI 1640, 10% FBS) before being added to MOLM-13 or MOLM-14 cells in a final DMSO concentration of 0.5%, final volume 1ml. Cells were incubated for 4 days at 37°C at which point 600 μl of cell suspension was removed for Mass spectrometry analysis of m6A. 600 μl of fresh media containing the appropriate concentration of METTL3 inhibitor/IFN γ was added to remaining cell suspensions. Cells were then cultured for a further 7 days, cell suspension was sampled for analysis of proliferation and Cell surface markers periodically.

[001016] Analysis of Cell proliferation

[001017] At regular time points (4,5,6 & 7) days cells were mixed to maintain a homogenous cell suspension. 25 μl of this cell suspension was removed and added to a white 384 well plate, 25 μl of Cell Titre Glo reagent (Promega) was added, and incubated for 10 mins at room temperature before measurement of luminescence intensity, as per the manufacturers instructions.

[001018] Analysis of Cell surface markers

[001019] Cell surface CD markers were measured via flow cytometry. 300 μl of a homogenous cell suspension was removed after 6 days. Samples were washed in PBS containing 0.5% BSA, and resuspended in 1ml PBS 0.5% BSA. 5 μl of anti-CD14-FITC, 5 μl of anti-CD11b-APC and 2 μl of DAPI were added to all samples and incubated in the dark at room temperature for 15 mins. Samples were analysed on Becton Dickinson LSR II.

[001020] Isolation of individual nucleosides from cellular samples.

[001021] Compound-treated cells were harvested by centrifugation and the total RNA content was extracted using a silica filter-based method (PureLink™ Pro 96 total RNA

Purification Kit ThermoFisher Scientific Catalog number: 12173011A). Up to 10µg of RNA was digested by adding 1µl digestion enzyme mix per well in a digest buffer, final concentrations: Tris-HCl pH 8 (4 mM), MgCl₂ (5 mM), NaCl (20 mM) in a total volume of up to 100µl.

5 **[001022]** The digestion enzyme mix was made by mixing benzonase (250 U/µl, Sigma Aldrich Cat# E1014-25KU), phosphodiesterase I from *Crotalus adamanteus* venom (10mU/µl, Sigma Aldrich Cat# P3243) and Antarctic phosphatase (5 U/µl, NEB Cat# M0289L) in a ratio of 1:10:20. This was incubated overnight at 37C.

10 **[001023]** The following day an equal volume of ¹³C, ¹⁵N-labelled Uridine (Sigma Aldrich Cat #645672 that had been previously dephosphorylated) in 0.1% formic acid was added to each reaction and this was subsequently prepared for LC-MSMS by filtration through 30kDa molecular weight cut-off filters (Sigma, Cat# UFC503096).

[001024] Mass Spectrometric analysis of m6A

15 **[001025]** Samples were resolved using a Thermo Scientific U3000 UPLC system on a gradient of 2-98% [0.1% formic acid/acetonitrile] through an Acquity 100mm x 2.1mm C-18 HSS T3 column and analysed on a QExactive-HF Orbitrap High Resolution Mass Spectrometer (ThermoFisher Scientific Cat# IQLAAEGAAPFALGMBFZ) in positive full-scan mode and the results were deconvoluted using the accompanying Xcalibur Software.

20 Nucleosides of interest (including adenosine, cytidine, guanosine, uridine, ¹³C, ¹⁵N-labelled uridine and m6A) were identified by both retention time and accurate masses and compared to purified standards and quantified accordingly.

[001026] A schematic of the timings of the processes outlined above is shown in Figure 1.

25

[001027] Results

[001028] METTL3 inhibitors Compound 15 (IC₅₀ 520nM), Compound 54 (16nM), Compound 55 (66nM), Compound 53 (27nM) tested in MOLM13 cells at concentrations ranging from 50-0.1µM

30 **[001029]** Total RNA isolated at day 4. METTL3 inhibitors show dose dependent decrease in m6A which correlates with their activity from primary enzyme screen, see Figure 2.

[001030] Proliferation measured every 24 hours (Day3- Day7). METTL3 inhibitors show dose dependent decrease in MOLM13 proliferation which correlates with their activity from primary enzyme screen and m6A levels, see Figure 3.

35

[001031] Expression of CD14 measured at day 6 via flow cytometry. METTL3 inhibitors show dose dependent increase of CD14 cell surface expression in MOLM13 cells which correlates with their activity from primary enzyme screen and m6A levels, see Figure 4.

- 5 **[001032]** Proliferation in other cell lines (MOLM14, Kasumi-1, NOMO-1, THP.1, and KCL-22) was investigated for Compound 54, see Figures 5 and 6. A similar potency profile was observed in other AML cell lines, indicating that this is not specific to one particular AML cell line.

MOLM13 CTG - Analysis of Cell proliferation

Example No	CTG MOLM13 cells IC50 GEOMEAN (nM)
72	8699
74	30000
78	6040
83	4117
87	30000
89	13090
93	6254
103	6796
104	8729
112	12700
114	2800
126	30000
127	30000
178	9890
193	2462
195	9768
203	8741
206	9134
207	10250
209	6577
210	5019
211	11390
212	1819
213	30000
214	7338
216	3508
217	2931
218	4708
225	649.3
226	1475
227	338
235	30000
236	11770
237	12900
248	1927
250	2999
251	727.1
252	714.5
253	2790
254	30000
255	9612
263	13850
265	12980
266	11140
267	30000
268	5334
269	1392

270	430.9
271	1167
273	9021
276	657.4
278	30000
279	1334
280	4505
281	30000
282	3423
283	10740
284	7402
285	7372
286	12320
287	30000
288	7315
290	6975
292	7191
293	4725
294	998.1
295	905.9
296	362.5
297	30000
298	30000
299	30000
300	30000
302	628.6
303	1440
304	1474
305	1831
306	3926
307	3681
308	5614
311	3680
313	11310
315	8360
316	12630
318	1183
319	4377
320	2762
322	11020
324	3276
325	7503
326	10680
327	1616
328	3253
330	30000
334	17930
337	5166
338	1189
339	3071
342	6710
343	929.8

CTG assay (Caov3 cell line)

Cell culture: Caov-3 cells (HTB-75, Lot number: 70016791, ATCC) were grown in DMEM (11960-04431053-028, Gibco) supplemented with 10% fetal bovine serum (1600-44, Gibco), 1 mM sodium pyruvate (11360-039, Gibco) and 2mM Glutamax (35050-038, Gibco) at 37°C with 5% CO₂.

Cell treatment and cell growth assessment: 18 hours post-seeding in white 384-Viewplate (6007480, PerkinElmer) at 1500 cells/well, Caov3 cells were treated for 120 hours with compounds inhibiting the METTL3/14 activity (10 serial semi-log dilutions, 30 µM as top concentration). Upon treatment, Coav-3 cells were incubated for 10 min at RT with the CellTiter-Glo reagent (G7571, Promega). Measurement of the luminescence signal was performed on a microplate reader (Ensign, PerkinElmer).

Caov3 CTG assay – Proliferation Assay

Example No	CTG Caov3 cells IC ₅₀ GEOMEAN nM
212	320
227	182
269	692
270	161
271	558
276	248
279	296
302	211
307	1770
327	572
337	3210
338	1110
339	849
343	554

Numbered Paragraphs

The following numbered paragraphs serve to define particular aspects and embodiments of the invention.

Paragraph 1. A compound of the formula (I), or a pharmaceutically acceptable salt thereof,

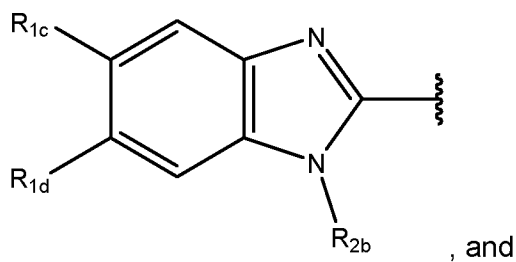
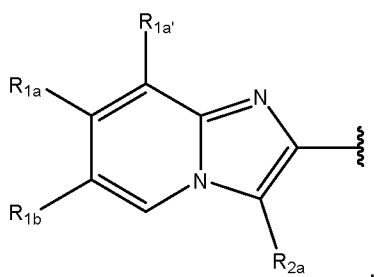
5



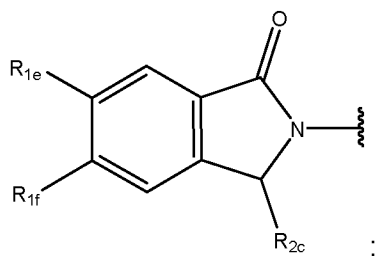
(I)

wherein:

X is selected from:



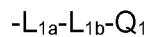
10



wherein:

R_{1a}, R_{1b}, R_{1c}, R_{1d}, R_{1e} and R_{1f} are independently selected from hydrogen, cyano, halo or a group of the formula:

15



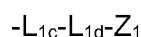
wherein

L_{1a} is absent or C₁₋₃alkylene, C₃₋₄cycloalkylene, optionally substituted by one or more substituents selected from C₁₋₂alkyl, halo, hydroxy, or oxo;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl; and

Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u, N(R_t)SO₂R_u or (CH₂)_zNR_tR_u (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



wherein

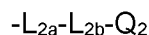
L_{1c} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

L_{1d} is absent or selected from C(O), O, C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

Z₁ is C₃₋₈cycloalkyl, heterocyclyl, phenyl or 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, C₁₋₄alkylamino, amino, cyano, hydroxyl, carboxy, carbamoyl or sulphamoyl; NR_{t1}R_{u1}, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, C(O)N(R_{t1})R_{u1}, N(R_{t1})C(O)R_{u1}, S(O)_yR_{t1} (where y is 0, 1 or 2), SO₂N(R_{t1})R_{u1}, N(R_{t1})SO₂R_{u1} or (CH₂)_zNR_{t1}R_{u1} (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C₁₋₄alkyl; and when Z₁ is C₃₋₈cycloalkyl or heterocyclyl, Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclyl;

R_{1a'} is selected from hydrogen and methyl;

R_{2a}, R_{2b} and R_{2c} are selected from hydrogen or a group of the formula:



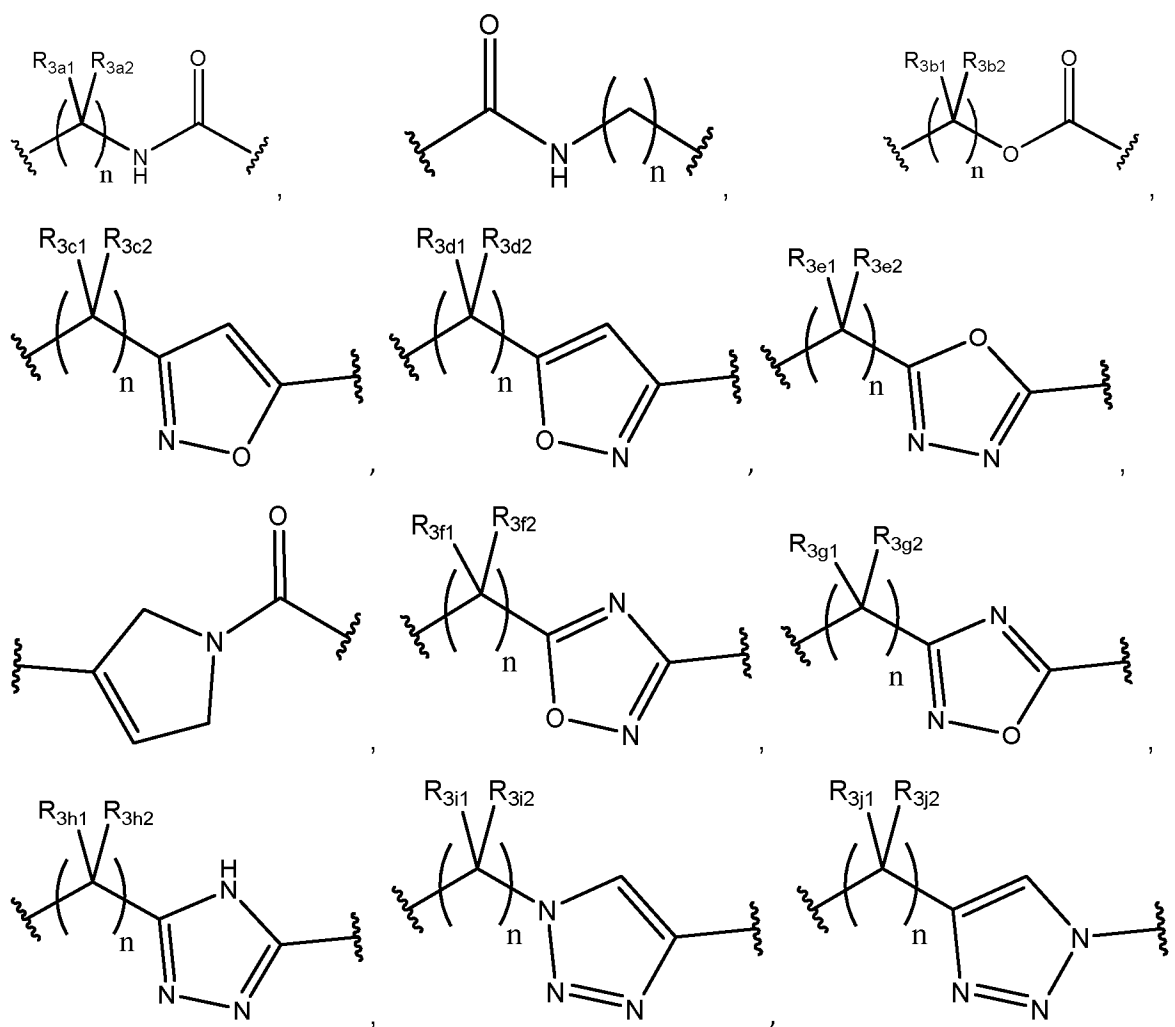
wherein

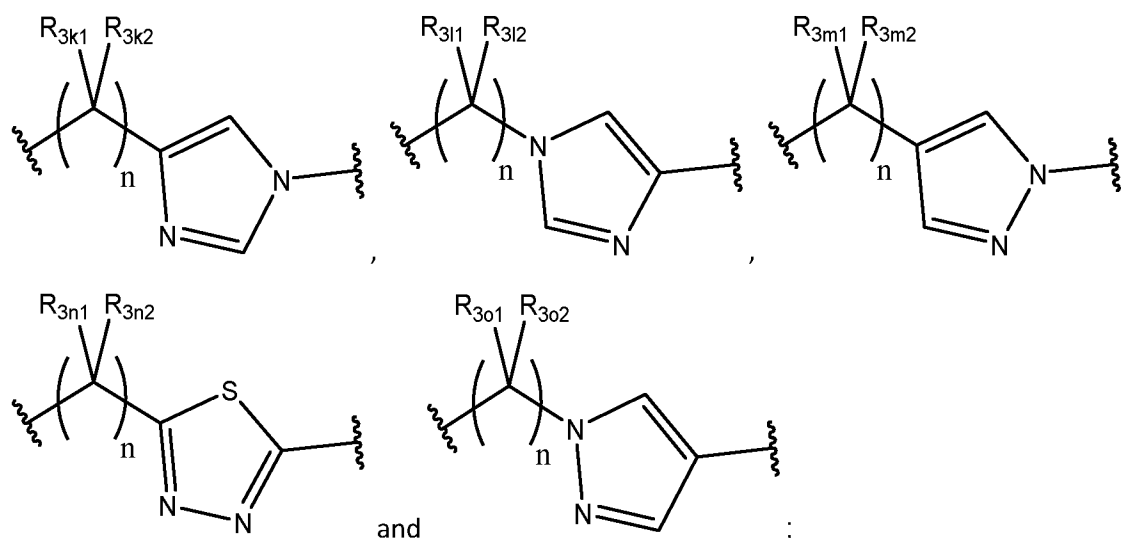
L_{2a} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

L_{2b} is selected from O, S, SO, SO₂, N(R_n), C(O), C(O)O, OC(O), C(O)N(R_n), N(R_n)C(O), N(R_n)C(O)N(R_o), S(O)₂N(R_n), or N(R_n)SO₂, wherein R_n and R_o are each independently selected from hydrogen or C₁₋₂alkyl; and

Q₂ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₆cycloalkyl, aryl, heterocyclyl or heteroaryl, each of which is optionally substituted by one or more substituents selected from halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, amino, carboxy, carbamoyl, sulphamoyl, C₁₋₄alkyl, NR_pR_q, OR_p, C(O)R_p, C(O)OR_p, OC(O)R_p, C(O)N(R_p)R_q, N(R_r)C(O)R_p, S(O)_yR_p (where y is 0, 1 or 2), SO₂N(R_p)R_q, N(R_r)SO₂R_p or (CH₂)_zNR_pR_q (where z is 1, 2 or 3), wherein R_p and R_q are each independently selected from hydrogen or C₁₋₄alkyl;

Y is selected from:





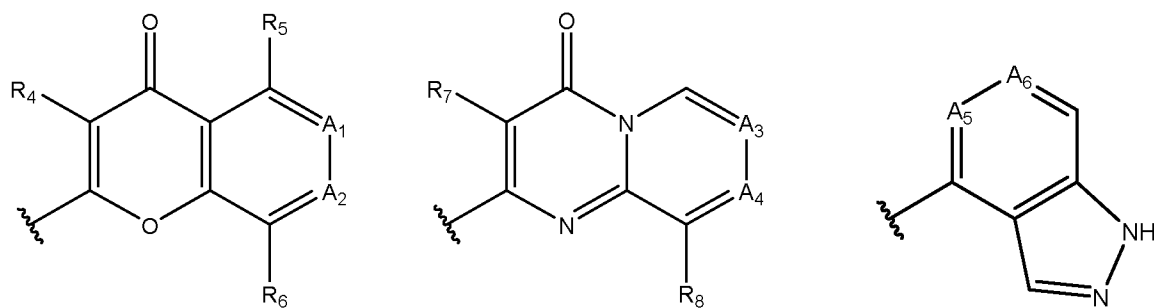
wherein:

R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} and R_{3o1} are independently selected from hydrogen, C_{1-6} alkyl, C_{3-4} cycloalkyl, hydroxy, and halo; and wherein C_{1-6} alkyl, or C_{3-4} cycloalkyl is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

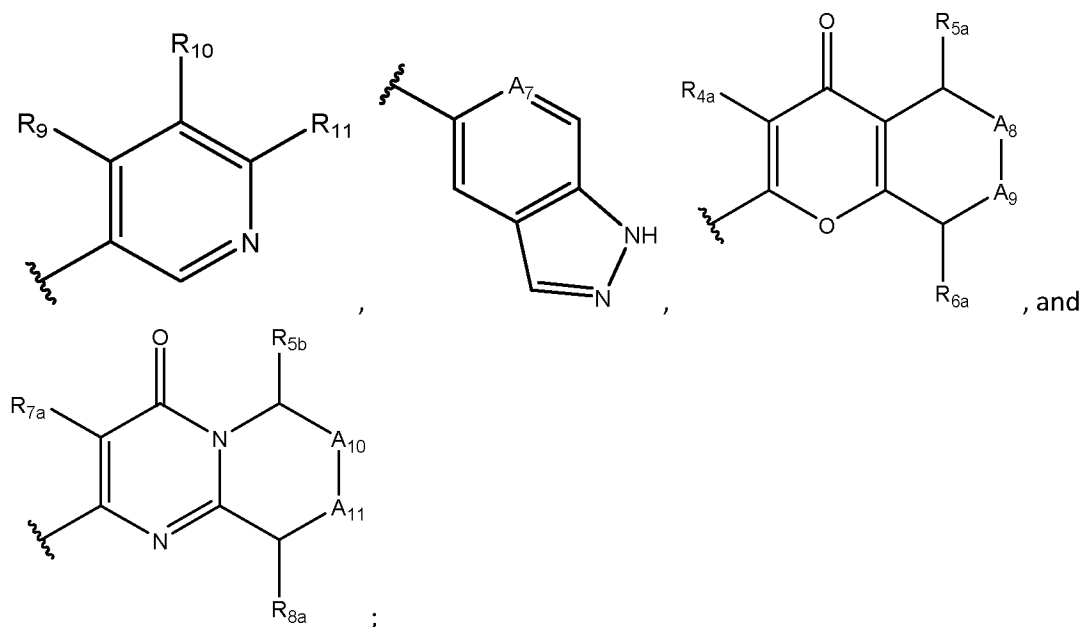
R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} and R_{3o2} are hydrogen;

or R_{3a1} and R_{3a2} , R_{3b1} and R_{3b2} , R_{3c1} and R_{3c2} , R_{3d1} and R_{3d2} , R_{3e1} and R_{3e2} , R_{3f1} and R_{3f2} , R_{3g1} and R_{3g2} , R_{3h1} and R_{3h2} , R_{3i1} and R_{3i2} , R_{3j1} and R_{3j2} , R_{3k1} and R_{3k2} , R_{3l1} and R_{3l2} , R_{3m1} and R_{3m2} , R_{3n1} and R_{3n2} , or R_{3o1} and R_{3o2} may be linked to form a spiro-fused C_{3-4} cycloalkyl which is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

Z is selected from:



and



wherein:

R_4 , R_7 , R_{4a} and R_{7a} are independently selected from hydrogen and methyl;

5 R_5 , R_{5a} and R_{5b} are independently selected from hydrogen and halo;

R_6 , R_8 , R_{6a} and R_{8a} are independently selected from hydrogen, halo and methyl;

R_9 , R_{10} and R_{11} are independently selected from hydrogen, NH_2 , halo, cyano, and C_{1-6} alkyl; or

10 R_9 and R_{10} may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system or R_{10} and R_{11} may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system;

A_1 is selected from CR_{12} and N;

A_2 is selected from CR_{13} and N;

A_3 is selected from CR_{14} and N;

15 A_4 is selected from CR_{15} and N;

A_5 is selected from CR_{16} and N;

A_6 is selected from CR_{17} and N;

A_7 is selected from CR_{18} and N;

A_8 is selected from $CR_{19}R_{20}$ and NR_{21} ;

20 A_9 is selected from $CR_{22}R_{23}$ and NR_{24} ;

A_{10} is selected from $CR_{25}R_{26}$ and NR_{27} ;

A₁₁ is selected from CR₂₈R₂₉ and NR₃₀;

R₁₂ and R₁₄ are independently selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₁₃ is selected from hydrogen, halo, cyano and methyl;

R₁₅ is selected from hydrogen, methoxy and methyl;

5 R₁₆ is selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₁₇ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl and a 5- or 6-membered heteroaryl;

R₁₈ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl and a 5- or 6-membered heteroaryl;

10 R₁₉, R₂₀, R₂₅ and R₂₆ are selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₂₂ and R₂₃ are selected from hydrogen, halo, cyano and methyl;

R₂₈ and R₂₉ are selected from hydrogen, methoxy and methyl;

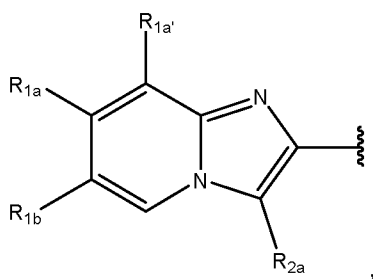
R₂₁, R₂₄, R₂₇ and R₃₀ are hydrogen; and

n is 0, 1 or 2.

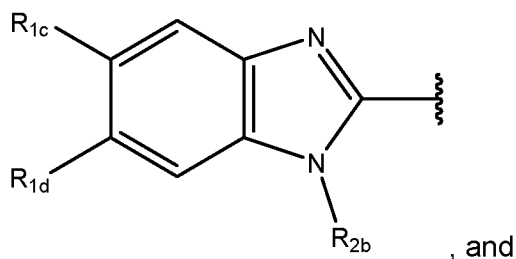
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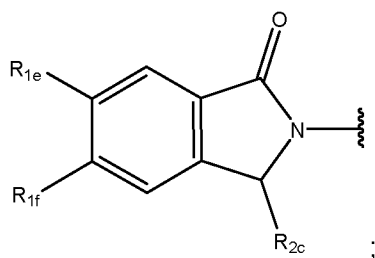
Paragraph 2. A compound of the formula (I), or a pharmaceutically acceptable salt thereof, according to Paragraph 1, wherein:

X is selected from:



20





wherein:

R_{1a} , R_{1b} , R_{1c} , R_{1d} , R_{1e} and R_{1f} are independently selected from hydrogen, cyano, halo or a group of the formula:



wherein

L_{1a} is absent or C_{1-3} alkylene, C_{3-4} cycloalkylene, optionally substituted by one or more substituents selected from C_{1-2} alkyl, halo, hydroxy, or oxo;

10 L_{1b} is absent or selected from O, S, SO, SO_2 , $N(R_r)$, C(O), $C(O)O$, $OC(O)$, $C(O)N(R_r)$, $N(R_r)C(O)$, $N(R_r)C(O)N(R_s)$, $S(O)_2N(R_r)$, or $N(R_r)SO_2$, wherein R_r and R_s are each independently selected from hydrogen or C_{1-2} alkyl; and

15 Q_1 is hydrogen, cyano, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u , OR_t , $C(O)R_t$, $C(O)OR_t$, $OC(O)R_t$, $C(O)N(R_t)R_u$, $N(R_t)C(O)R_u$, $S(O)_yR_t$ (where y is 0, 1 or 2), $SO_2N(R_t)R_u$, $N(R_t)SO_2R_u$ or $(CH_2)_zNR_tR_u$ (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C_{1-4} alkyl; or

Q_1 is optionally substituted by a group of the formula:



wherein

L_{1c} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

25 L_{1d} is absent or selected from C(O), $C(O)O$, $OC(O)$, $C(O)N(R_v)$, $N(R_v)C(O)$, $N(R_v)C(O)N(R_w)$, $S(O)_2N(R_v)$, or $N(R_v)SO_2$, wherein R_v and R_w are each independently selected from hydrogen or C_{1-2} alkyl; and

Z_1 is phenyl or 5-6 membered heteroaryl; wherein Z_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, C_{1-4} haloalkyl, C_{1-4} haloalkoxy,

C₁₋₄alkoxy, C₁₋₄alkylamino, amino, cyano, hydroxyl, carboxy, carbamoyl or sulphamoyl;

R_{1a}' is selected from hydrogen and methyl;

R_{2a}, R_{2b} and R_{2c} are selected from hydrogen or a group of the formula:



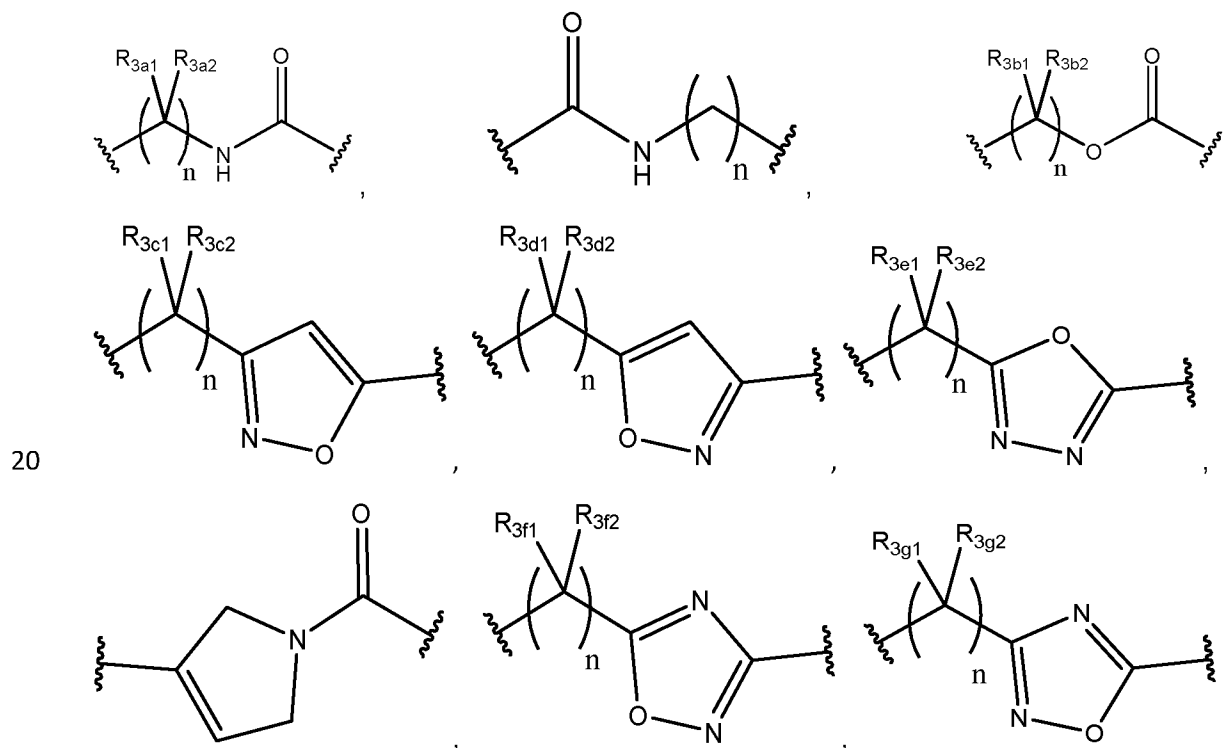
wherein

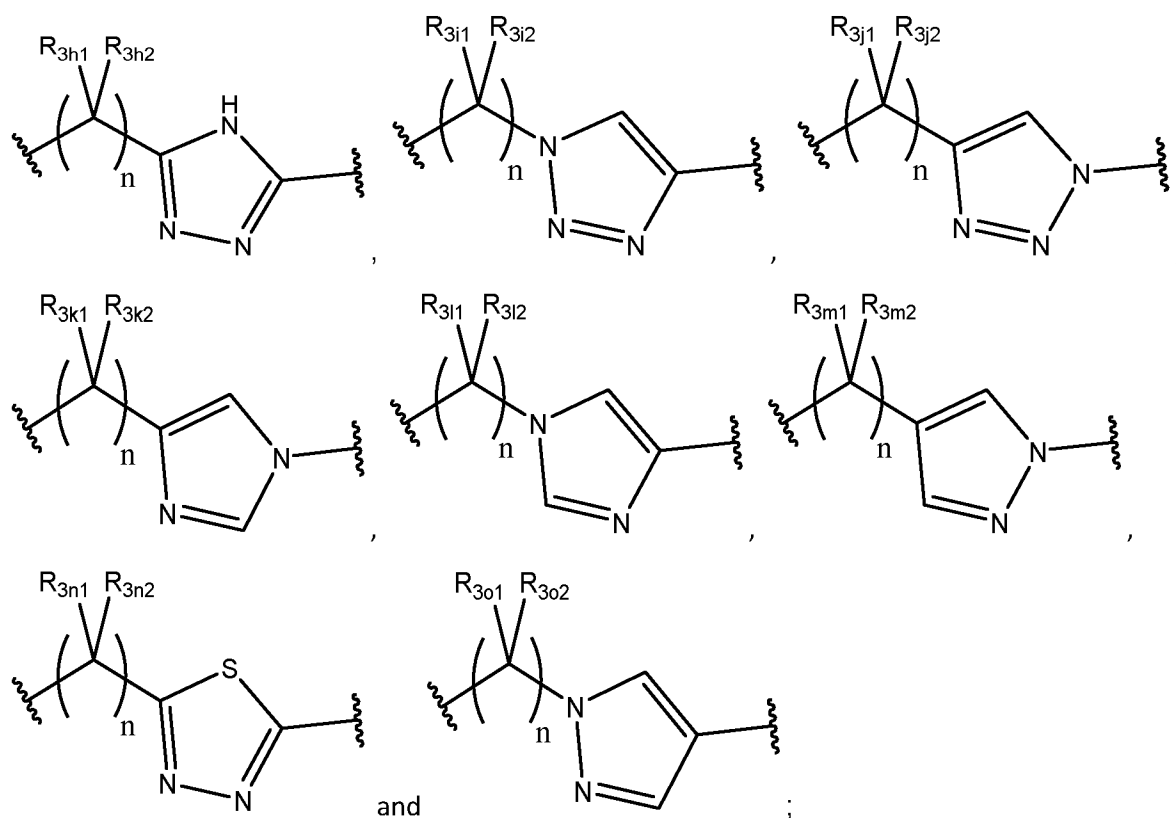
L_{2a} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂ alkyl or oxo;

L_{2b} is selected from O, S, SO, SO₂, N(R_n), C(O), C(O)O, OC(O), C(O)N(R_n),
N(R_n)C(O), N(R_n)C(O)N(R_o), S(O)₂N(R_n), or N(R_n)SO₂, wherein R_n and R_o are each
10 independently selected from hydrogen or C₁₋₂alkyl; and

Q₂ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₆cycloalkyl, aryl, heterocyclyl or heteroaryl, each
of which is optionally substituted by one or more substituents selected from halo,
trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, amino, carboxy, carbamoyl,
sulphamoyl, C₁₋₄alkyl, NR_pR_q, OR_p, C(O)R_p, C(O)OR_p, OC(O)R_p, C(O)N(R_p)R_q,
15 N(R_r)C(O)R_p, S(O)_yR_p (where y is 0, 1 or 2), SO₂N(R_p)R_q, N(R_r)SO₂R_p or (CH₂)_zNR_pR_q
(where z is 1, 2 or 3), wherein R_p and R_q are each independently selected from
hydrogen or C₁₋₄alkyl;

Y is selected from:





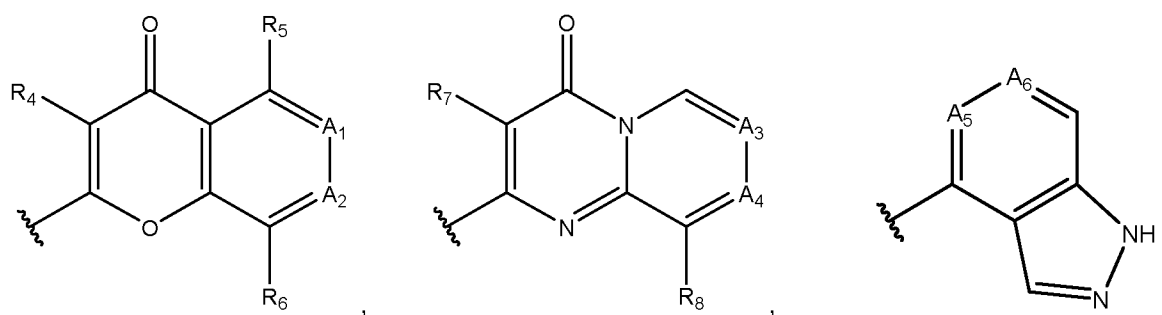
wherein:

5 R_{3a1}, R_{3b1}, R_{3c1}, R_{3d1}, R_{3e1}, R_{3f1}, R_{3g1}, R_{3h1}, R_{3i1}, R_{3j1}, R_{3k1}, R_{3l1}, R_{3m1}, R_{3n1} and R_{3o1} are independently selected from hydrogen, C₁₋₆alkyl, C₃₋₄ cycloalkyl, hydroxy, and halo; and wherein C₁₋₆alkyl, or C₃₋₄ cycloalkyl is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

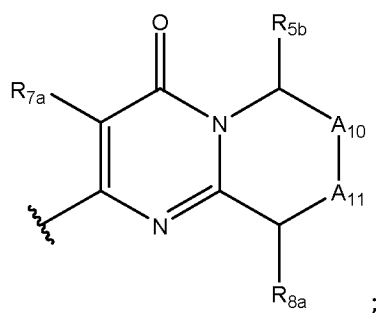
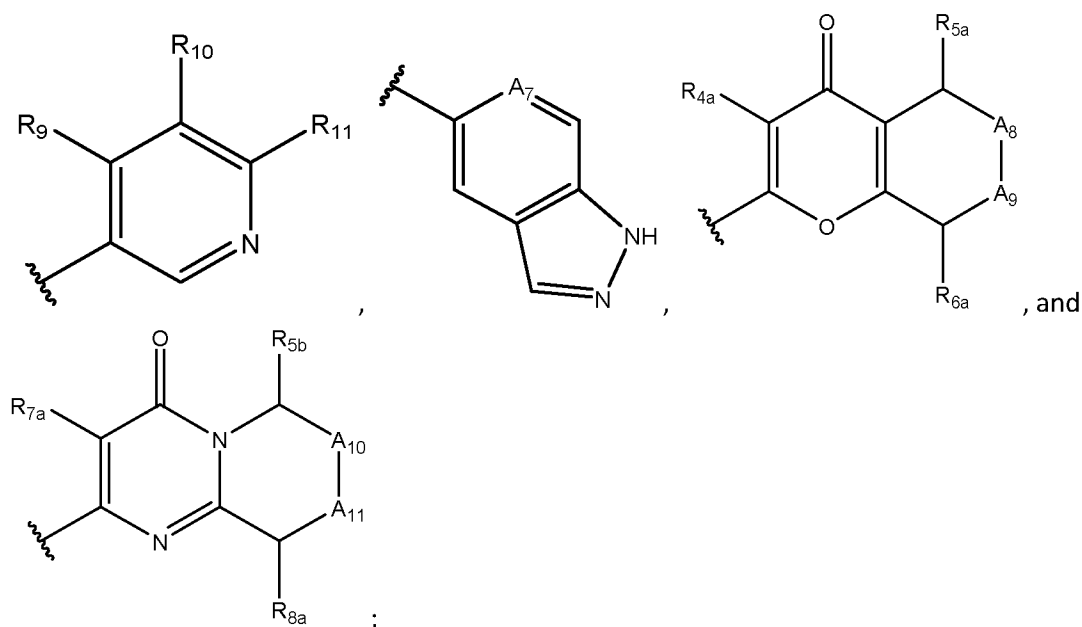
10 R_{3a2}, R_{3b2}, R_{3c2}, R_{3d2}, R_{3e2}, R_{3f2}, R_{3g2}, R_{3h2}, R_{3i2}, R_{3j2}, R_{3k2}, R_{3l2}, R_{3m2}, R_{3n2} and R_{3o2} are hydrogen;

or R_{3a1} and R_{3a2}, R_{3b1} and R_{3b2}, R_{3c1} and R_{3c2}, R_{3d1} and R_{3d2}, R_{3e1} and R_{3e2}, R_{3f1} and R_{3f2}, R_{3g1} and R_{3g2}, R_{3h1} and R_{3h2}, R_{3i1} and R_{3i2}, R_{3j1} and R_{3j2}, R_{3k1} and R_{3k2}, R_{3l1} and R_{3l2}, R_{3m1} and R_{3m2}, R_{3n1} and R_{3n2}, or R_{3o1} and R_{3o2} may be linked to form a spiro-fused C₃-C₄cycloalkyl which is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

Z is selected from:



and



5 wherein:

R_4 , R_7 , R_{4a} and R_{7a} are independently selected from hydrogen and methyl;

R_5 , R_{5a} and R_{5b} are independently selected from hydrogen and halo;

R_6 , R_8 , R_{6a} and R_{8a} are independently selected from hydrogen, halo and methyl;

10 R_9 , R_{10} and R_{11} are independently selected from hydrogen, NH_2 , halo, cyano, and C_{1-6} alkyl; or

R_9 and R_{10} may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system or R_{10} and R_{11} may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system;

A_1 is selected from CR_{12} and N ;

15 A_2 is selected from CR_{13} and N ;

A_3 is selected from CR_{14} and N ;

A_4 is selected from CR_{15} and N ;

A₅ is selected from CR₁₆ and N;

A₆ is selected from CR₁₇ and N;

A₇ is selected from CR₁₈ and N;

A₈ is selected from CR₁₉R₂₀ and NR₂₁;

5 A₉ is selected from CR₂₂R₂₃ and NR₂₄;

A₁₀ is selected from CR₂₅R₂₆ and NR₂₇;

A₁₁ is selected from CR₂₈R₂₉ and NR₃₀;

R₁₂ and R₁₄ are independently selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₁₃ is selected from hydrogen, halo, cyano and methyl;

10 R₁₅ is selected from hydrogen, methoxy and methyl;

R₁₆ is selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₁₇ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl and a 5- or 6-membered heteroaryl;

15 R₁₈ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl and a 5- or 6-membered heteroaryl;

R₁₉, R₂₀, R₂₅ and R₂₆ are selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

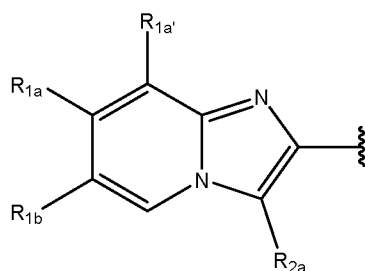
R₂₂ and R₂₃ are selected from hydrogen, halo, cyano and methyl;

R₂₈ and R₂₉ are selected from hydrogen, methoxy and methyl;

R₂₁, R₂₄, R₂₇ and R₃₀ are hydrogen; and

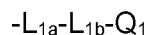
20 n is 0, 1 or 2.

Paragraph 3. A compound according to Paragraph 1, or a pharmaceutically acceptable salt thereof, wherein X is:



25 and R_{1a}, R_{1b}, R_{1a'} and R_{2a} are each as defined in claim 1.

Paragraph 4. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein one of R_{1a} and R_{1b} , R_{1c} and R_{1d} , R_{1e} and R_{1f} is selected from hydrogen, halo, C_{1-6} alkyl, C_{2-3} alkenyl or $-O-C_{1-6}$ alkyl, and the other is selected from hydrogen, cyano, halo or a group of the formula:



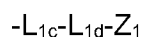
wherein

L_{1a} is absent or C_{1-3} alkylene, C_{3-4} cycloalkylene, optionally substituted by one or more substituents selected from C_{1-2} alkyl, halo, hydroxy, or oxo;

L_{1b} is absent or selected from O, S, SO, SO_2 , $N(R_r)$, $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_r)$, $N(R_r)C(O)$, $N(R_r)C(O)N(R_s)$, $S(O)_2N(R_r)$, or $N(R_r)SO_2$, wherein R_r and R_s are each independently selected from hydrogen or C_{1-2} alkyl; and

Q_1 is hydrogen, cyano, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u , OR_t , $C(O)R_t$, $C(O)OR_t$, $OC(O)R_t$, $C(O)N(R_t)R_u$, $N(R_t)C(O)R_u$, $S(O)_yR_t$ (where y is 0, 1 or 2), $SO_2N(R_t)R_u$, $N(R_t)SO_2R_u$ or $(CH_2)_zNR_tR_u$ (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C_{1-4} alkyl; or

Q_1 is optionally substituted by one or more groups of the formula:



wherein

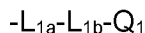
L_{1c} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

L_{1d} is absent or selected from $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_v)$, $N(R_v)C(O)$, $N(R_v)C(O)N(R_w)$, $S(O)_2N(R_v)$, or $N(R_v)SO_2$, wherein R_v and R_w are each independently selected from hydrogen or C_{1-2} alkyl; and

Z_1 is phenyl or 5-6 membered heteroaryl; wherein Z_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, C_{1-4} alkylamino, amino, cyano, hydroxyl, carboxy, carbamoyl or sulphamoyl.

Paragraph 5. A compound according to Paragraph 4, or a pharmaceutically acceptable salt thereof, wherein R_{1a} , R_{1c} and R_{1e} are selected from hydrogen, halo, C_{1-6} alkyl, C_{2-3} alkenyl or $-O-C_{1-6}$ alkyl

and R_{1b} , R_{1d} , and R_{1f} are selected from hydrogen, cyano, halo or a group of the formula:



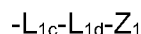
wherein

L_{1a} is absent or C_{1-3} alkylene, C_{3-4} cycloalkylene, optionally substituted by one or more substituents selected from C_{1-2} alkyl, halo, hydroxy, or oxo;

L_{1b} is absent or selected from O, S, SO, SO_2 , $N(R_r)$, $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_r)$, $N(R_r)C(O)$, $N(R_r)C(O)N(R_s)$, $S(O)_2N(R_r)$, or $N(R_r)SO_2$, wherein R_r and R_s are each independently selected from hydrogen or C_{1-2} alkyl; and

Q_1 is hydrogen, cyano, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u , OR_t , $C(O)R_t$, $C(O)OR_t$, $OC(O)R_t$, $C(O)N(R_t)R_u$, $N(R_t)C(O)R_u$, $S(O)_yR_t$ (where y is 0, 1 or 2), $SO_2N(R_t)R_u$, $N(R_t)SO_2R_u$ or $(CH_2)_zNR_tR_u$ (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C_{1-4} alkyl; or

Q_1 is optionally substituted by one or more groups of the formula:



wherein

L_{1c} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

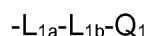
L_{1d} is absent or selected from $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_v)$, $N(R_v)C(O)$, $N(R_v)C(O)N(R_w)$, $S(O)_2N(R_v)$, or $N(R_v)SO_2$, wherein R_v and R_w are each independently selected from hydrogen or C_{1-2} alkyl; and

Z_1 is phenyl or 5-6 membered heteroaryl; wherein Z_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, C_{1-4} alkylamino, amino, cyano, hydroxyl, carboxy, carbamoyl or sulphamoyl.

Paragraph 6. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein R_{1a} , R_{1c} and R_{1e} are selected from hydrogen, halo, C_{1-4} alkyl, C_{2-3} alkenyl and $-O-C_{1-4}$ alkyl.

5 **Paragraph 7.** A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein:

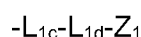
R_{1b} , R_{1d} and R_{1f} are selected from hydrogen, halo, cyano or from a group of formula:



wherein

10 L_{1a} is absent or C_{1-3} alkylene, optionally substituted by one or more hydroxy;
 L_{1b} is absent or $N(R_r)$ wherein R_r is hydrogen; and
 Q_1 is C_{1-6} alkyl, C_{2-3} alkenyl, C_{3-6} cycloalkyl, aryl, heterocyclyl or heteroaryl; and wherein
 Q_1 is optionally substituted by one or more substituents selected from halo, carboxy,
15 or C_{1-4} alkyl; or

Q_1 is optionally substituted by one or more groups of the formula:



wherein

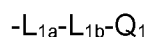
L_{1c} is absent;

20 L_{1d} is absent; and

Z_1 is 5-6 membered heteroaryl; wherein Z_1 is optionally substituted by one or more C_{1-4} alkyl.

Paragraph 8. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein:

25 R_{1b} , R_{1d} and R_{1f} are selected from hydrogen, halo, cyano or from a group of formula:



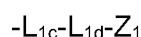
wherein

L_{1a} is absent or C_{1-3} alkylene;

30 L_{1b} is absent or $N(R_r)$ wherein R_r is hydrogen; and

Q_1 is C_{1-6} alkyl, and wherein

Q_1 is substituted by a group of the formula:



wherein

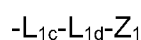
L_{1c} is absent;

L_{1d} is absent; and

Z₁ is phenyl.

- 5 **Paragraph 9.** A compound according to any one of Paragraphs 1 to 8, or a pharmaceutically acceptable salt thereof, wherein Q₁ is a 5- or 6-membered aryl, a 5- or 6-membered heteroaryl, or a 5- or 6-membered heterocyclyl, wherein Q₁ is optionally substituted by one or more substituents selected from halo, NR_tR_u, OR_t wherein R_t and R_u are independently selected from hydrogen or C₁₋₄alkyl; or

- 10 Q₁ is optionally substituted by one or more groups of the formula:



wherein

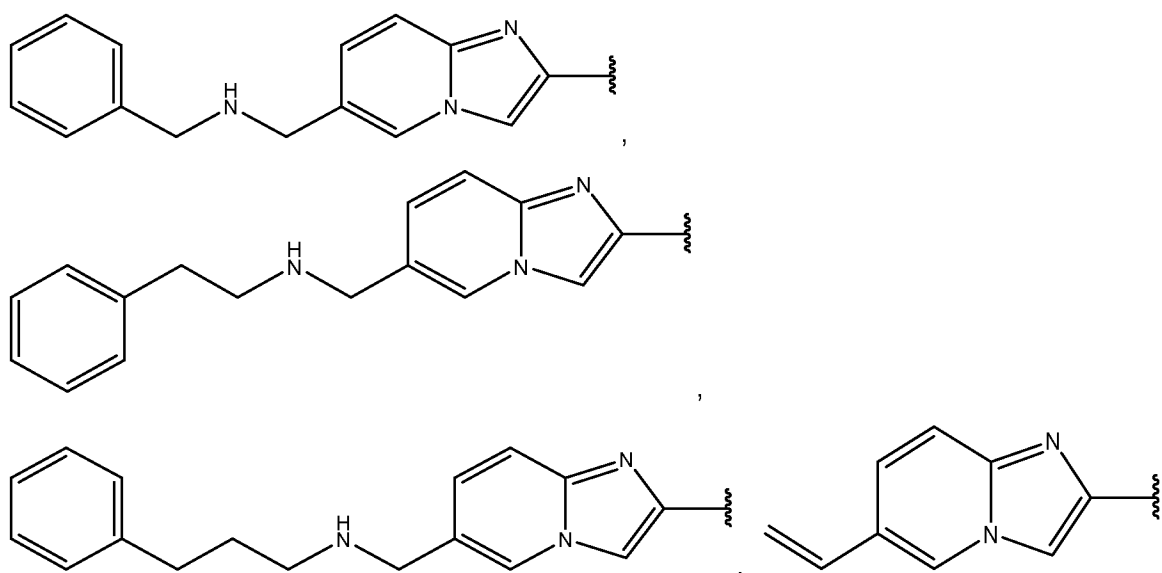
L_{1c} is absent;

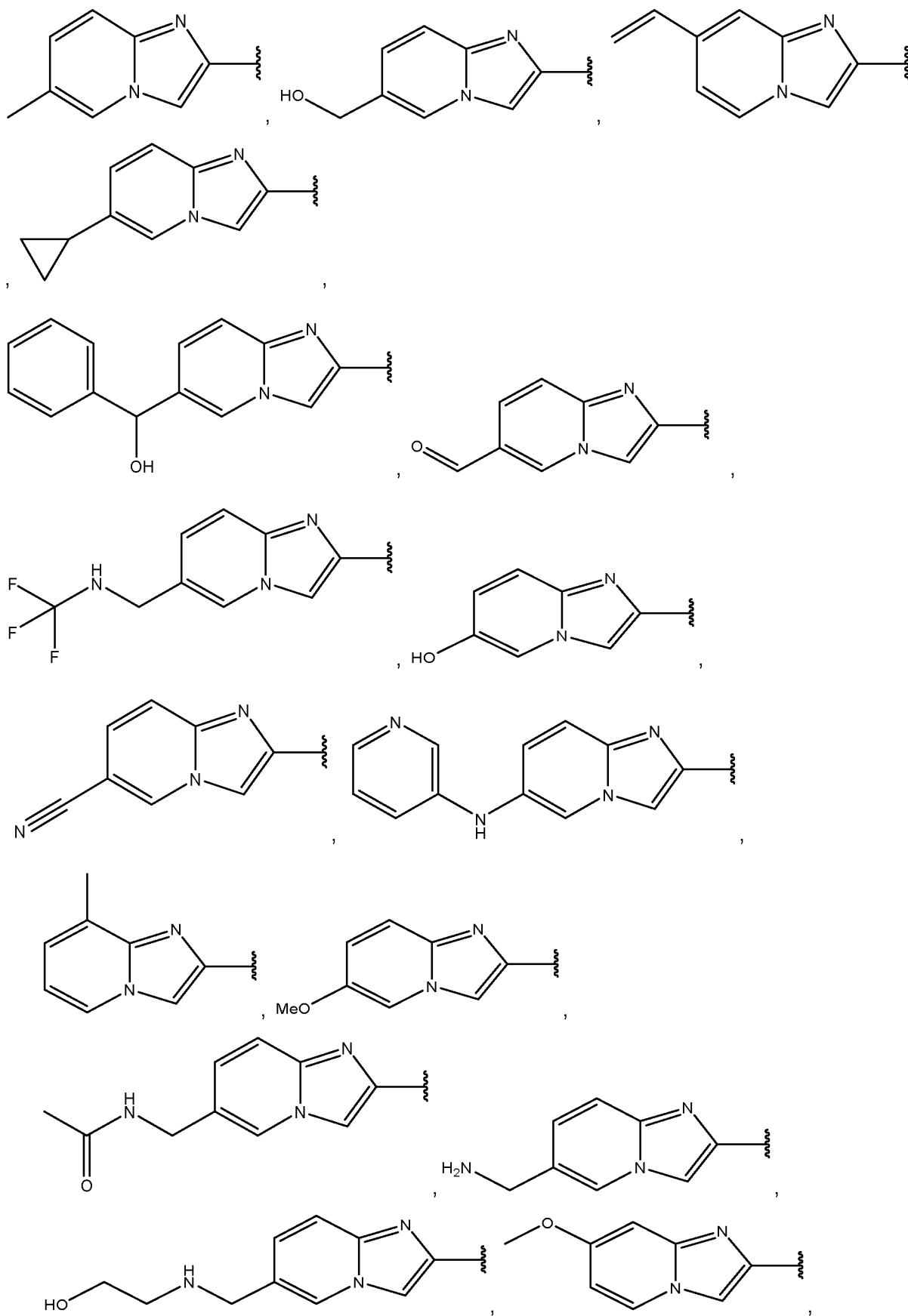
L_{1d} is absent; and

- 15 Z₁ is 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more C₁₋₄alkyl.

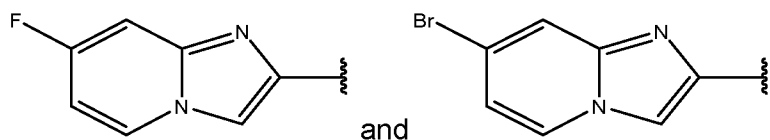
Paragraph 10. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein R_{2a}, R_{2b} and R_{2c} are hydrogen.

- 20 **Paragraph 11.** A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein X is selected from

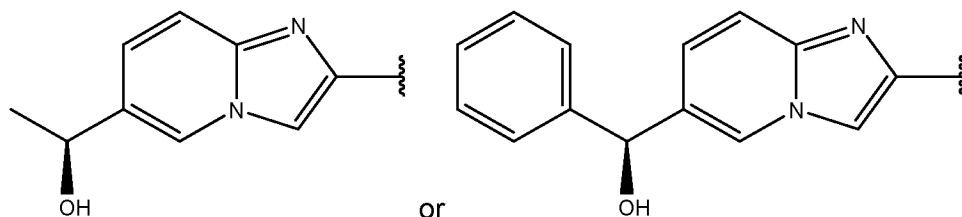






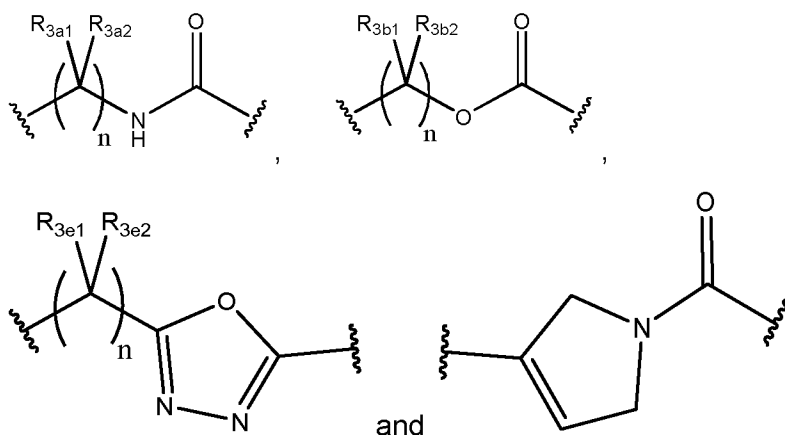


Paragraph 12. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein X is



5

Paragraph 13. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein Y is selected from:



10

Paragraph 14. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} and R_{3o1} are independently selected from hydrogen and C_{1-6} alkyl; and wherein C_{1-6} alkyl is optionally substituted with one or more hydroxy substituents.

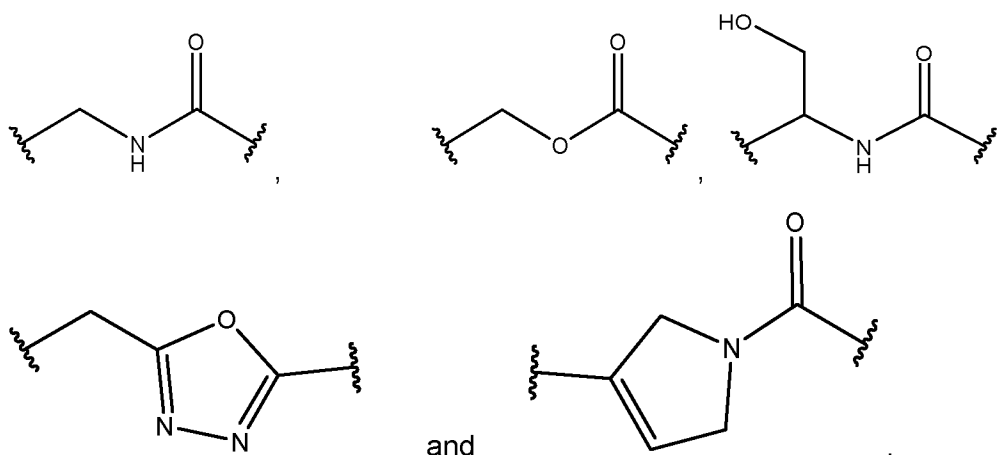
15

Paragraph 15. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} and R_{3o2} are hydrogen.

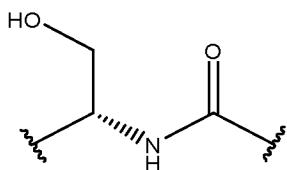
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Paragraph 16. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein n is 1.

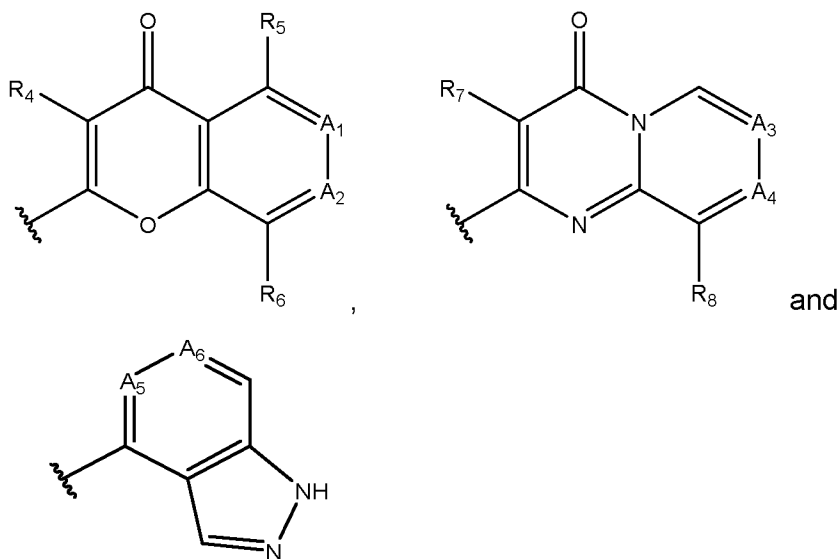
Paragraph 17. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein Y is selected from:



Paragraph 18. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein Y is



Paragraph 19. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein Z is selected from:



Paragraph 20. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein R_4 , R_5 , R_6 , R_7 , R_8 , R_{4a} , R_{5a} , R_{5b} , R_{6a} , R_{7a} and R_{8a} are hydrogen.

5 **Paragraph 21.** A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein A_1 is CR_{12} and wherein R_{12} is hydrogen.

10 **Paragraph 22.** A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein A_2 is CR_{13} and wherein R_{13} is hydrogen.

15 **Paragraph 23.** A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein A_3 is CR_{14} and wherein R_{14} is hydrogen or chloro.

Paragraph 24. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein A_4 is CR_{15} and wherein R_{15} is hydrogen or methoxy.

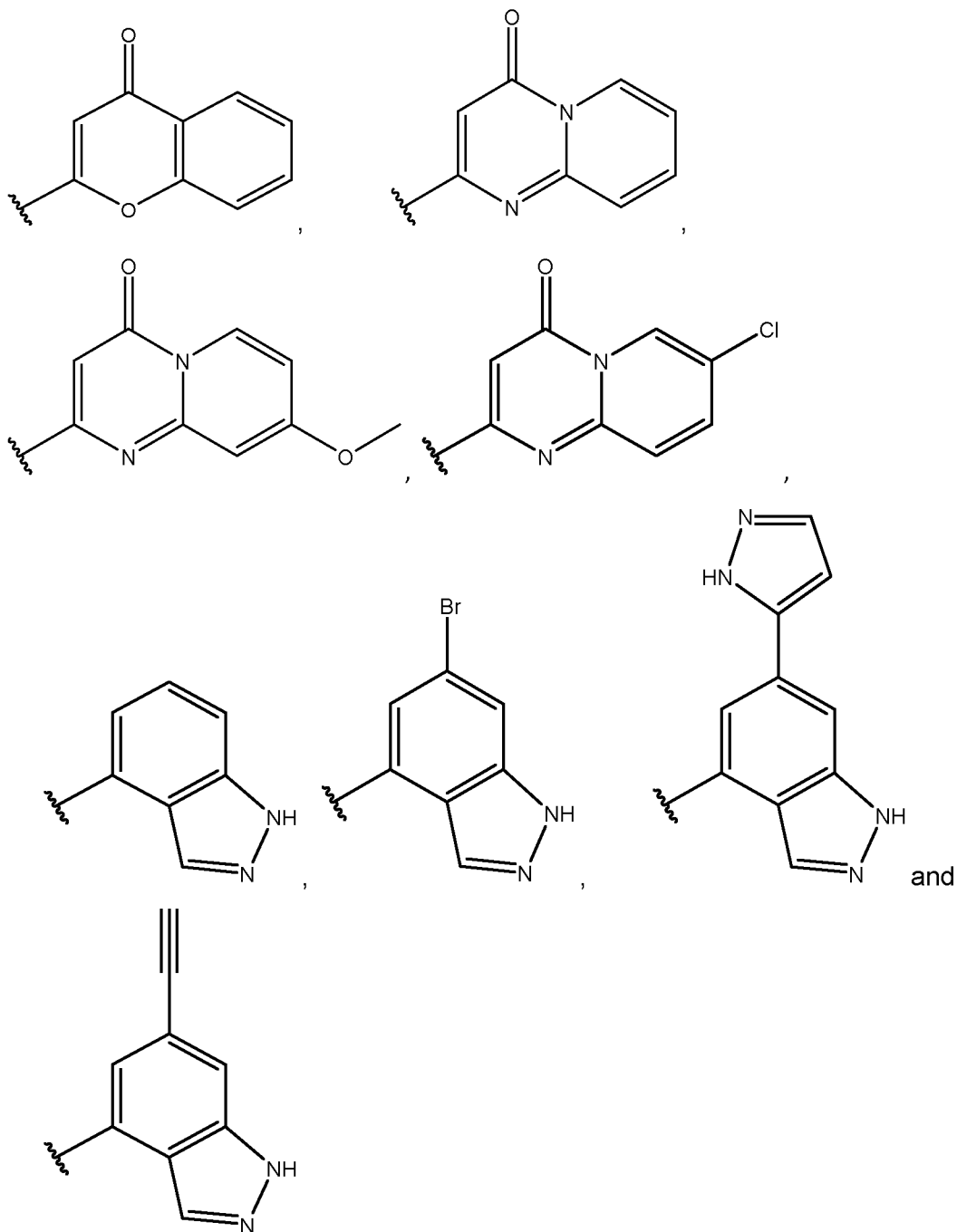
20

Paragraph 25. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein A_5 is CR_{16} and wherein R_{16} is hydrogen.

25 **Paragraph 26.** A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein A_6 is CR_{17} and wherein R_{17} is selected from hydrogen, halo, C_{1-4} alkynyl and a 5- or 6-membered heteroaryl.

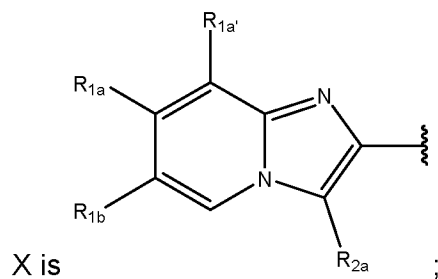
30 **Paragraph 27.** A compound according to Paragraph 26, or a pharmaceutically acceptable salt thereof, wherein R_{17} is a 5-membered heteroaryl.

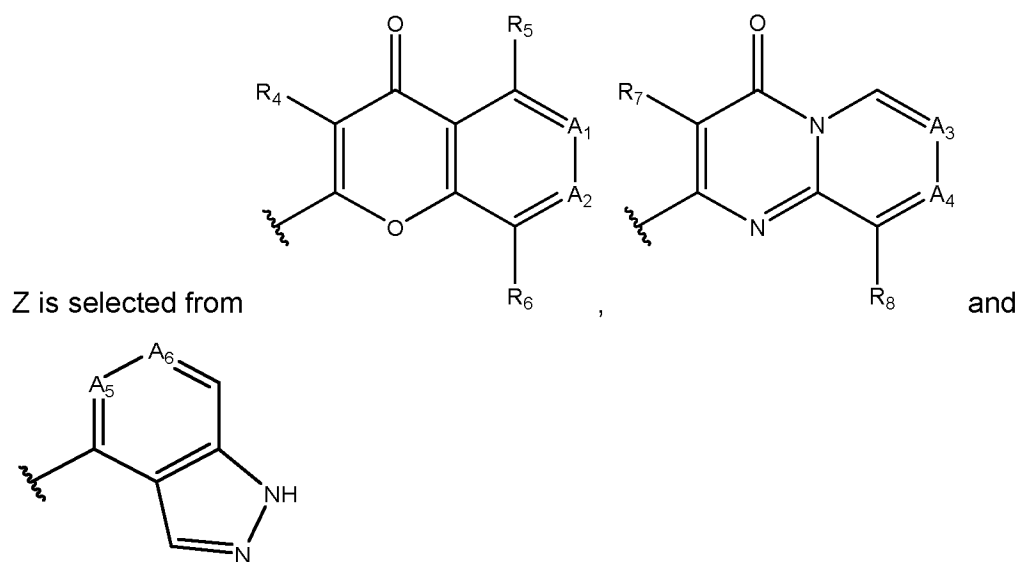
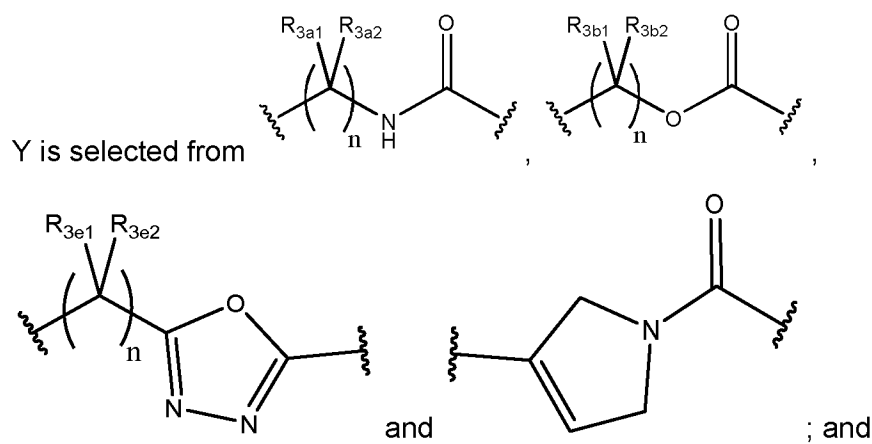
Paragraph 28. A compound according to any one of the preceding Paragraphs, or a pharmaceutically acceptable salt thereof, wherein Z is selected from:



5

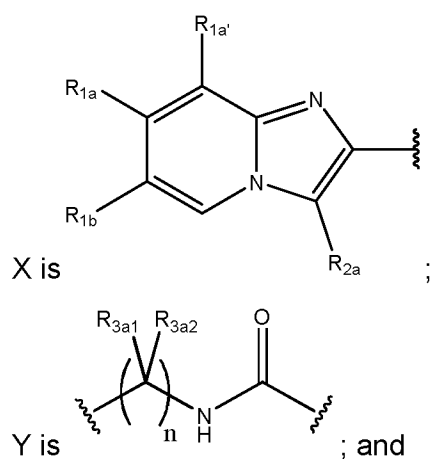
Paragraph 29. A compound according to Paragraph 1 or Paragraph 2, or a pharmaceutically acceptable salt thereof, wherein:

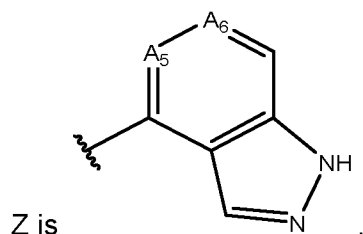




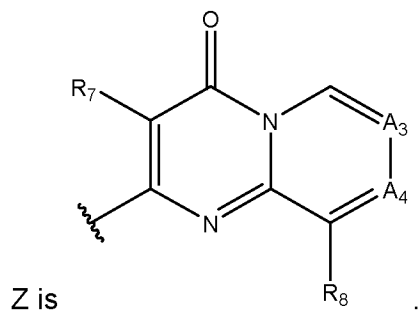
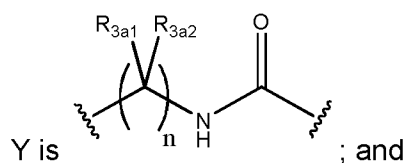
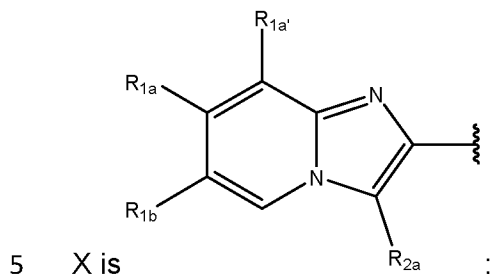
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Paragraph 30. A compound according to Paragraph 29, or a pharmaceutically acceptable salt thereof, wherein:





Paragraph 31. A compound according to Paragraph 29, or a pharmaceutically acceptable salt thereof, wherein:



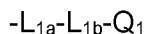
Paragraph 32. A compound according to Paragraph 1 or Paragraph 2, or a pharmaceutically acceptable salt thereof, wherein:

R₉ and R₁₀ are linked together to form a fused 5- or 6-membered unsaturated ring system or R₁₀ and R₁₁ may be linked together to form a fused 5- or 6-membered unsaturated ring system.

Paragraph 33. A compound according to Paragraph 1, or a pharmaceutically acceptable salt thereof, wherein:

R_{1a}, R_{1c} and R_{1e} are independently selected from hydrogen, C₂₋₃alkenyl, cyano, halo, C₁₋₆alkyl, OR^t, wherein R^t is C₁₋₄alkyl; and

R_{1b}, R_{1d} and R_{1f} are independently selected from hydrogen, cyano, halo, and a group of the formula:



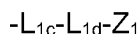
wherein

L_{1a} is absent or C_{1-3} alkylene, C_{3-4} cycloalkylene, optionally substituted by one or more substituents selected from C_{1-2} alkyl, halo, hydroxy, or oxo;

L_{1b} is absent or selected from O, S, SO, SO_2 , $N(R_r)$, $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_r)$, $N(R_r)C(O)$, $N(R_r)C(O)N(R_s)$, $S(O)_2N(R_r)$, or $N(R_r)SO_2$, wherein R_r and R_s are each independently selected from hydrogen or C_{1-2} alkyl; and

Q_1 is hydrogen, cyano, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphonamoyl, NR_tR_u , OR_t , $C(O)R_t$, $C(O)OR_t$, $OC(O)R_t$, $C(O)N(R_t)R_u$, $N(R_t)C(O)R_u$, $S(O)_yR_t$ (where y is 0, 1 or 2), $SO_2N(R_t)R_u$, $N(R_t)SO_2R_u$ or $(CH_2)_zNR_tR_u$ (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C_{1-4} alkyl; or

Q_1 is optionally substituted by one or more groups of the formula:



wherein

L_{1c} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

L_{1d} is absent or selected from $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_v)$, $N(R_v)C(O)$,

$N(R_v)C(O)N(R_w)$, $S(O)_2N(R_v)$, or $N(R_v)SO_2$, wherein R_v and R_w are each independently selected from hydrogen or C_{1-2} alkyl; and

Z_1 is phenyl or 5-6 membered heteroaryl; wherein Z_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, C_{1-4} alkylamino, amino, cyano, hydroxyl, carboxy, carbamoyl or sulphonamoyl.

Paragraph 34. A compound, or a pharmaceutically acceptable salt thereof, selected from any one of the following:

N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({7-bromoimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-bromoimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-chloroimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({7-fluoroimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-fluoroimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({7-methoxyimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

- N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-6-(1H-pyrazol-5-yl)-1H-indazole-4-carboxamide;
- N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;
- 6-bromo-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;
- 5 6-bromo-N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;
- N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
- N-({imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
- 6-ethynyl-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;
- N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
- 10 carboxamide;
- N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
- N-({7-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-cyanoimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
- 15 carboxamide;
- 8-methoxy-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-5-carboxamide;
- 7-chloro-N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
- 20 carboxamide;
- N-({6-fluoroimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-bromoimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-({6-methoxyimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({7-methoxyimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-({8-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-pyrazolo[4,3-c]pyridine-4-carboxamide;
- N-({7-bromoimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-(2-hydroxy-1-{6-methylimidazo[1,2-a]pyridin-2-yl}ethyl)-1H-indazole-4-carboxamide;
- 5 4-(3-{imidazo[1,2-a]pyridin-2-yl}-2,5-dihydro-1H-pyrrole-1-carbonyl)-1H-indazole;
- N-[(6-{[(pyridin-3-yl)methyl]amino}imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-{[(1-methyl-1H-imidazol-4-yl)methyl]amino}imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 10 N-[(6-(3-methoxyphenyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-(1H-pyrazol-5-yl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-(3-chlorophenyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-({6-[(pyridin-3-yl)amino]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- N-({6-[(piperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- 15 N-[(6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-(acetamidomethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- {6-methylimidazo[1,2-a]pyridin-2-yl)methyl 1H-indazole-4-carboxylate;
- {6-methylimidazo[1,2-a]pyridin-2-yl)methyl 1H-indazole-4-carboxylate hydrochloride;
- N-[(6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 20 N-({6-hydroxyimidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- N-({6-[(methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- N-({6-[(methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide dihydrochloride;
- N-[(6-{[(2-hydroxyethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-
- 25 carboxamide;
- N-[(6-{[(2,2,2-trifluoroethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-({6-[hydroxy(phenyl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;

- N-({6-formylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-[(6-{{(2,2,2-trifluoroethyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-{{(2-hydroxyethyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-{{(2-phenylethyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-({6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-{{(3-phenylpropyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-({6-[hydroxy(phenyl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-ethenylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-({6-cyclopropylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({7-ethenylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-{{6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 2-(1H-indazol-4-yl)-5-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]-1,3,4-oxadiazole;
- N-{{6-(2-aminoethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H,6H,7H,8H,9H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- 4-oxo-N-{{6-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- tert-butyl N-(2-{2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridin-6-yl}ethyl)carbamate;
- 5 N-benzyl-2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridine-6-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 7-chloro-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 10 6-chloro-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H,6H,7H,8H,9H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 6-amino-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]pyridine-3-carboxamide;
- N-[(6-[(benzyloxy)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 20 N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-7-fluoro-4-oxo-4H-chromene-2-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-7-methyl-4-oxo-4H-chromene-2-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 25 8-chloro-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 6-bromo-N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 30 N-[(6-[(cyclohexylmethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]quinoline-3-carboxamide;

N-[(6-{1-[(cyclohexylmethyl)amino]ethyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

6-chloro-N-[(6-{[(cyclohexylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;

5 4-[5-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1,3,4-thiadiazol-2-yl]-1H-indazole;

4-[1-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole;

N-[(6-{[(3-chlorophenyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

10 N-[(6-{[(1-cyclohexyl-2-hydroxyethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

4-oxo-N-{[6-({[(pyridin-3-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-{[6-({[(4-methoxyphenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

15 N-[(6-{[(cyclohexylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-{[6-({[(4-chlorophenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

20 N-[(6-{[benzyl(methyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

4-oxo-N-{[6-({[(1R)-1-phenylethyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

25 4-oxo-N-{[6-({[(1S)-1-phenylethyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-{[6-({[(2-fluorophenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

4-oxo-N-[(6-{[(2-phenylpropan-2-yl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

30 N-{[6-({[(3-fluorophenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-{[6-({[(4-fluorophenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

35 4-oxo-N-[(6-{[(4,4,4-trifluorobutyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-[[6-({[(oxan-4-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(3,3-difluorocyclobutyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-[[6-({[(cyclopropylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[[6-({[(3,3,3-trifluoropropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(cyclohexylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-
- 10 a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-({[(3-(trifluoromethyl)bicyclo[1.1.1]pentan-1-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(oxan-2-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 4-oxo-N-[[6-({[(3-phenyloxetan-3-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(oxan-3-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(1-fluorocyclohexyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-
- 20 4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(3-cyclopropylphenyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(3,3-dimethylbutyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 4-oxo-N-{{6-({[(2-(trifluoromethoxy)ethyl)amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-({[(oxolan-2-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(2-methanesulfonyl)ethyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-
- 30 pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-[(3-phenylpyrrolidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(1-cyclohexylcyclopropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 4-oxo-N-{{6-({[(1,3-thiazol-5-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- tert-butyl 3-[[[2-[[[4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amino]methyl]piperidine-1-carboxylate;
 N-[[6-[[[4,4-difluorocyclohexyl)methyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 tert-butyl 2-[[[2-[[[4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amino]methyl]piperidine-1-carboxylate;
 N-[[6-[[[2-cyclopropylethyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-([6-[[[piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-
- 10 a]pyrimidine-2-carboxamide;
 4-oxo-N-([6-[[[1-(2,2,2-trifluoroethyl)-1H-pyrazol-3-yl]methyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-[[[1-methylcyclohexyl)methyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 4-oxo-N-([6-[[[2-(pyridin-3-yl)ethyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-[[[1,4-dioxan-2-yl)methyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-([6-[[[cyclopropylamino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-
- 20 a]pyrimidine-2-carboxamide;
 N-[[6-[[[3,3-difluorocyclobutyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-[[[oxetan-3-yl)methyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 4-oxo-N-([6-[[[1R,2R)-2-(trifluoromethyl)cyclopropyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-[[[2,2-dimethylpropyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-[[[cyclohexylmethyl](methyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-
- 30 pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-[[[4,4-difluorocyclohexyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-([6-[[[bicyclo[1.1.1]pentan-1-yl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 4-oxo-N-([6-[[[2S]-oxolan-2-yl)methyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- 4-oxo-N-({6-([[(2R)-oxolan-2-yl]methyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(2,2-difluoroethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-({6-([[(oxolan-3-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(1-methylcyclopropyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 4-oxo-N-({6-([[(oxolan-3-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 methyl 3-methyl-2-[(2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl)amino]butanoate;
 N-({6-([[(oxan-3-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 4-oxo-N-({6-([[(2S)-3,3,3-trifluoro-2-hydroxypropyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(cyclobutyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(tert-butylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-
- 20 a]pyrimidine-2-carboxamide;
 N-({6-([[(2-fluoroethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(4,4-difluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 4-oxo-N-({6-([[(4-phenylpiperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(1,2,3,4-tetrahydroisoquinolin-2-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-([[(diethylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-
- 30 a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(pyrrolidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-([[(3-(pyridin-2-yl)azetidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-({6-([[(dicyclopropylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-[(6-[(cyclopropylmethyl)(methyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(4-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-[(6-[(4-(trifluoromethyl)piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(3-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-[(spiro[2.2]pentan-1-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-
- 10 4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(3,3-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-[(3-(trifluoromethyl)piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-[(6-[(5,5-dimethyloxolan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(4-fluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(3-methoxypropyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-
- 20 pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(1-methylcyclohexyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(4,4-dimethyloxolan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-[(6-[(1-methylcyclopentyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-[(propylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(3,3-dimethyloxolan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-
- 30 oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(2-methylpropyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(2-(tert-butoxy)ethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-[(6-[(4-chlorophenyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-{{6-({[2-(oxan-2-yl)ethyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(4-benzylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-{{6-[(4-phenoxy piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2,2-difluorocyclopropyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2,2-dimethylcyclopropyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-{{6-({[(2-methyloxolan-2-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(4-tert-butylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-{{6-({[(4-tert-butylcyclohexyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2-cyclopentylethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(4-(2,2-dimethylpropanoyl)piperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-{{6-[(4-acetyl piperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[7-azabicyclo[2.2.1]heptan-7-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-{{6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(2,2-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-({[(2,3,3-trimethylbutan-2-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-{{6-({[(5-fluoropyridin-2-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[1,1'-bi(cyclopropane)]-1-yl)amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-{{6-({[(1-fluorocyclopentyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-({6-[(2,6-dimethylmorpholin-4-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
methyl 1-({2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl)piperidine-3-carboxylate;
- 5 N-[(6-[(2-fluoro-2-methylpropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(1-cyclohexylethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(2-cyclopropylethyl)(methyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-
- 10 4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(2,2-dimethylpropyl)(methyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(1-fluorocyclobutyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-({6-[(4-fluoro-4-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-({6-[(3,3-difluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(1-hydroxycyclohexyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-
- 20 4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(cyclopentylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(3,3-difluorocyclopentyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-[(6-[(cyclobutylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(2-(3,3-difluorocyclobutyl)ethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(2-fluorocyclobutyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-
- 30 pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-[(2S)-3,3-dimethylbutan-2-yl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
N-[(6-({6-azaspiro[2.5]octan-6-yl)methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 4-oxo-N-({6-[(1R,3R)-3-fluorocyclobutyl]methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- 4-oxo-N-({6-[(2-phenylethyl)amino]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-[2-(benzylamino)ethyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-({6-[2-(cyclohexylamino)ethyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-({6-[(phenylformamido)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(cyclohexylformamido)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 4-oxo-N-{{6-({[(piperidin-3-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-{{6-({[(piperidin-2-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-[(6-{{[(azetidin-3-yl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-({6-[(cyclohexylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
- N-[(6-{{[(2-cyclopropylethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-chromene-2-carboxamide;
- 20 4-oxo-N-({6-[(piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-chromene-2-carboxamide;
- N-{{6-({[(4-chlorophenyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-chromene-2-carboxamide;
- 25 N-({6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
- N-{{6-({[(1-methylcyclohexyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-chromene-2-carboxamide;
- N-[(6-{{[(2,2-dimethylpropyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-chromene-2-carboxamide;
- 30 4-oxo-N-[(7-{{[(2-phenylethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(7-{{[(cyclohexylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-[(7-{{[(cyclopropylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-[(6-{1-[(cyclohexylmethyl)amino]cyclopropyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-{[6-(2-amino-3-phenylpropyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

5 (cyclohexylmethyl)[(2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amine;

N-(cyclohexylmethyl)-2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridine-6-carboxamide;

10 (2,2-dimethylpropyl)[(2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amine;

4-[1-({6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole;

[(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl][(3,3-difluorocyclobutyl)methyl]amine;

15 [(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl](2,2-dimethylpropyl)amine;

[(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl](cyclohexylmethyl)amine;

20 6-bromo-4-[1-({6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole;

(2-{[4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methanol;

(2,2-dimethylpropyl)[(2-{[4-(1H-indazol-5-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amine;

25 ((cyclohexylmethyl)[1-(2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)ethyl]amine;

(2,2-dimethylpropyl)({2-[(4-{1H-pyrazolo[3,4-c]pyridin-4-yl}-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl)amine;

30 {2-[(4-{1H-pyrazolo[3,4-c]pyridin-4-yl}-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methanol;

N-({6-[(3R,5S)-5-tert-butylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-({6-[(3S,5R)-5-tert-butylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

35 N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;

N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;

5 N-({6-[4-(2,2-dimethylpropyl)morpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-({6-[(3S,5R)-5-methylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; and

10 N-({6-[(9-methoxy-2,3,4,5-tetrahydro-1,4-benzoxazepin-3-yl)imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide.

Paragraph 35. A pharmaceutical composition comprising a compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, and one
15 or more pharmaceutically acceptable excipients.

Paragraph 36. A compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35, for use in therapy.
20

Paragraph 37. A compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35, for use in the treatment of a proliferative condition.

25 **Paragraph 38.** A compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35, for use in the treatment of cancer.

Paragraph 39. A compound according to any one of Paragraphs 1 to 34 or a
30 pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35, for use in the treatment of leukaemia.

Paragraph 40. A compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to
35 Paragraph 35, for use in the treatment of AML leukaemia or chronic myeloid leukaemia.

Paragraph 41. A compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35, for use in the inhibition of METTL3 activity.

5 **Paragraph 42.** A compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35, for use in the treatment of an autoimmune disease, a neurological disease, an inflammatory disease or an infectious disease.

10 **Paragraph 43.** Use of a compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a proliferative condition.

Paragraph 44. Use of a compound according to any one of Paragraphs 1 to 34, or a
15 pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cancer.

Paragraph 45. Use of a compound according to any one of Paragraphs 1 to 34, or a
20 pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of leukaemia.

Paragraph 46. Use of a compound according to any one of Paragraphs 1 to 34, or a
25 pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of AML leukaemia or chronic myeloid leukaemia.

Paragraph 47. Use of a compound according to any one of Paragraphs 1 to 34, or a
30 pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of an autoimmune disease, a neurological disease, an inflammatory disease or an infectious disease.

Paragraph 48. Use of a compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the inhibition of METTL3 activity.

35 **Paragraph 49.** A method of treating a proliferative disorder, said method comprising administering to a subject in need thereof a therapeutically effective amount of a

compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35.

Paragraph 50. A method of treating cancer, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35.

Paragraph 51. A method of treating leukaemia, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35.

Paragraph 52. A method of treating AML leukaemia or chronic myeloid leukaemia, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35.

Paragraph 53. A method of treating an autoimmune disease, a neurological disease, an inflammatory disease or an infectious disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35.

Paragraph 54. A method of inhibiting METTL3 activity *in vitro* or *in vivo*, said method comprising contacting a cell with an effective amount of a compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35.

Paragraph 55. A method of inhibiting metastasis *in vitro* or *in vivo*, said method comprising contacting a cell with an effective amount of a compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to Paragraph 35.

Paragraph 56. A combination comprising a compound according to any one of Paragraphs 1 to 34, or a pharmaceutically acceptable salt there, with one or more additional therapeutic agents.

CLAIMS

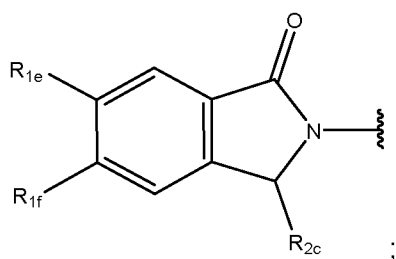
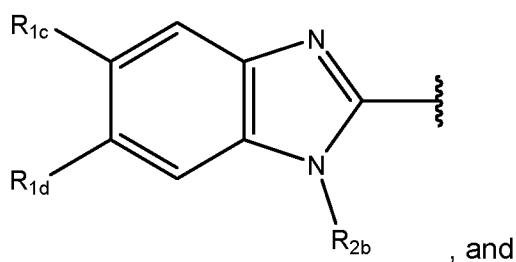
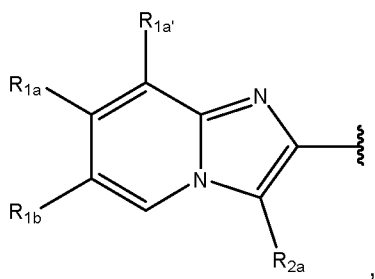
1. A compound of the formula (I), or a pharmaceutically acceptable salt thereof,



(I)

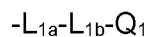
- 5 wherein:

X is selected from:



- 10 wherein:

R_{1a}, R_{1b}, R_{1c}, R_{1d}, R_{1e} and R_{1f} are independently selected from hydrogen, cyano, halo or a group of the formula:



wherein

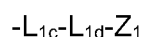
- 15 L_{1a} is absent or selected from C₁₋₃alkylene and C₃₋₅cycloalkylene, wherein C₁₋₃alkylene and C₃₋₅cycloalkylene are optionally substituted by one or more substituents selected from aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl, C₁₋₃alkyl, cyano, C₁₋₃alkoxy, halo, hydroxy, C₁₋₃haloalkoxy, -O-C₃₋₄cycloalkyl, NH₂ or oxo; wherein any -O-

C₃₋₆cycloalkyl aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl or C₁₋₃alkyl is optionally further substituted by one or more substituents selected from cyano, hydroxy, C₁₋₃alkoxy, halo, C₁₋₃haloalkoxy, -O-C₃₋₄cycloalkyl, or NH₂; wherein -O-C₃₋₆cycloalkyl is optionally further substituted with halo, cyano or hydroxy; ; or C₁₋₃alkylene is optionally spiro-fused to a 3- to 5-membered cycloalkyl or heterocyclic ring, or a spirocyclic ring system, each of which is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo or C₁₋₂haloalkoxy;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₃alkyl, wherein C₁₋₃alkyl is optionally further substituted by cyano, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, NH₂, C₃₋₆cycloalkyl or a 3 to 6 membered heterocyclyl, wherein the C₃₋₆cycloalkyl or a 3 to 6 membered heterocyclyl in turn are optionally further substituted by halo, hydroxy, C₁₋₂alkoxy or C₁₋₂haloalkoxy; and

Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₈cycloalkyl (e.g. C₃₋₆cycloalkyl), C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, oxo, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, -S(O)₀₋₂R_tR_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u, N(R_t)SO₂R_u or (CH₂)_zNR_tR_u (where z is 1, 2 or 3), wherein C₁₋₄alkyl is in turn optionally substituted by one more substituents selected from cyano, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, -O-C₃cycloalkyl, wherein -O-C₃cycloalkyl is optionally substituted with halo, cyano or hydroxy; and wherein R_t and R_u are each independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



wherein

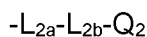
L_{1c} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

L_{1d} is absent or selected from C(O), O, C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl), heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system), aryl or heteroaryl, ; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, cyano, hydroxyl, NR_{t1}R_{u1}, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, C(O)N(R_{t1})R_{u1}, N(R_{t1})C(O)R_{u1}, -S(O)₀₋₂R_{t1}R_{u1}, S(O)_yR_{t1} (where y is 0, 1 or 2), SO₂N(R_{t1})R_{u1}, N(R_{t1})SO₂R_{u1} or (CH₂)_zNR_{t1}R_{u1} (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C₁₋₄alkyl; and when Z₁ is C₃₋₈cycloalkyl or heterocyclyl, Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclyl ring;

R_{1a}' is selected from hydrogen, halo and methyl;

R_{2a}, R_{2b} and R_{2c} are selected from hydrogen, halo or a group of the formula:



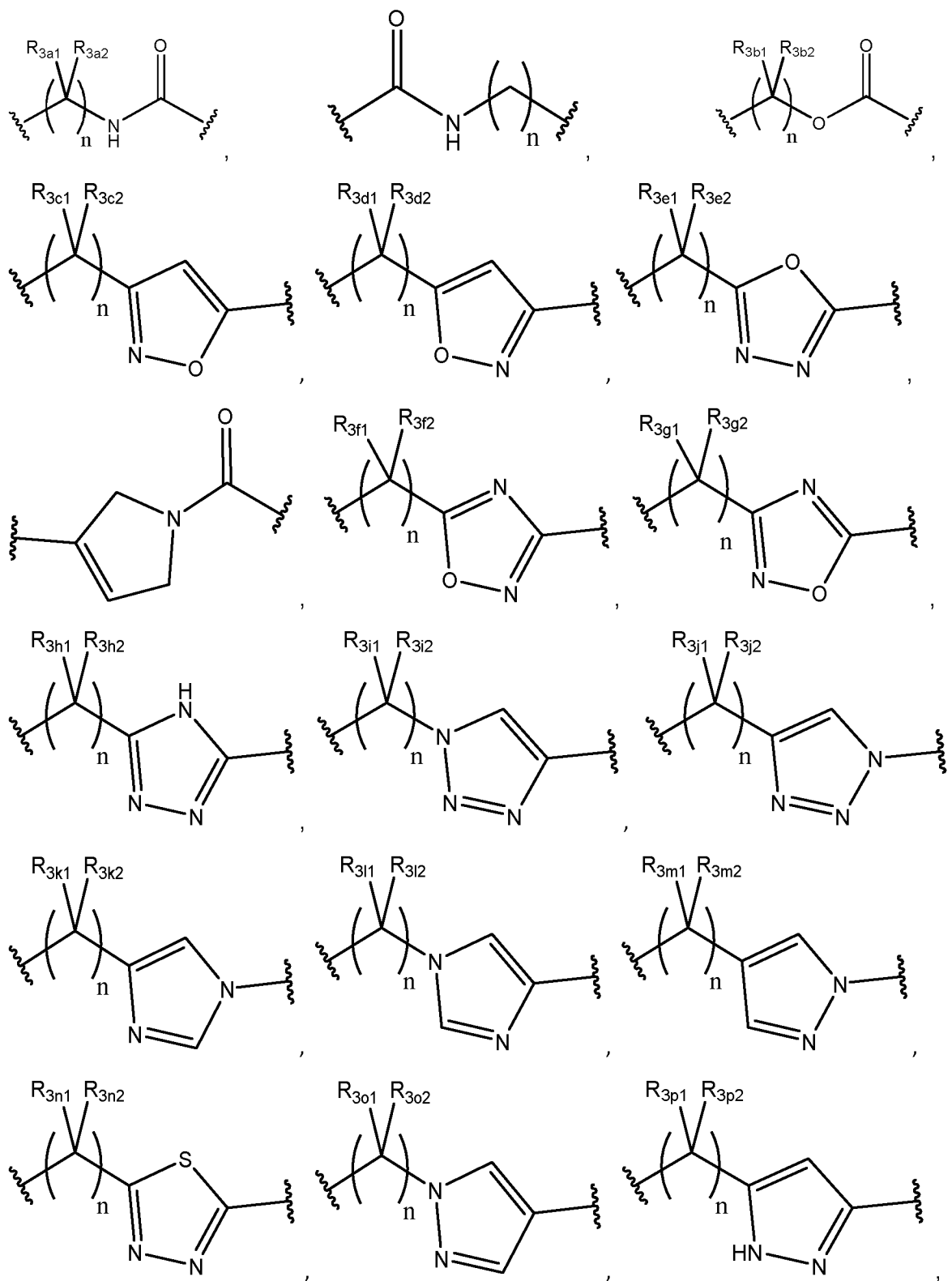
wherein

L_{2a} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂ alkyl or oxo;

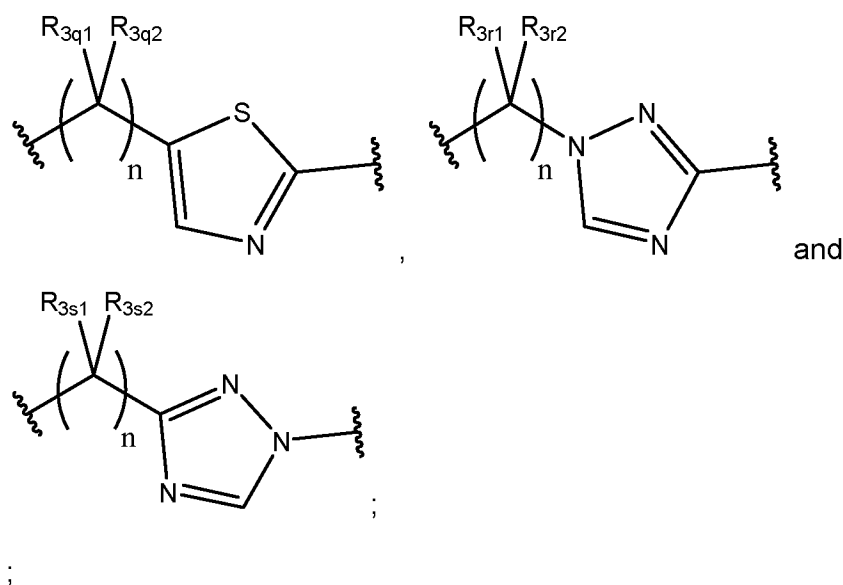
L_{2b} is absent or selected from O, S, SO, SO₂, N(R_n), C(O), C(O)O, OC(O), C(O)N(R_n), N(R_n)C(O), N(R_n)C(O)N(R_o), S(O)₂N(R_n), or N(R_n)SO₂, wherein R_n and R_o are each independently selected from hydrogen or C₁₋₂alkyl; and

Q₂ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₆cycloalkyl, aryl, heterocyclyl or heteroaryl, each of which is optionally substituted by one or more substituents selected from halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, amino, carboxy, carbamoyl, sulphamoyl, C₁₋₄alkyl, NR_pR_q, OR_p, C(O)R_p, C(O)OR_p, OC(O)R_p, C(O)N(R_p)R_q, N(R_r)C(O)R_p, S(O)_yR_p (where y is 0, 1 or 2), SO₂N(R_p)R_q, N(R_r)SO₂R_p or (CH₂)_zNR_pR_q (where z is 1, 2 or 3), wherein R_p and R_q are each independently selected from hydrogen or C₁₋₄alkyl;

Y is selected from:



5



wherein:

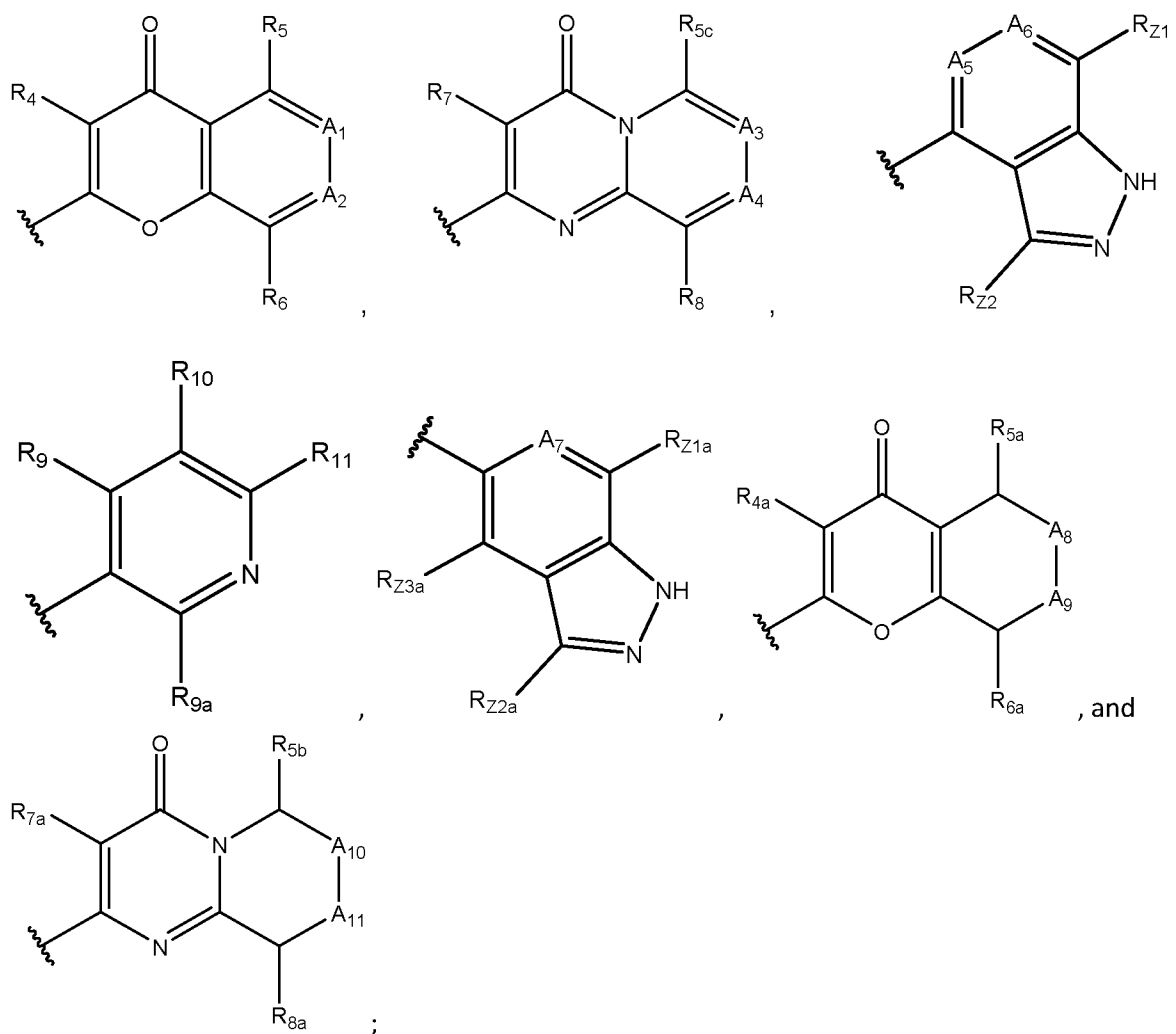
5 R_{3a1}, R_{3b1}, R_{3c1}, R_{3d1}, R_{3e1}, R_{3f1}, R_{3g1}, R_{3h1}, R_{3i1}, R_{3j1}, R_{3k1}, R_{3l1}, R_{3m1}, R_{3n1}, R_{3o1}, R_{3p1}, R_{3q1}, R_{3r1} and R_{3s1} are independently selected from hydrogen (including deuterium), C₁₋₆alkyl, C₃₋₄ cycloalkyl, hydroxy, and halo; and wherein C₁₋₆alkyl, or C₃₋₄ cycloalkyl is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

10 R_{3a2}, R_{3b2}, R_{3c2}, R_{3d2}, R_{3e2}, R_{3f2}, R_{3g2}, R_{3h2}, R_{3i2}, R_{3j2}, R_{3k2}, R_{3l2}, R_{3m2}, R_{3n2}, R_{3o2}, R_{3p2}, R_{3q2}, R_{3r2} and R_{3s2} are hydrogen or halo;

with the proviso that R_{3a1}, R_{3b1}, R_{3i1}, R_{3l1}, R_{3o1}, R_{3r1}, R_{3a2}, R_{3b2}, R_{3i2}, R_{3l2}, R_{3o2} and R_{3s1} cannot be halo when n=1 or when n=2 and the carbon atom to which they are attached is linked to an oxygen or nitrogen atom;

15 or R_{3a1} and R_{3a2}, R_{3b1} and R_{3b2}, R_{3c1} and R_{3c2}, R_{3d1} and R_{3d2}, R_{3e1} and R_{3e2}, R_{3f1} and R_{3f2}, R_{3g1} and R_{3g2}, R_{3h1} and R_{3h2}, R_{3i1} and R_{3i2}, R_{3j1} and R_{3j2}, R_{3k1} and R_{3k2}, R_{3l1} and R_{3l2}, R_{3m1} and R_{3m2}, R_{3n1} and R_{3n2}, R_{3o1} and R_{3o2}, R_{3p1} and R_{3p2}, R_{3q1} and R_{3q2}, or R_{3r1} and R_{3r2} or R_{3s1} and R_{3s2} may be linked such that, together with the carbon atom to which they are attached, they form a spiro-fused C₃₋₄cycloalkyl which is optionally substituted with one
20 or more substituents selected from halo, methyl, amino, cyano, and hydroxy;

Z is selected from:



wherein:

- 5 R₄, R₇, R_{4a} and R_{7a} are independently selected from hydrogen, halo, cyano and methyl;
R₅, R_{5a}, R_{5b} and R_{5c} are independently selected from hydrogen, halo, cyano and methyl;
R₆, R₈, R_{6a} and R_{8a} are independently selected from hydrogen, halo, cyano and methyl;
R₉, R_{9a}, R₁₀ and R₁₁ are independently selected from hydrogen, NH₂, halo, cyano, and
C₁₋₆ alkyl; or
- 10 R₉ and R₁₀ may be linked together to form a fused 5- or 6-membered saturated or
unsaturated ring system or R₁₀ and R₁₁ may be linked together to form a fused 5- or 6-
membered saturated or unsaturated ring system; wherein either of the fused 5- or 6-
membered saturated or unsaturated ring system may be optionally substituted by one
or more substituents selected from C₁₋₂alkyl, cyano, C₁₋₂haloalkyl, hydroxy, C₁₋₂alkoxy,
15 halo, C₁₋₂haloalkoxy, NR_{1ia}R_{1ja} or -S(O)₀₋₂R_{1ia}R_{1ja}, wherein R_{1ia} and R_{1ja} are H or C₁₋₂alkyl;

R_{Z1} and R_{Z1a} are selected from hydrogen, C₁₋₄alkyl, cyano, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, C₃₋₆cycloalkyl and -O-C₃₋₆cycloalkyl, wherein C₃₋₆cycloalkyl and -O-C₃₋₆cycloalkyl are optionally substituted by one or more of halo, methyl or methoxy;

R_{Z2} and R_{Z2a} are selected from hydrogen, C₁₋₄alkyl, cyano, halo, NH₂ and C₁₋₄alkoxy;

5 R_{Z3a} is selected from hydrogen, C₁₋₄alkyl, cyano, halo, NH₂ and C₁₋₄alkoxy

A₁ is selected from CR₁₂ and N;

A₂ is selected from CR₁₃ and N;

A₃ is selected from CR₁₄ and N;

A₄ is selected from CR₁₅ and N;

10 A₅ is selected from CR₁₆ and N;

A₆ is selected from CR₁₇ and N;

A₇ is selected from CR₁₈ and N;

A₈ is selected from CR₁₉R₂₀ and NR₂₁;

A₉ is selected from CR₂₂R₂₃ and NR₂₄;

15 A₁₀ is selected from CR₂₅R₂₆ and NR₂₇;

A₁₁ is selected from CR₂₈R₂₉ and NR₃₀;

R₁₂ and R₁₄ are independently selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₁₃ is selected from hydrogen, halo, cyano, methoxy and methyl;

R₁₅ is selected from hydrogen, halo, cyano methoxy and methyl;

20 R₁₆ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₃₋₄cycloalkyl, a 3- to 4-membered heterocyclyl and C₃₋₄cycloalkoxy;

R₁₇ is selected from hydrogen, hydroxy, halo, cyano, C₁₋₅ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, C₂₋₄ alkenyl, C₂₋₄ alkynyl, phenyl, a 5- or 6-membered or heteroaryl, C₃₋₆cycloalkyl, -O-C₃₋₆cycloalkyl, heterocyclyl, -O-heterocyclyl (carbon-

25 linked), -(OCH₂CH₂)_m-NR_qR_r, -(OCH₂CH₂)_m-OCH₃ wherein m is an integer from 1 to 6, NR_qR_r, -C(O)-NR_qR_r, -C(O)OR_q;

wherein R_q and R_r are each independently hydrogen, C₁₋₅ alkyl, C₃₋₆cycloalkyl, a 3- to 6- membered carbon-linked heterocyclyl, wherein C₁₋₅ alkyl, C₃₋₆cycloalkyl, a 3- to 6-membered carbon-linked heterocyclyl may be optionally substituted by one or more substituents selected from C₁₋₂alkyl, cyano, C₁₋₂haloalkyl, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, NR_{1ea}R_{1fa} or -S(O)₀₋₂R_{1ea}R_{1fa}, wherein R_{1ea} and R_{1fa} are H or C₁₋₂alkyl;

30

or R_q and R_r are linked together such that, together with the nitrogen atom to which they are attached, they form a 3- to 6-membered heterocyclic ring, which may be optionally substituted by one or more substituents selected from C₁₋₂alkyl, cyano, C₁₋₂haloalkyl, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy;

5 wherein any C₁₋₅alkyl, C₁₋₄alkoxy, C₂₋₄alkenyl, C₂₋₄alkynyl, phenyl, 5- or 6-membered or heteroaryl, C₃₋₆cycloalkyl, -O-C₃₋₆cycloalkyl, heterocyclyl or -O-heterocyclyl (carbon-linked) is optionally further substituted by one or more substituents selected from C₁₋₂alkyl, cyano, C₁₋₂haloalkyl, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, NR_{1ea}R_{1fa} or -S(O)₀₋₂R_{1ea}R_{1fa}, wherein R_{1ea} and R_{1fa} are H or C₁₋₂alkyl;

10 R₁₈ is selected from hydrogen, halo, cyano, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, a 5- or 6-membered heteroaryl, C₁₋₄alkoxy, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₃₋₄cycloalkyl, a 3- to 4-membered heterocyclyl and C₃₋₄cycloalkoxy;

R₁₉, R₂₀, R₂₅ and R₂₆ are selected from hydrogen, halo, cyano and C₁₋₄alkyl;

R₂₂ and R₂₃ are selected from hydrogen, halo, cyano and methyl;

15 R₂₈ and R₂₉ are selected from hydrogen, methoxy and methyl;

R₂₁, R₂₄, R₂₇ and R₃₀ are hydrogen; and

n is 0, 1 or 2;

with the proviso that the compound is not:

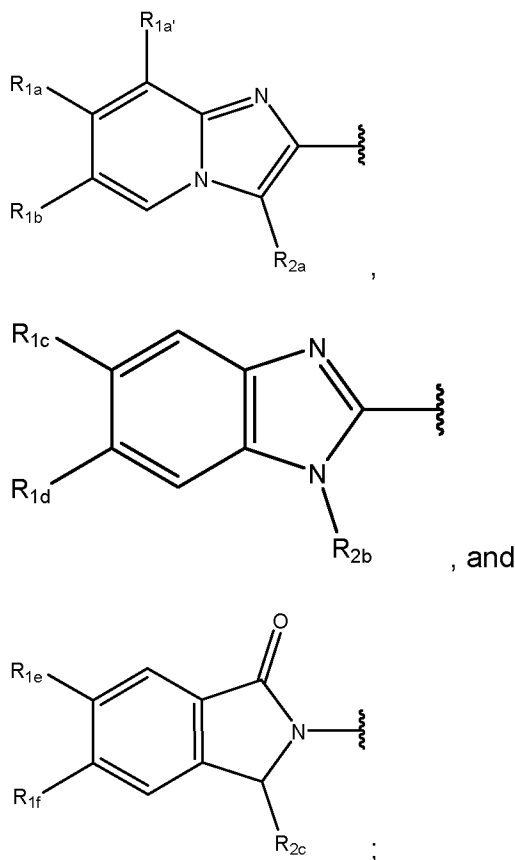
2-((1H-benzo[d]imidazol-2-yl)methyl)-5-(pyridin-3-yl)-1,3,4-oxadiazole;

20 2-((6-chloro-1-phenyl-1H-benzo[d]imidazol-2-yl)methyl)-5-(pyridin-3-yl)-1,3,4-oxadiazole;

N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-5-carboxamide.

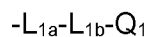
2. A compound of the formula (I), or a pharmaceutically acceptable salt thereof,
25 according to claim 1, wherein:

X is selected from:



wherein:

- 5 R_{1a} , R_{1b} , R_{1c} , R_{1d} , R_{1e} and R_{1f} are independently selected from hydrogen, cyano, halo or a group of the formula:



wherein

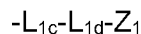
- 10 L_{1a} is absent or C_{1-3} alkylene, C_{3-4} cycloalkylene, optionally substituted by one or more substituents selected from C_{1-2} alkyl, halo, hydroxy, or oxo;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C_{1-2} alkyl; and

- 15 Q_1 is hydrogen, cyano, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u,

$N(R_t)SO_2R_u$ or $(CH_2)_zNR_tR_u$ (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C_{1-4} alkyl; or

Q_1 is optionally substituted by a group of the formula:



5 wherein

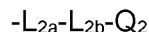
L_{1c} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

L_{1d} is absent or selected from $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_v)$, $N(R_v)C(O)$, $N(R_v)C(O)N(R_w)$, $S(O)_2N(R_v)$, or $N(R_v)SO_2$, wherein R_v and R_w are each independently selected from hydrogen or C_{1-2} alkyl; and

10 Z_1 is phenyl or 5-6 membered heteroaryl; wherein Z_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, halo, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, C_{1-4} alkylamino, amino, cyano, hydroxyl, carboxy, carbamoyl or sulphamoyl;

$R_{1a'}$ is selected from hydrogen and methyl;

15 R_{2a} , R_{2b} and R_{2c} are selected from hydrogen or a group of the formula:



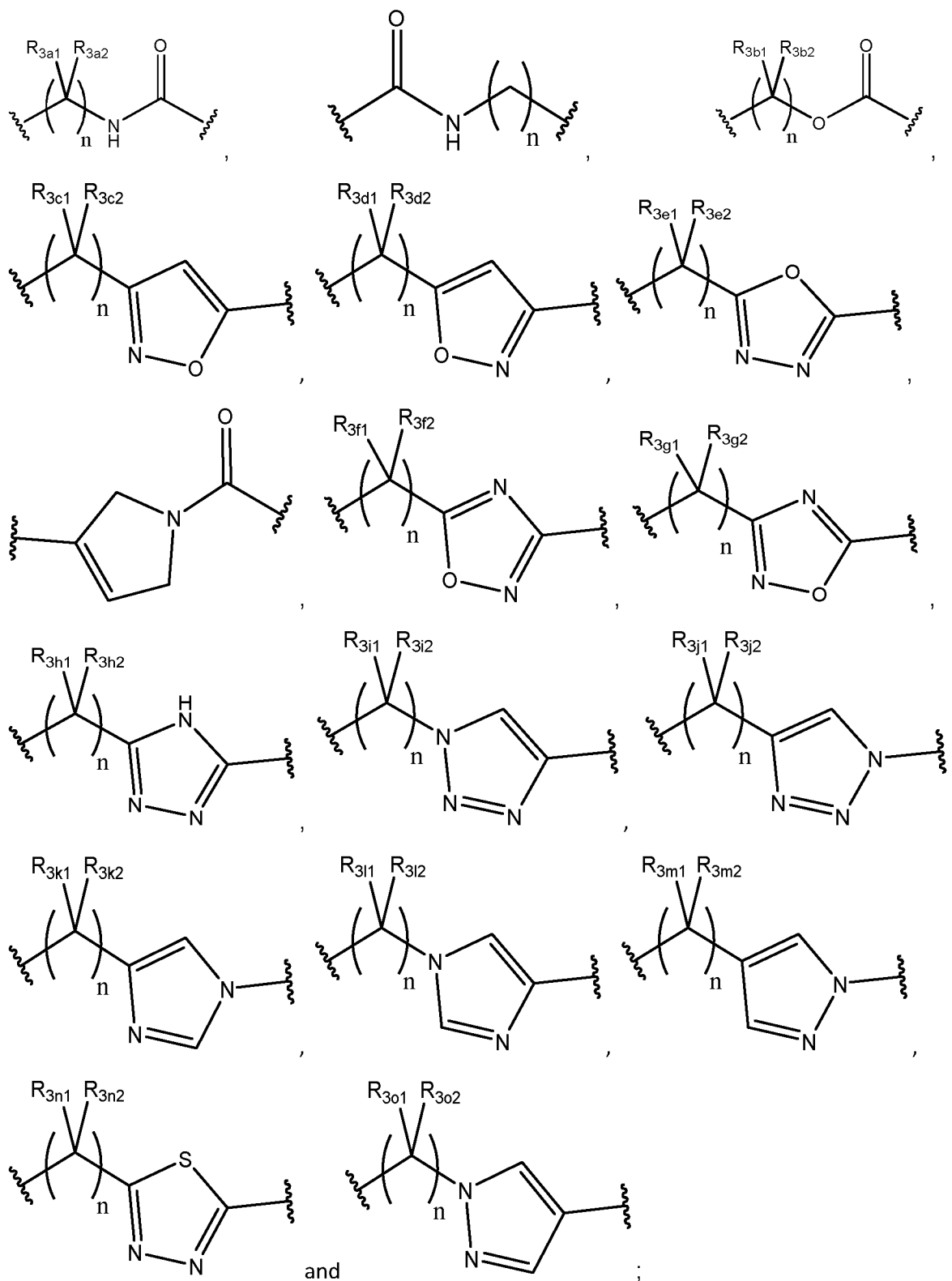
wherein

L_{2a} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

20 L_{2b} is selected from O , S , SO , SO_2 , $N(R_n)$, $C(O)$, $C(O)O$, $OC(O)$, $C(O)N(R_n)$, $N(R_n)C(O)$, $N(R_n)C(O)N(R_o)$, $S(O)_2N(R_n)$, or $N(R_n)SO_2$, wherein R_n and R_o are each independently selected from hydrogen or C_{1-2} alkyl; and

25 Q_2 is hydrogen, cyano, C_{1-6} alkyl, C_{3-6} cycloalkyl, aryl, heterocyclyl or heteroaryl, each of which is optionally substituted by one or more substituents selected from halo, trifluoromethyl, trifluoromethoxy, amino, cyano, hydroxy, amino, carboxy, carbamoyl, sulphamoyl, C_{1-4} alkyl, NR_pR_q , OR_p , $C(O)R_p$, $C(O)OR_p$, $OC(O)R_p$, $C(O)N(R_p)R_q$, $N(R_r)C(O)R_p$, $S(O)_yR_p$ (where y is 0, 1 or 2), $SO_2N(R_p)R_q$, $N(R_r)SO_2R_p$ or $(CH_2)_zNR_pR_q$ (where z is 1, 2 or 3), wherein R_p and R_q are each independently selected from hydrogen or C_{1-4} alkyl;

Y is selected from:



wherein:

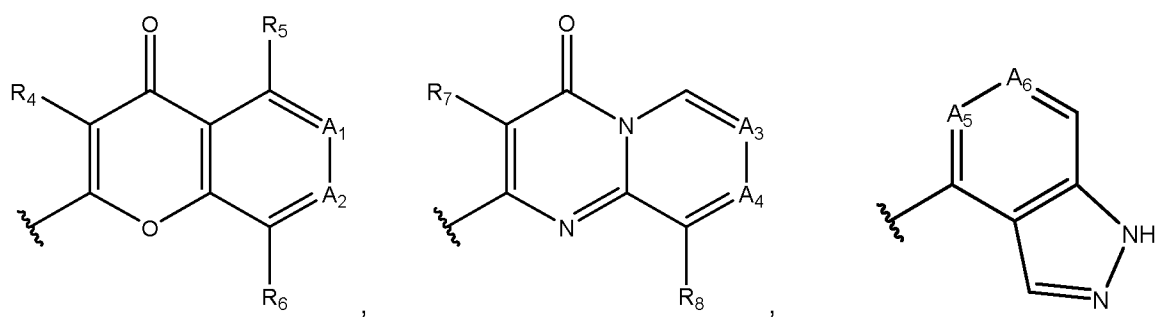
R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} and R_{3o1} are independently selected from hydrogen, C_{1-6} alkyl, C_{3-4} cycloalkyl, hydroxy, and halo; and

wherein C₁₋₆alkyl, or C₃₋₄ cycloalkyl is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

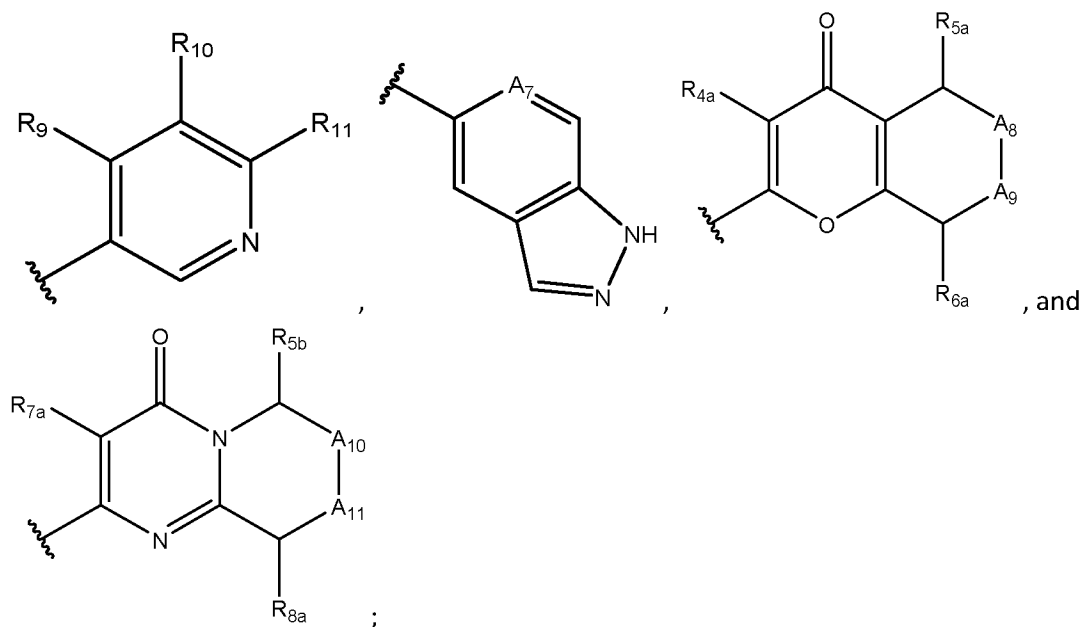
R_{3a2}, R_{3b2}, R_{3c2}, R_{3d2}, R_{3e2}, R_{3f2}, R_{3g2}, R_{3h2}, R_{3i2}, R_{3j2}, R_{3k2}, R_{3l2}, R_{3m2}, R_{3n2} and R_{3o2} are hydrogen;

- 5 or R_{3a1} and R_{3a2}, R_{3b1} and R_{3b2}, R_{3c1} and R_{3c2}, R_{3d1} and R_{3d2}, R_{3e1} and R_{3e2}, R_{3f1} and R_{3f2}, R_{3g1} and R_{3g2}, R_{3h1} and R_{3h2}, R_{3i1} and R_{3i2}, R_{3j1} and R_{3j2}, R_{3k1} and R_{3k2}, R_{3l1} and R_{3l2}, R_{3m1} and R_{3m2}, R_{3n1} and R_{3n2}, or R_{3o1} and R_{3o2} may be linked to form a spiro-fused C₃₋₄cycloalkyl which is optionally substituted with one or more substituents selected from halo, amino, cyano, and hydroxy;

- 10 Z is selected from:



and



- 15 wherein:

R₄, R₇, R_{4a} and R_{7a} are independently selected from hydrogen and methyl;

R₅, R_{5a} and R_{5b} are independently selected from hydrogen and halo;

R₆, R₈, R_{6a} and R_{8a} are independently selected from hydrogen, halo and methyl;

R₉, R₁₀ and R₁₁ are independently selected from hydrogen, NH₂, halo, cyano, and C₁₋₆ alkyl; or

R₉ and R₁₀ may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system or R₁₀ and R₁₁ may be linked together to form a fused 5- or 6-membered saturated or unsaturated ring system;

A₁ is selected from CR₁₂ and N;

A₂ is selected from CR₁₃ and N;

A₃ is selected from CR₁₄ and N;

A₄ is selected from CR₁₅ and N;

A₅ is selected from CR₁₆ and N;

A₆ is selected from CR₁₇ and N;

A₇ is selected from CR₁₈ and N;

A₈ is selected from CR₁₉R₂₀ and NR₂₁;

A₉ is selected from CR₂₂R₂₃ and NR₂₄;

A₁₀ is selected from CR₂₅R₂₆ and NR₂₇;

A₁₁ is selected from CR₂₈R₂₉ and NR₃₀;

R₁₂ and R₁₄ are independently selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₁₃ is selected from hydrogen, halo, cyano and methyl;

R₁₅ is selected from hydrogen, methoxy and methyl;

R₁₆ is selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

R₁₇ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl and a 5- or 6-membered heteroaryl;

R₁₈ is selected from hydrogen, halo, cyano, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl and a 5- or 6-membered heteroaryl;

R₁₉, R₂₀, R₂₅ and R₂₆ are selected from hydrogen, halo, cyano and C₁₋₄ alkyl;

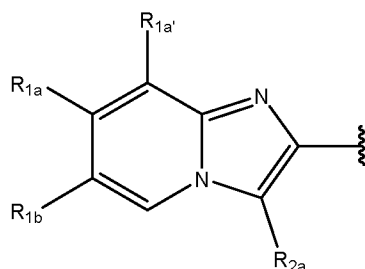
R₂₂ and R₂₃ are selected from hydrogen, halo, cyano and methyl;

R₂₈ and R₂₉ are selected from hydrogen, methoxy and methyl;

R₂₁, R₂₄, R₂₇ and R₃₀ are hydrogen; and

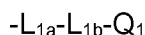
n is 0, 1 or 2.

3. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein X is:



- 5 and R_{1a}, R_{1b}, R_{1a'} and R_{2a} are each as defined in claim 1.
4. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein one of R_{1a} and R_{1b}, R_{1c} and R_{1d}, R_{1e} and R_{1f} is selected from hydrogen, halo, C₁₋₆alkyl, C₂₋₃alkenyl or -O-C₁₋₆alkyl,

and the other is selected from hydrogen, cyano, halo or a group of the formula:



wherein

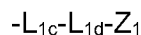
L_{1a} is absent or C₁₋₃alkylene, C₃₋₄cycloalkylene, optionally substituted by one or more substituents selected from aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl, C₁₋₂alkyl, cyano, halo, hydroxy, or oxo, wherein any aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl or C₁₋₂alkyl is optionally further substituted by one or more substituents selected from halo, cyano or hydroxy;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl, wherein C₁₋₂alkyl is optionally further substituted by C₃₋₆cycloalkyl or a 3 to 6 membered heterocyclyl, which in turn are optionally further substituted by halo, hydroxy, C₁₋₂alkoxy or C₁₋₂haloalkoxy; and

Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₈cycloalkyl (e.g. C₃₋₆cycloalkyl), C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, oxo cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1

or 2), $\text{SO}_2\text{N}(\text{R}_t)\text{R}_u$, $\text{N}(\text{R}_t)\text{SO}_2\text{R}_u$ or $(\text{CH}_2)_z\text{NR}_t\text{R}_u$ (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C_{1-4} alkyl; or

Q_1 is optionally substituted by one or more groups of the formula:



5 wherein

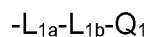
L_{1c} is absent or C_{1-3} alkylene optionally substituted by C_{1-2} alkyl or oxo;

L_{1d} is absent or selected from $\text{C}(\text{O})$, O , $\text{C}(\text{O})\text{O}$, $\text{OC}(\text{O})$, $\text{C}(\text{O})\text{N}(\text{R}_v)$, $\text{N}(\text{R}_v)\text{C}(\text{O})$, $\text{N}(\text{R}_v)\text{C}(\text{O})\text{N}(\text{R}_w)$, $\text{S}(\text{O})_2\text{N}(\text{R}_v)$, or $\text{N}(\text{R}_v)\text{SO}_2$, wherein R_v and R_w are each independently selected from hydrogen or C_{1-2} alkyl; and

10 Z_1 is C_{3-8} cycloalkyl (including a spirocyclic carbocyclic and a bridged C_{3-8} cycloalkyl), heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system), phenyl or 5-6 membered heteroaryl; wherein Z_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, C_{3-6} cycloalkyl, heterocyclyl, halo, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, cyano, hydroxyl, $\text{NR}_{t1}\text{R}_{u1}$, OR_{t1} , $\text{C}(\text{O})\text{R}_{t1}$, $\text{C}(\text{O})\text{OR}_{t1}$, $\text{OC}(\text{O})\text{R}_{t1}$, $\text{C}(\text{O})\text{N}(\text{R}_{t1})\text{R}_{u1}$, $\text{N}(\text{R}_{t1})\text{C}(\text{O})\text{R}_{u1}$, $\text{S}(\text{O})_y\text{R}_{t1}$ (where y is 0, 1 or 2), $\text{SO}_2\text{N}(\text{R}_{t1})\text{R}_{u1}$, $\text{N}(\text{R}_{t1})\text{SO}_2\text{R}_{u1}$ or $(\text{CH}_2)_z\text{NR}_{t1}\text{R}_{u1}$ (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C_{1-4} alkyl; and when Z_1 is C_{3-8} cycloalkyl or heterocyclyl, Z_1 is optionally spiro-fused to a C_{3-6} cycloalkyl or heterocyclyl ring.

5. A compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein R_{1a} , R_{1c} and R_{1e} are selected from hydrogen, halo, C_{1-6} alkyl, C_{2-3} alkenyl or -O- C_{1-6} alkyl

25 and R_{1b} , R_{1d} , and R_{1f} are selected from hydrogen, cyano, halo or a group of the formula:



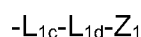
wherein

30 L_{1a} is absent or C_{1-3} alkylene, C_{3-4} cycloalkylene, optionally substituted by one or more substituents selected from aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl, C_{1-2} alkyl, cyano, halo, hydroxy, or oxo, wherein any aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl or C_{1-2} alkyl is optionally further substituted by one or more substituents selected from halo, cyano or hydroxy;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl, wherein C₁₋₂alkyl is optionally further substituted by C₃₋₆cycloalkyl or a 3 to 6 membered heterocyclyl, which in turn are optionally further substituted by halo, hydroxy, C₁₋₂alkoxy or C₁₋₂haloalkoxy; and

Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₈cycloalkyl (e.g. C₃₋₆cycloalkyl), C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, oxo, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u, N(R_t)SO₂R_u or (CH₂)_zNR_tR_u (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



wherein

L_{1c} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

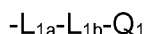
L_{1d} is absent or selected from C(O), O, C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl), heterocyclyl, phenyl or 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, cyano, hydroxyl, NR_{t1}R_{u1}, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, C(O)N(R_{t1})R_{u1}, N(R_{t1})C(O)R_{u1}, S(O)_yR_{t1} (where y is 0, 1 or 2), SO₂N(R_{t1})R_{u1}, N(R_{t1})SO₂R_{u1} or (CH₂)_zNR_{t1}R_{u1} (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C₁₋₄alkyl; and when Z₁ is C₃₋₈cycloalkyl or heterocyclyl, Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclyl ring.

6. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R_{1a}, R_{1c} and R_{1e} are selected from hydrogen, halo, C₁₋₄alkyl, C₂₋₃alkenyl and -O-C₁₋₄alkyl.

7. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein:

R_{1b} , R_{1d} and R_{1f} are selected from hydrogen, halo, cyano or from a group of formula:



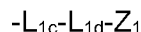
5 wherein

L_{1a} is absent or C_{1-3} alkylene, optionally substituted by one or more hydroxy;

L_{1b} is absent or $N(R_r)$ wherein R_r is hydrogen or C_{1-4} alkyl; and

10 Q_1 is C_{1-6} alkyl, C_{2-3} alkenyl, C_{3-6} cycloalkyl, aryl, heterocyclyl or heteroaryl; and wherein Q_1 is optionally substituted by one or more substituents selected from halo, carboxy, trifluoromethyl, NR_tR_u , OR_t wherein R_t and R_u are independently selected from hydrogen or C_{1-4} alkyl; or

Q_1 is optionally substituted by one or more groups of the formula:



wherein

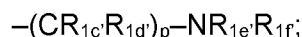
15 L_{1c} is absent;

L_{1d} is absent; and

20 Z_1 is is phenyl, 5-6 membered heteroaryl, C_{3-8} cycloalkyl or heterocyclyl; wherein Z_1 is optionally substituted by one or more substituents selected from C_{1-4} alkyl, C_{3-6} cycloalkyl, heterocyclyl, halo, C_{1-4} haloalkyl, OR_{t1} , $C(O)R_{t1}$, $C(O)OR_{t1}$, $OC(O)R_{t1}$, wherein R_{t1} and R_{u1} are each independently selected from hydrogen or C_{1-4} alkyl; and Z_1 is optionally spiro-fused to a C_{3-6} cycloalkyl or heterocyclyl ring.

8. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:

25 R_{1b} , R_{1d} and R_{1f} are independently selected from hydrogen, halo, cyano, hydroxy, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, or a group of the formula:



wherein

p is an integer selected from 1 or 2;

$R_{1c'}$ and $R_{1d'}$ are independently selected from:

30 (i) hydrogen (including deuterium),

(ii) C₁₋₃alkyl which is optionally substituted by one more substituents selected from cyano, hydroxy, C₁₋₃alkoxy, halo, C₁₋₃haloalkoxy, -O-C₃₋₄cycloalkyl, or NH₂; wherein -O-C₃₋₆cycloalkyl is optionally substituted with halo, cyano or hydroxy,

5 (iii) or R_{1c'} and R_{1d'} are linked together such that, together with the carbon atom to which they are attached, they form a 3- to 5-membered cycloalkyl or heterocyclic ring, or a spirocyclic ring system, each of which is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo or C₁₋₂haloalkoxy;

10 R_{1e'} is selected from:

- (i) hydrogen (including deuterium);
- (ii) C₁₋₃alkyl which is optionally substituted by one more substituents selected from cyano, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy and NH₂;

R_{1f} is a group with the formula:

15
$$-(CR_{1g}R_{1h})_q-T_1$$

wherein:

q is 0, 1 or 2;

R_{1g} and R_{1h} are independently selected from:

- a) hydrogen (including deuterium); or
- 20 b) C₁₋₃alkyl, which is optionally substituted by one more substituents selected from cyano, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, -O-C₃cycloalkyl, wherein -O-C₃cycloalkyl is optionally substituted with halo, cyano or hydroxy;

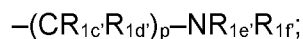
25 and T₁ is selected from C₃₋₈cycloalkyl, aryl, heterocyclyl, heteroaryl, a spirocyclic carbocyclic or heterocyclic ring system, a bridged C₃₋₈cycloalkyl, or a bridged heterocyclic ring system, each of which is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo or C₁₋₂haloalkoxy;

30 or R_{1e'} and R_{1f} are linked such that, together with the nitrogen atom to which they are attached, they form a mono- or bicyclic-heterocyclic ring, which is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, NR_{1i}R_{1j} or -S(O)₀₋₂R_{1i}R_{1j}, wherein R_{1i} and R_{1j} are H or C₁₋₂alkyl, and/or the mono- or bicyclic heterocyclic ring formed by R_{1e} and R_{1f} is optionally

spiro-fused to a C₃₋₆cycloalkyl or a heterocyclic ring, which in turn is optionally substituted by one or more substituents selected from C₁₋₂alkyl, cyano, hydroxy, C₁₋₂alkoxy, halo, C₁₋₂haloalkoxy, NR_{1i}R_{1j} or -S(O)₀₋₂R_{1i}R_{1j}, wherein R_{1i} and R_{1j} are H or C₁₋₂alkyl.

- 5 9. A compound according to claim 1 or 8, or a pharmaceutically acceptable salt thereof, wherein

R_{1d} and R_{1f} are independently selected from hydrogen, halo, cyano, hydroxy, methyl and methoxy; and R_{1b} is a group of the formula:



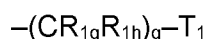
10 wherein

p is 1;

R_{1c'} and R_{1d'} are independently selected from hydrogen (including deuterium) or C₁₋₂alkyl;

R_{1e'} is selected from hydrogen (including deuterium) or C₁₋₂alkyl; and

15 R_{1f'} is a group with the formula:



wherein:

q is 1;

20 R_{1g} and R_{1h} are independently selected from hydrogen (including deuterium) or C₁₋₂alkyl;

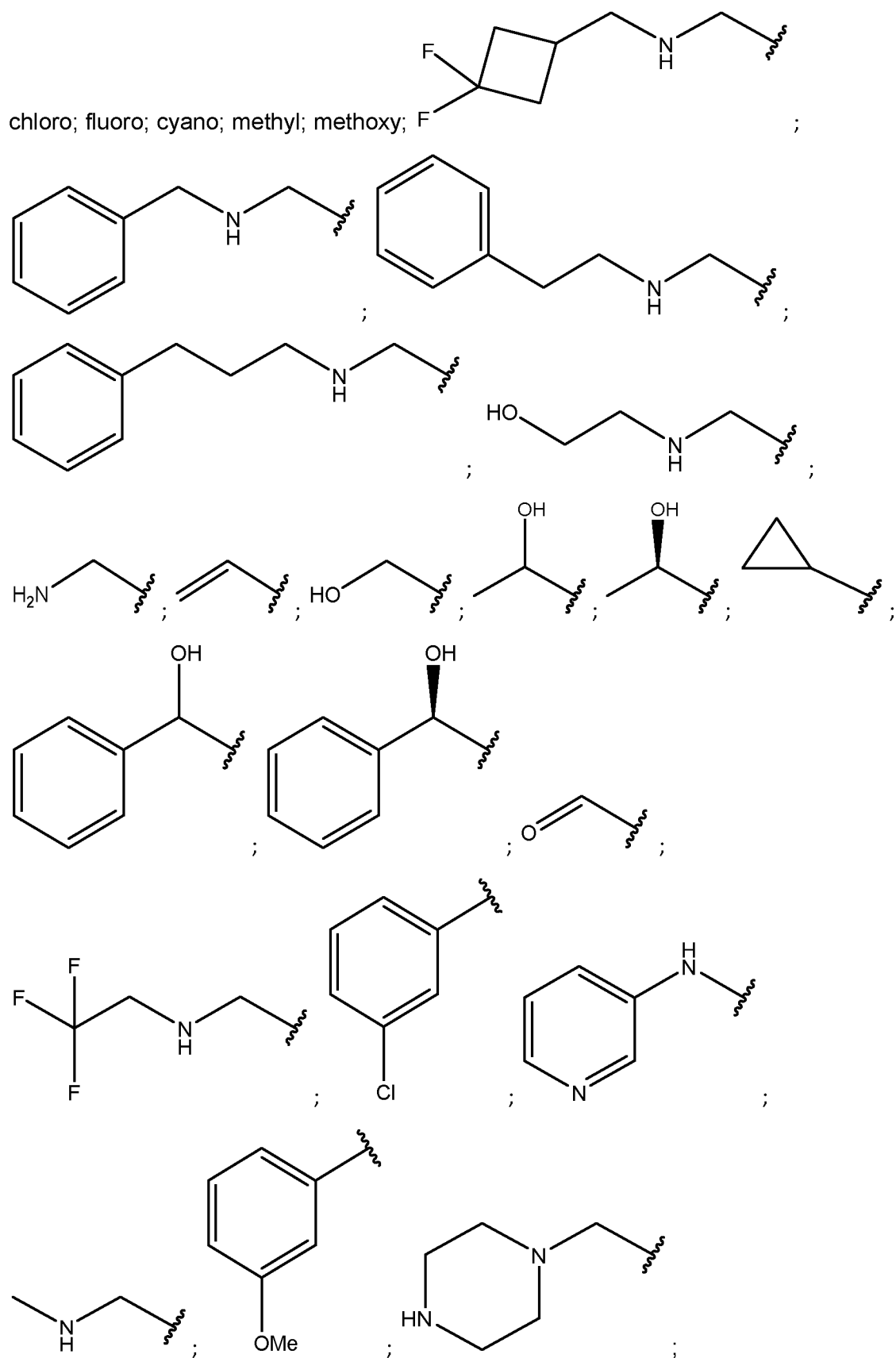
and T₁ is selected from C₃₋₄cycloalkyl, heterocyclyl, a spirocyclic carbocyclic or heterocyclic ring system, a bridged C₃₋₈cycloalkyl, or a bridged heterocyclic ring system, each of which is optionally substituted by one or more substituents selected from C₁₋₂alkyl, C₁₋₂haloalkyl, cyano, hydroxy, C₁₋₂alkoxy, halo or C₁₋₂haloalkoxy.

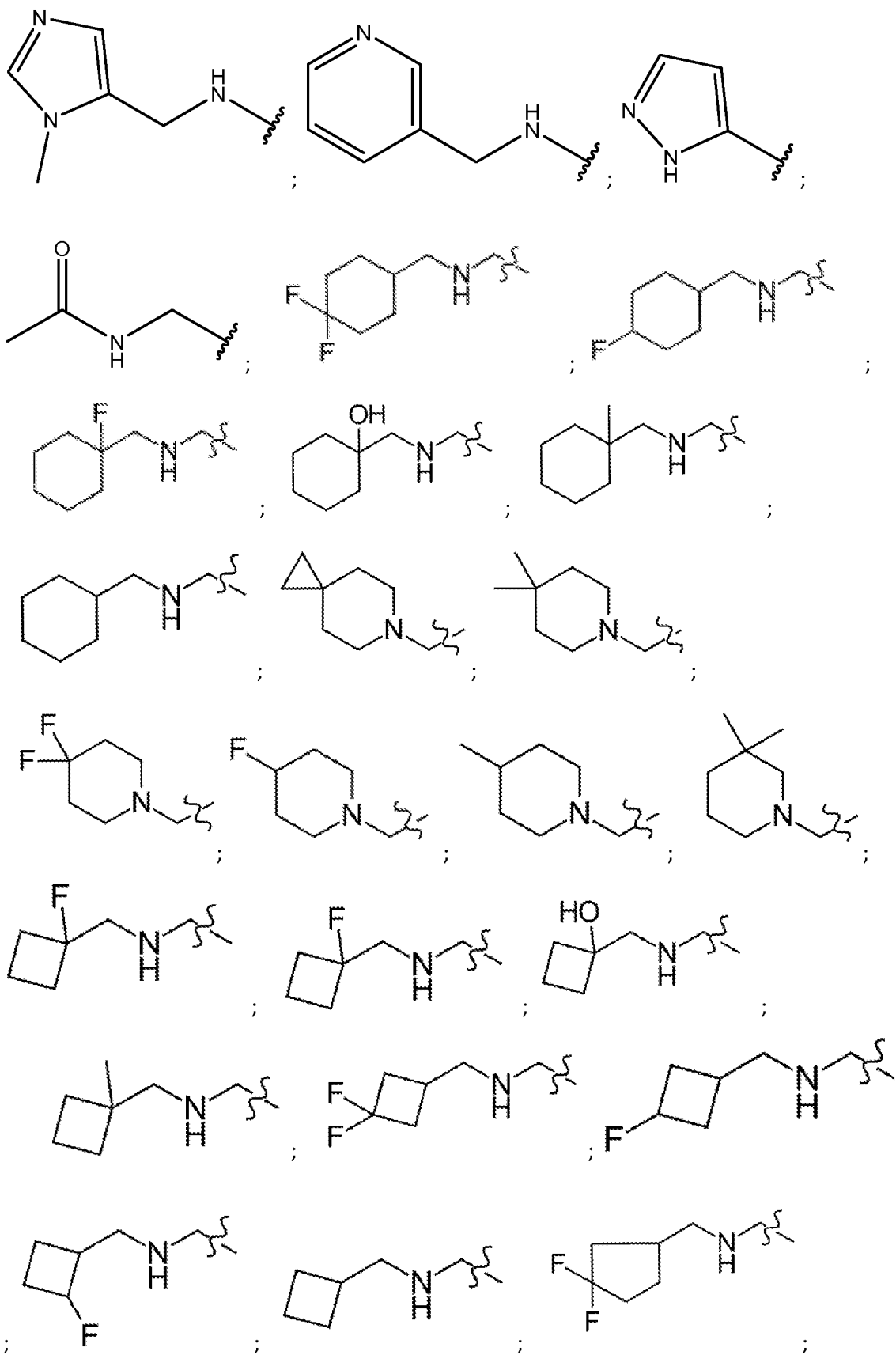
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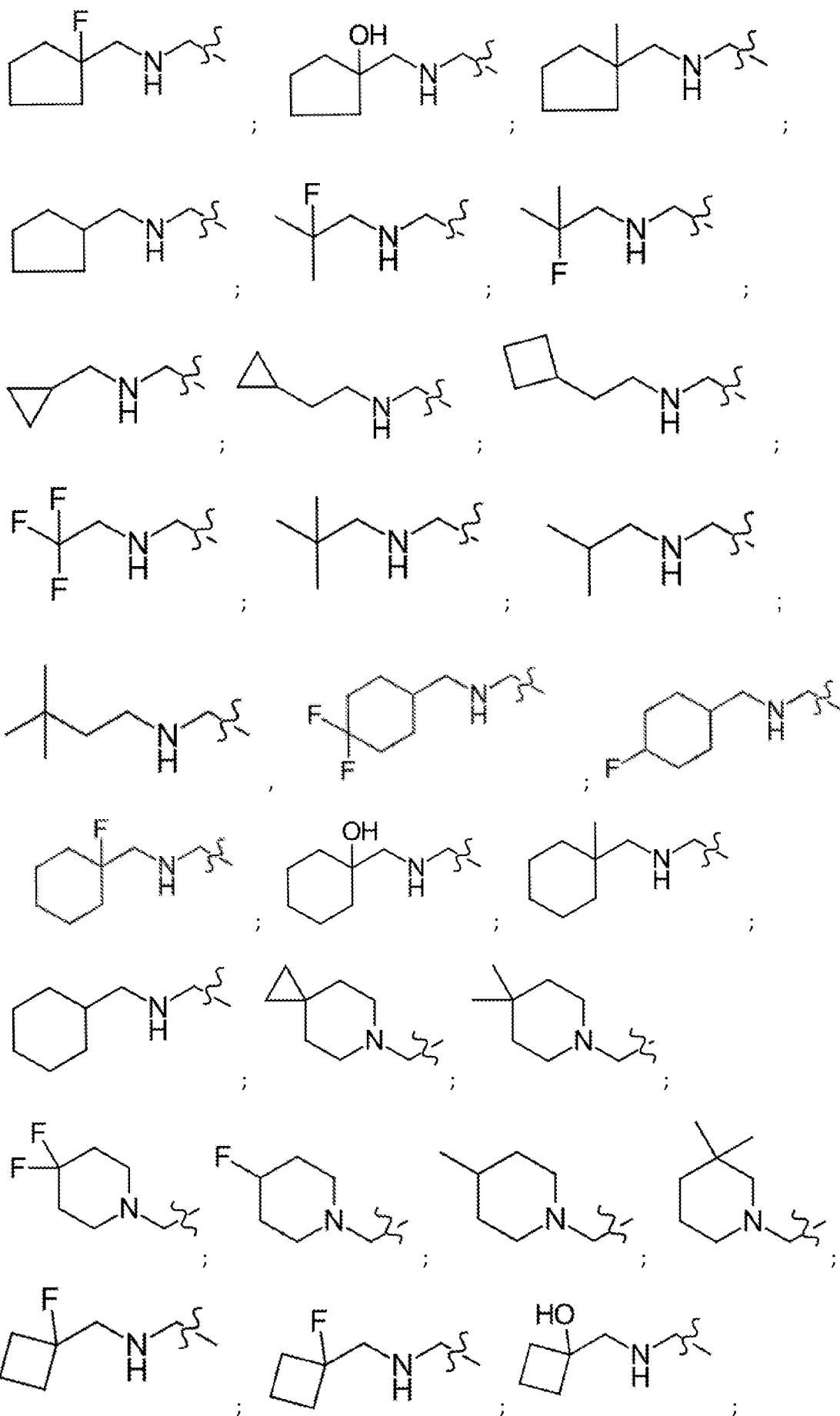
10. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R_{2a}, R_{2b} and R_{2c} are hydrogen.

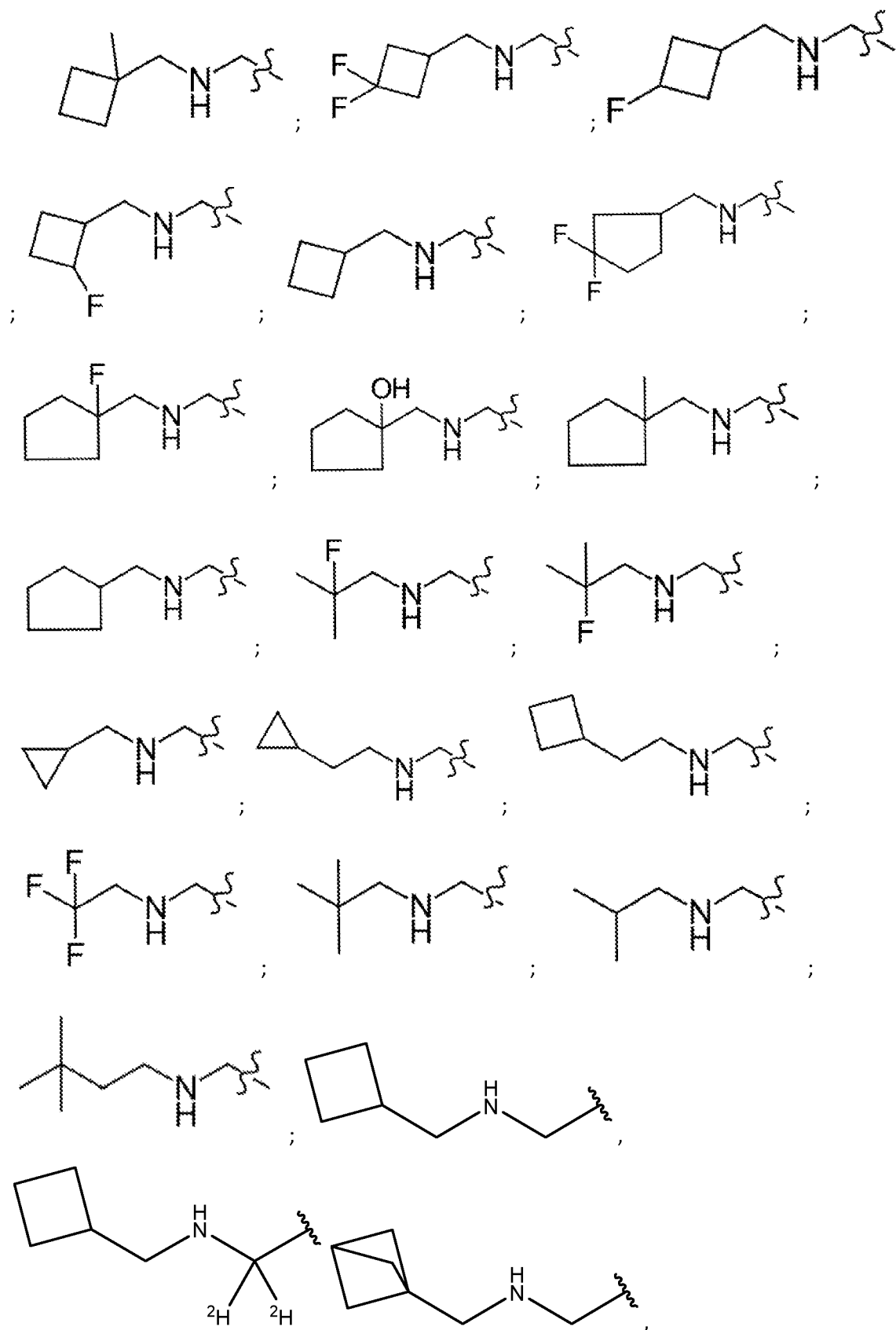
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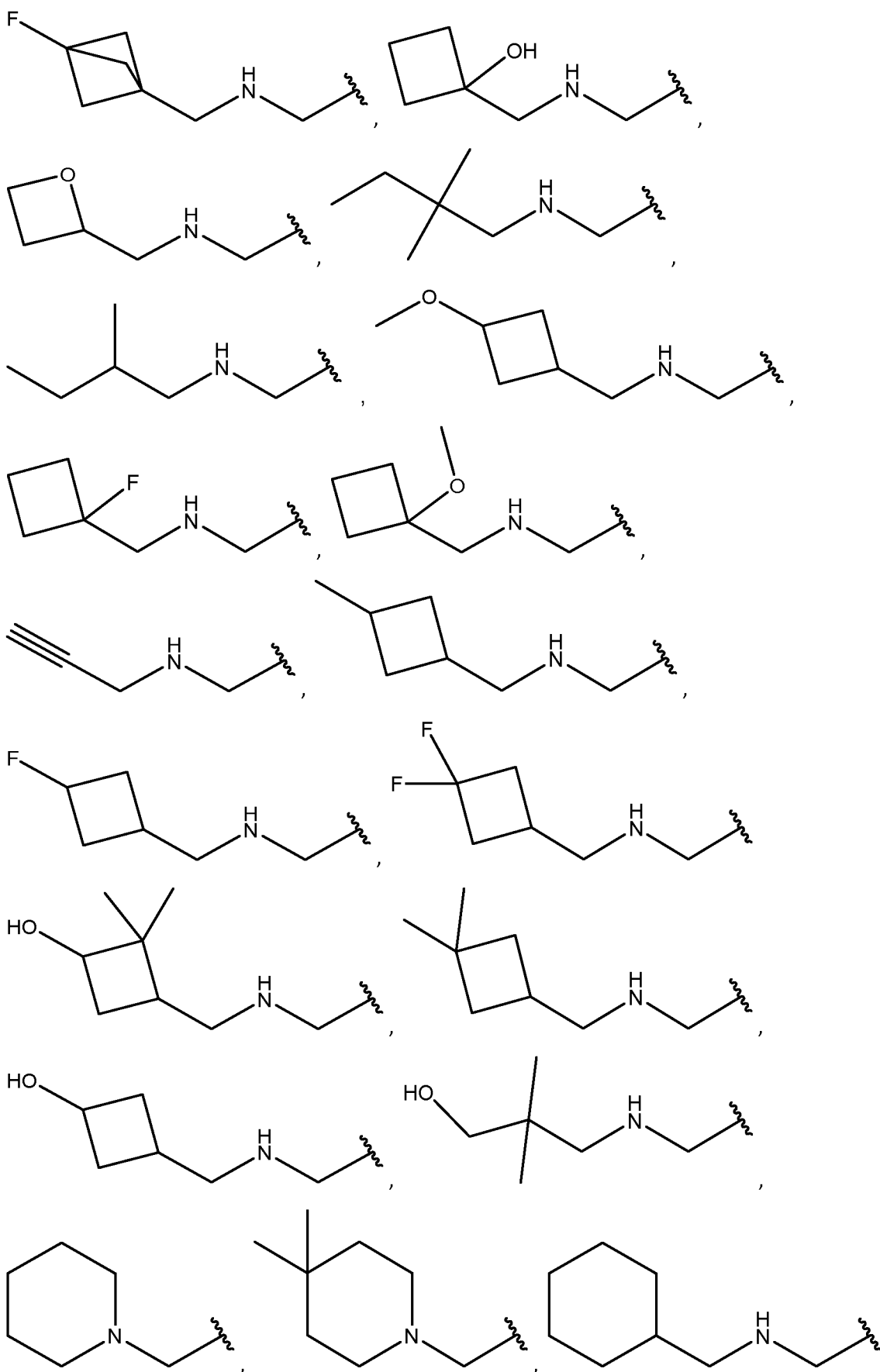
11. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R_{1b}, R_{1d} and R_{1f} are selected from hydrogen; bromo;

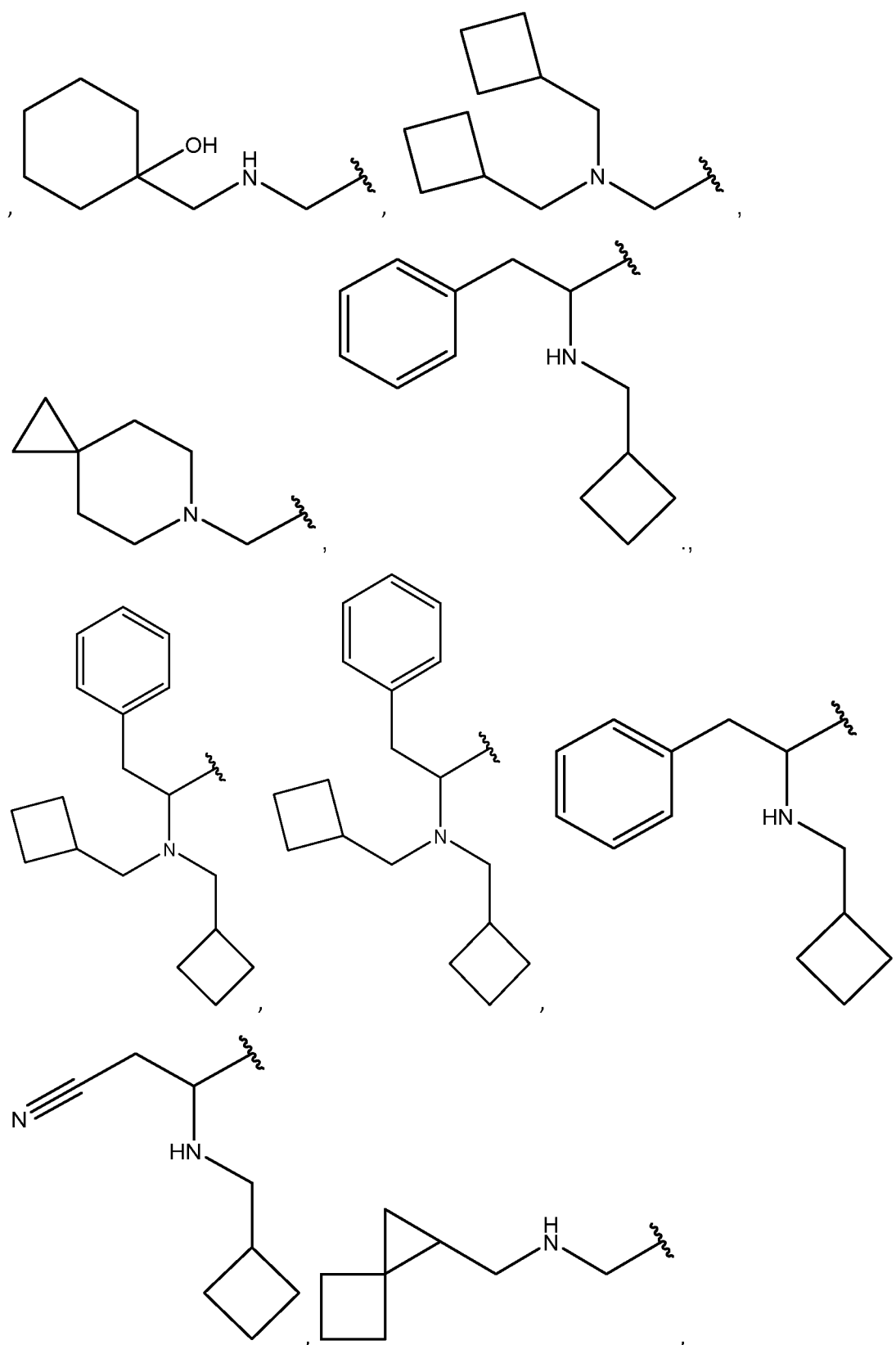


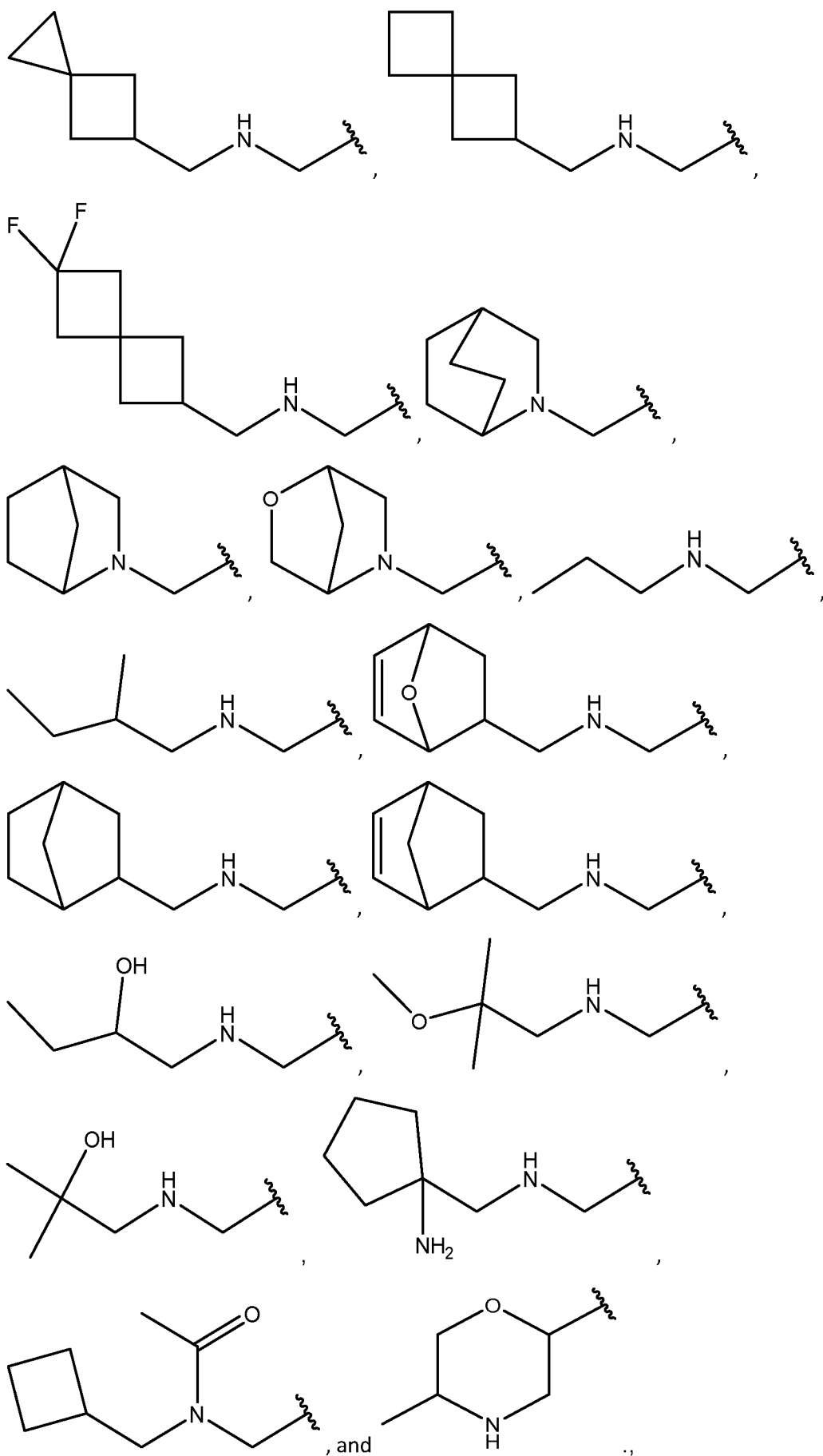




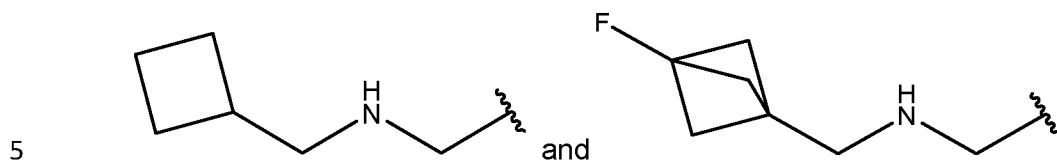




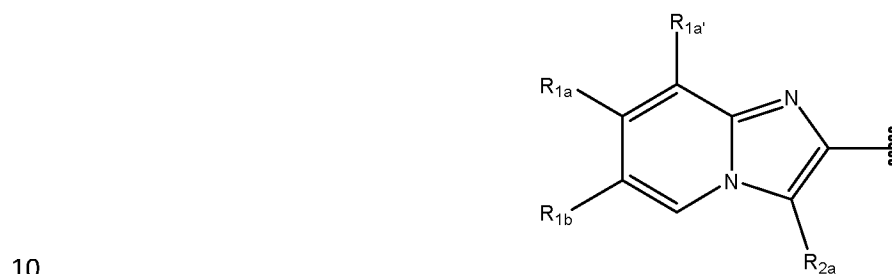




12. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R_{1b} , R_{1d} and R_{1f} are selected from;

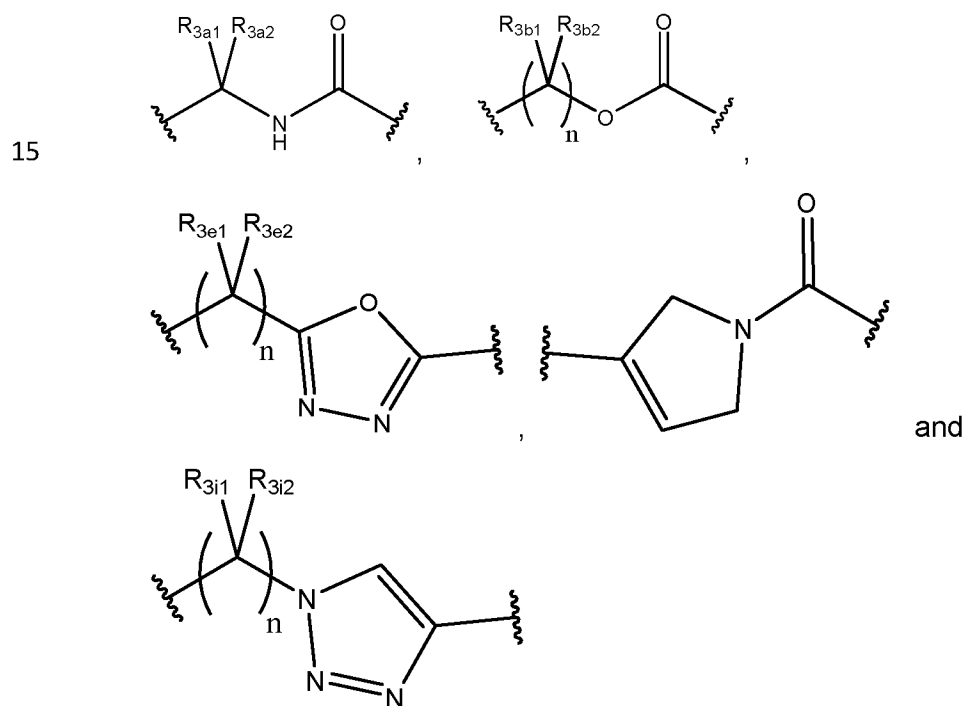


13. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein X is:



and R_{1a} , R_{1b} , $R_{1a'}$ and R_{2a} are as defined in any of the preceding claims.

14. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein Y is selected from:

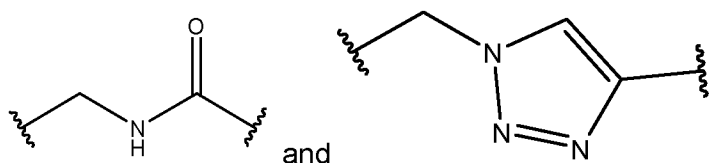


15. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein , R_{3a1} , R_{3b1} , R_{3c1} , R_{3d1} , R_{3e1} , R_{3f1} , R_{3g1} , R_{3h1} , R_{3i1} , R_{3j1} , R_{3k1} , R_{3l1} , R_{3m1} , R_{3n1} , R_{3o1} , R_{3p1} , R_{3q1} , R_{3r1} and R_{3s1} are independently selected from hydrogen and C_{1-6} alkyl; and wherein C_{1-6} alkyl is optionally substituted with one or more hydroxy substituents.

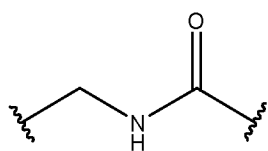
16. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R_{3a2} , R_{3b2} , R_{3c2} , R_{3d2} , R_{3e2} , R_{3f2} , R_{3g2} , R_{3h2} , R_{3i2} , R_{3j2} , R_{3k2} , R_{3l2} , R_{3m2} , R_{3n2} , R_{3o2} , R_{3p2} , R_{3q2} , R_{3r2} and R_{3s2} are hydrogen.

17. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein n is 1.

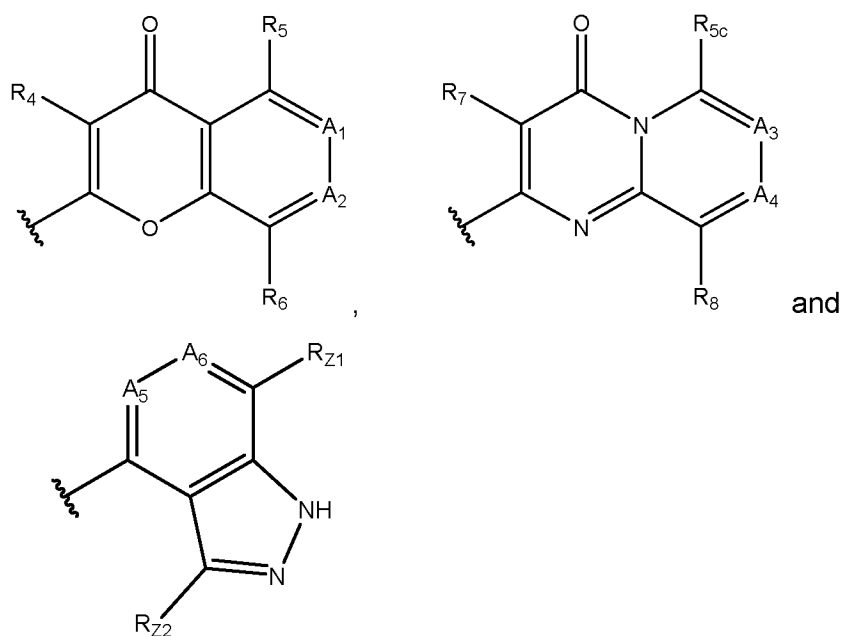
18. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein Y is selected from:



19. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein Y is



20. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein Z is selected from:



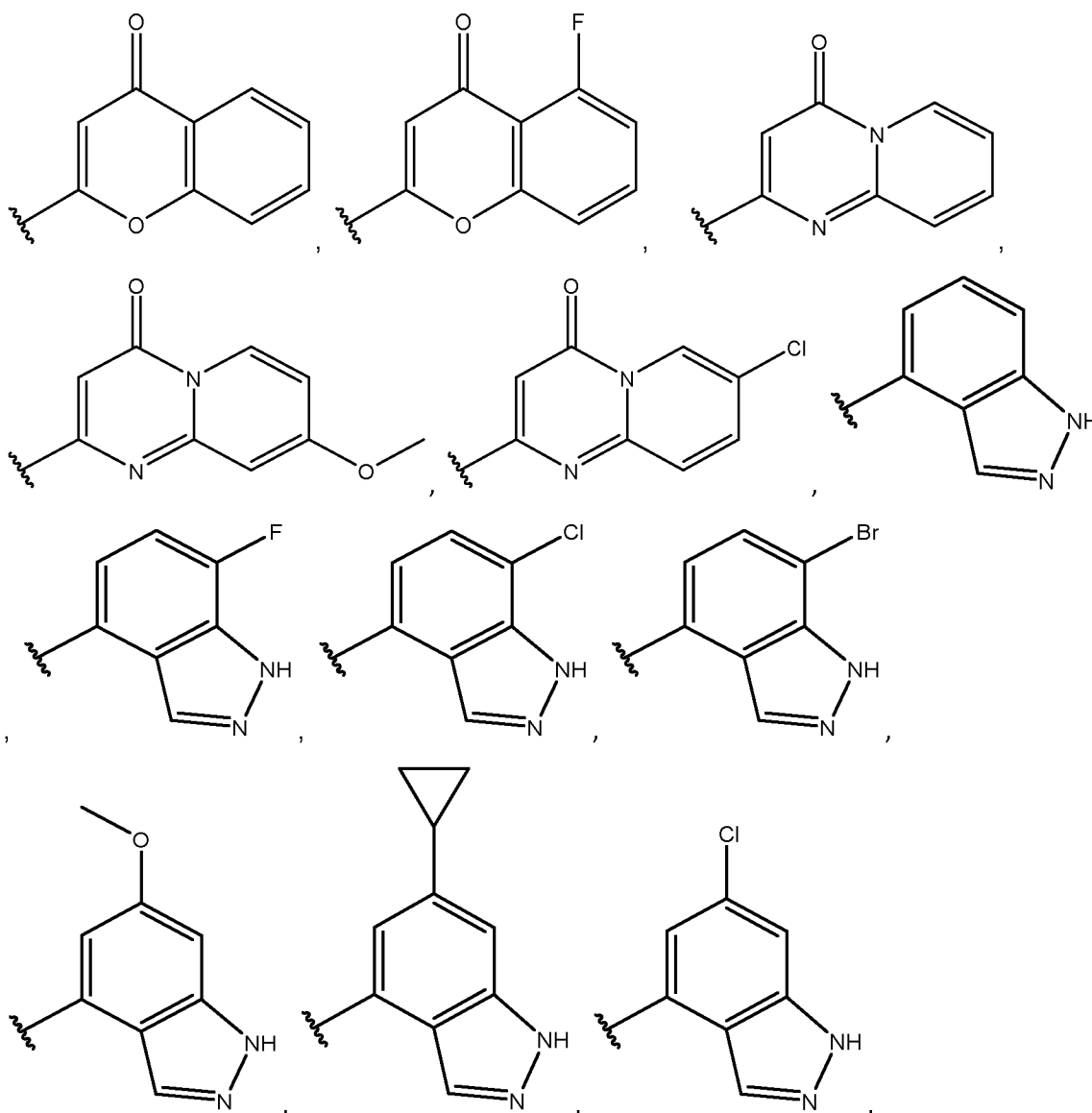
21. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R_4 , R_{4a} , R_5 , R_{5a} , R_{5b} , R_{5c} , R_6 , R_{6a} , R_7 , R_{7a} , R_8 , R_{8a} , R_9 , R_{10} and R_{11} are hydrogen.
22. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein A_1 is CR_{12} and wherein R_{12} is hydrogen.
23. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein A_2 is CR_{13} and wherein R_{13} is hydrogen.
24. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein A_3 is CR_{14} and wherein R_{14} is hydrogen or chloro.
25. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein A_4 is CR_{15} and wherein R_{15} is hydrogen or methoxy.
26. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein A_5 is CR_{16} and wherein R_{16} is hydrogen.
27. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein A_6 is CR_{17} and wherein R_{17} is selected from selected from hydrogen, halo, cyano, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl, $-O-C_{3-4}$ cycloalkyl, heterocyclyl, $-(OCH_2CH_2)_m-OCH_3$

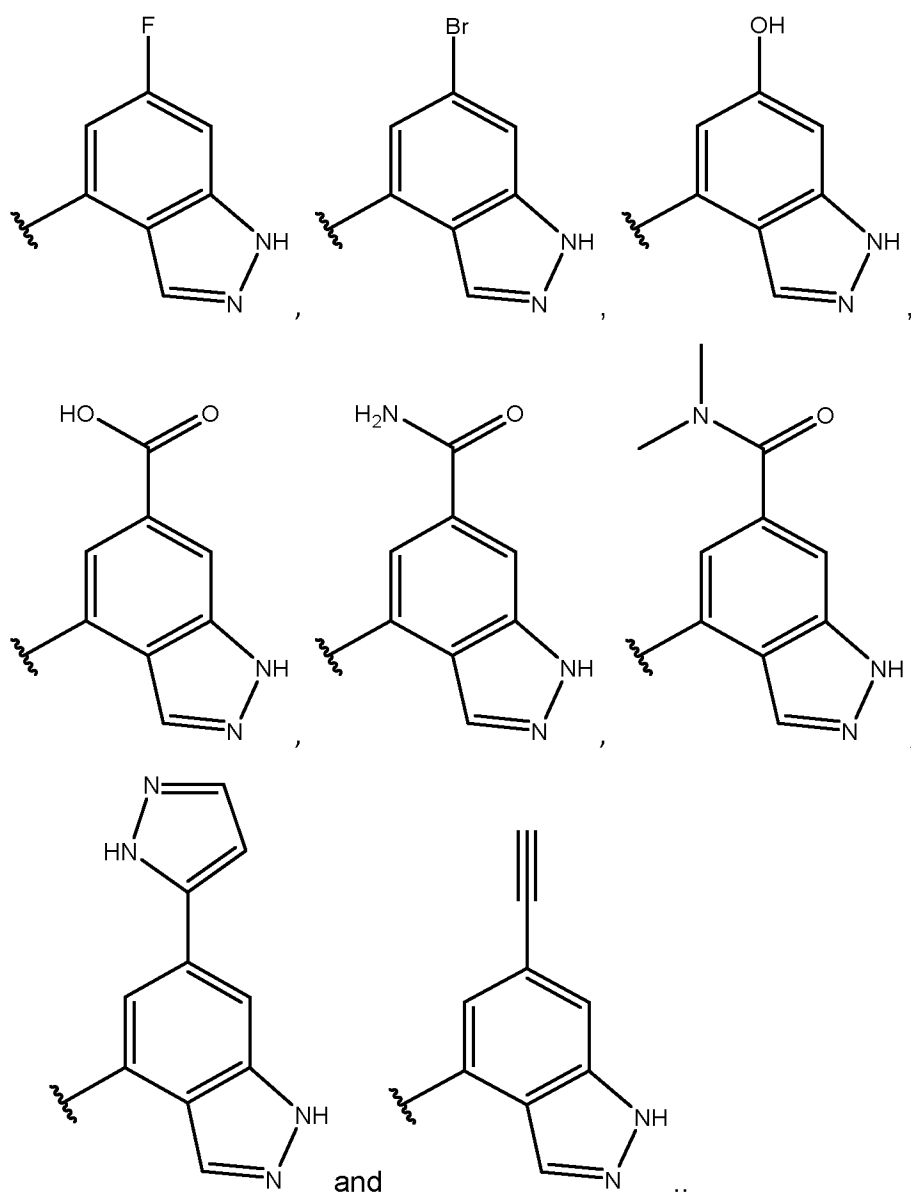
wherein m is 1, 2 or 3, NR_qR_r , wherein R_q and R_r are each independently hydrogen or C_{1-2} alkyl;

wherein any C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl, $-\text{O}-\text{C}_{3-4}$ cycloalkyl, heterocyclyl, system is optionally further substituted by one or more substituents selected from C_{1-2} alkyl, C_{1-2} haloalkyl, cyano, hydroxy, C_{1-2} alkoxy, halo and C_{1-2} haloalkoxy.

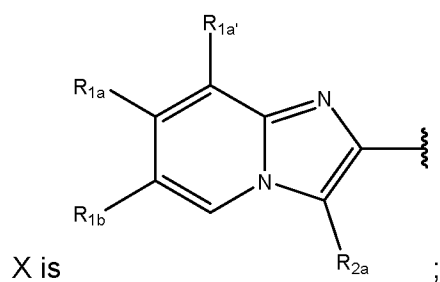
28. A compound according to claim 27, or a pharmaceutically acceptable salt thereof, wherein R_{17} is selected from hydrogen, halo, C_{1-4} alkoxy or C_{1-4} haloalkoxy.

29. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein Z is selected from:

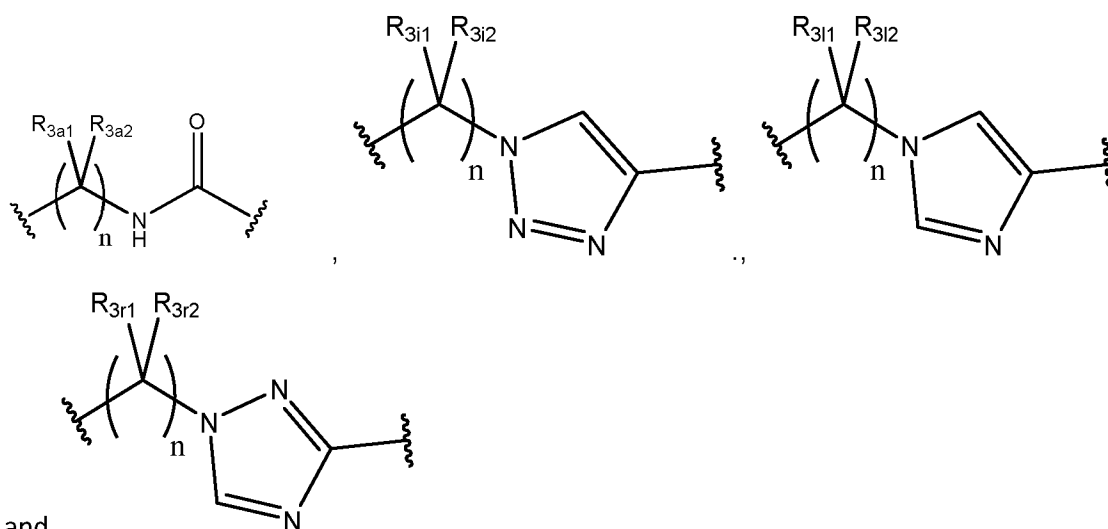




- 5 30. A compound according to claim 1 or claim 2, or a pharmaceutically acceptable salt thereof, wherein:



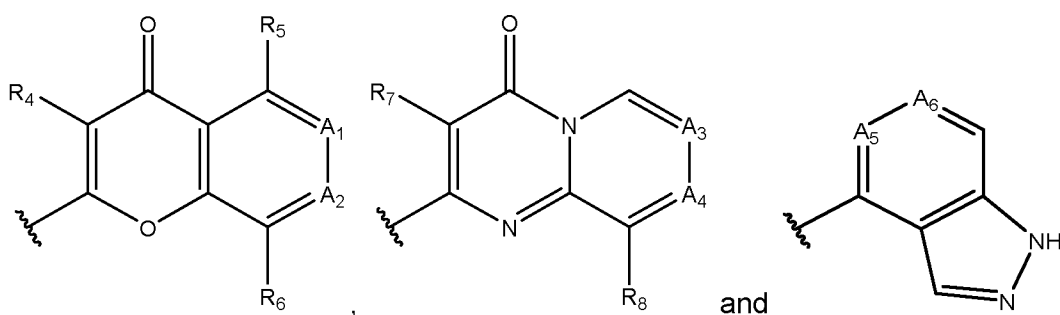
Y is selected from



and

; and

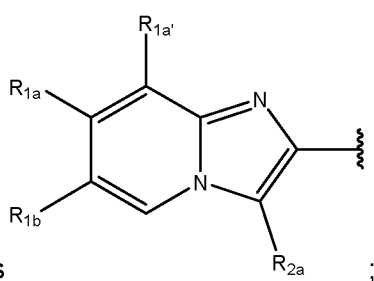
5 Z is selected from:



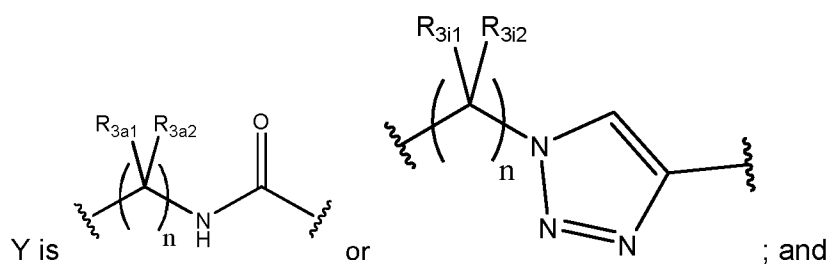
31. A compound according to claim 30, or a pharmaceutically acceptable salt thereof, wherein:

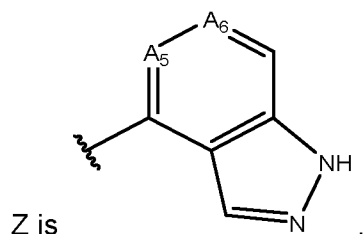
10

X is

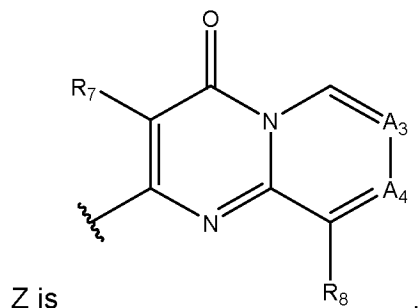
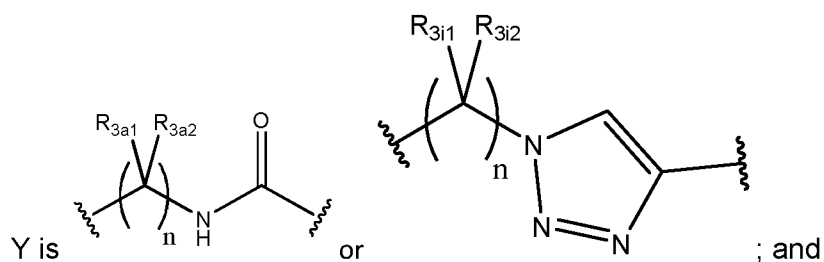
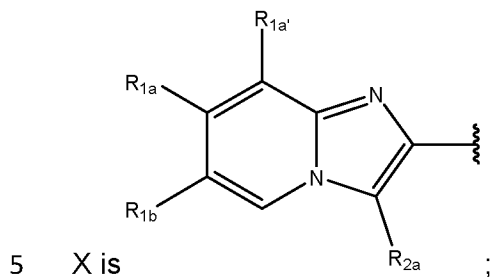


Y is

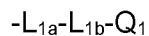




32. A compound according to claim 30, or a pharmaceutically acceptable salt thereof, wherein:



- 10 33. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:
- R_{1a}, R_{1c} and R_{1e} are independently selected from hydrogen, C₂₋₃alkenyl, cyano, halo, C₁₋₆alkyl, OR^t, wherein R^t is C₁₋₄alkyl; and
- 15 R_{1b}, R_{1d} and R_{1f} are independently selected from hydrogen, cyano, halo, and a group of the formula:



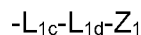
wherein

L_{1a} is absent or C₁₋₃alkylene, C₃₋₄cycloalkylene, optionally substituted by one or more substituents selected from aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl, C₁₋₂alkyl, cyano, halo, hydroxy, or oxo, wherein any aryl, aryl-(1-2C)alkyl, heteroaryl, aryl-(1-2C)alkyl or C₁₋₂alkyl is optionally further substituted by one or more substituents selected from halo, cyano or hydroxy;

L_{1b} is absent or selected from O, S, SO, SO₂, N(R_r), C(O), C(O)O, OC(O), C(O)N(R_r), N(R_r)C(O), N(R_r)C(O)N(R_s), S(O)₂N(R_r), or N(R_r)SO₂, wherein R_r and R_s are each independently selected from hydrogen or C₁₋₂alkyl, wherein C₁₋₂alkyl is optionally further substituted by C₃₋₆cycloalkyl or a 3 to 6 membered heterocyclyl, which in turn are optionally further substituted by halo, hydroxy, C₁₋₂alkoxy or C₁₋₂haloalkoxy; and

Q₁ is hydrogen, cyano, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, heterocyclyl or heteroaryl; and wherein Q₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, halo, trifluoromethyl, trifluoromethoxy, amino, oxo, cyano, hydroxy, carboxy, carbamoyl, sulphamoyl, NR_tR_u, OR_t, C(O)R_t, C(O)OR_t, OC(O)R_t, C(O)N(R_t)R_u, N(R_t)C(O)R_u, S(O)_yR_t (where y is 0, 1 or 2), SO₂N(R_t)R_u, N(R_t)SO₂R_u or (CH₂)_zNR_tR_u (where z is 1, 2 or 3), wherein R_t and R_u are each independently selected from hydrogen or C₁₋₄alkyl; or

Q₁ is optionally substituted by one or more groups of the formula:



wherein

L_{1c} is absent or C₁₋₃alkylene optionally substituted by C₁₋₂alkyl or oxo;

L_{1d} is absent or selected from C(O), O, C(O)O, OC(O), C(O)N(R_v), N(R_v)C(O), N(R_v)C(O)N(R_w), S(O)₂N(R_v), or N(R_v)SO₂, wherein R_v and R_w are each independently selected from hydrogen or C₁₋₂alkyl; and

Z₁ is C₃₋₈cycloalkyl (including a spirocyclic carbocyclic and a bridged C₃₋₈cycloalkyl), heterocyclyl (including a mono- or bicyclic-heterocyclic ring system, a spirocyclic heterocyclic ring system, or a bridged heterocyclic ring system), phenyl or 5-6 membered heteroaryl; wherein Z₁ is optionally substituted by one or more substituents selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocyclyl, halo, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkoxy, cyano, hydroxyl, NR_{t1}R_{u1}, OR_{t1}, C(O)R_{t1}, C(O)OR_{t1}, OC(O)R_{t1}, C(O)N(R_{t1})R_{u1}, N(R_{t1})C(O)R_{u1}, S(O)_yR_{t1} (where y is 0, 1 or 2), SO₂N(R_{t1})R_{u1}, N(R_{t1})SO₂R_{u1} or (CH₂)_zNR_{t1}R_{u1} (where z is 1, 2 or 3), wherein R_{t1} and R_{u1} are each independently

selected from hydrogen or C₁₋₄alkyl; and when Z₁ is C₃₋₈cycloalkyl or heterocyclyl, Z₁ is optionally spiro-fused to a C₃₋₆cycloalkyl or heterocyclyl ring.

34. A compound, or a pharmaceutically acceptable salt thereof, selected from any one of the following:

N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({7-bromoimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-bromoimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-chloroimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

10 N-({7-fluoroimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-fluoroimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({7-methoxyimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-6-(1H-pyrazol-5-yl)-1H-indazole-4-carboxamide;

15 N-({7-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

6-bromo-N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

6-bromo-N-({7-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-chromene-2-carboxamide;

N-({imidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-chromene-2-carboxamide;

20 6-ethynyl-N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-4-carboxamide;

N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

N-({7-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-chromene-2-carboxamide;

N-({7-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-

25 carboxamide;

N-({6-cyanoimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

8-methoxy-N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

30 N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-indazole-5-carboxamide;

- 7-chloro-N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-fluoroimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-({6-bromoimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-methoxyimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-({7-methoxyimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({imidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({8-methylimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-methylimidazo[1,2-a]pyridin-2-yl}methyl)-1H-pyrazolo[4,3-c]pyridine-4-carboxamide;
- 15 N-({7-bromoimidazo[1,2-a]pyridin-2-yl}methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-(2-hydroxy-1-({6-methylimidazo[1,2-a]pyridin-2-yl}ethyl)-1H-indazole-4-carboxamide;
- 4-(3-({imidazo[1,2-a]pyridin-2-yl}-2,5-dihydro-1H-pyrrole-1-carbonyl)-1H-indazole;
- N-[(6-[(pyridin-3-yl)methyl]amino)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-
- 20 carboxamide;
- N-[(6-[(1-methyl-1H-imidazol-4-yl)methyl]amino)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-(3-methoxyphenyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-(1H-pyrazol-5-yl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 25 N-[(6-(3-chlorophenyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-[(pyridin-3-yl)amino]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-[(piperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-(acetamidomethyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 30 {6-methylimidazo[1,2-a]pyridin-2-yl}methyl 1H-indazole-4-carboxylate;

- {6-methylimidazo[1,2-a]pyridin-2-yl)methyl 1H-indazole-4-carboxylate hydrochloride;
- N-{{6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- N-{{6-hydroxyimidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- N-{{6-[(methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- 5 N-{{6-[(methylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide dihydrochloride;
- N-{{6-[[{(2-hydroxyethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- N-{{6-[[{(2,2,2-trifluoroethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-
- 10 carboxamide;
- N-{{6-[(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- N-{{6-[hydroxy(phenyl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- N-{{6-formylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-{{6-(aminomethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-[[{(2,2,2-trifluoroethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[[{(2-hydroxyethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-
- 20 a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-[[{(2-phenylethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 4-oxo-N-{{6-[[{(3-phenylpropyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[hydroxy(phenyl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-[(1-hydroxyethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-
- 30 carboxamide;

- N-({6-ethenylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-cyclopropylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-({7-ethenylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-(hydroxymethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 2-(1H-indazol-4-yl)-5-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]-1,3,4-oxadiazole;
- 10 N-{{6-(2-aminoethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H,6H,7H,8H,9H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-
- 15 carboxamide;
- tert-butyl N-(2-{2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)]formamido)methyl}imidazo[1,2-a]pyridin-6-yl)ethyl)carbamate;
- N-benzyl-2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)]formamido)methyl}imidazo[1,2-a]pyridine-6-carboxamide;
- 20 N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 7-chloro-N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 6-chloro-N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-
- 25 4H-chromene-2-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H,6H,7H,8H,9H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 6-amino-N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]pyridine-3-carboxamide;
- 30 N-({6-[(benzyloxy)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-({6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-indazole-4-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-7-fluoro-4-oxo-4H-chromene-2-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-7-methyl-4-oxo-4H-chromene-2-carboxamide;
- 5 N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 8-chloro-N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 10 6-bromo-N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]quinoline-3-carboxamide;
- N-[(6-{1-[(cyclohexylmethyl)amino]ethyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 6-chloro-N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-1H-indazole-4-carboxamide;
- 4-[5-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1,3,4-thiadiazol-2-yl]-1H-indazole;
- 4-[1-({6-methylimidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl]-1H-indazole;
- 20 N-[(6-[(3-chlorophenyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(1-cyclohexyl-2-hydroxyethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-[(pyridin-3-yl)methyl]amino}methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-{{6-[(4-methoxyphenyl)methyl]amino}methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(cyclohexylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-{{6-[(4-chlorophenyl)methyl]amino}methyl}imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[[benzyl(methyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- 4-oxo-N-{{6-({[(1R)-1-phenylethyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-({[(1S)-1-phenylethyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-{{6-({[(2-fluorophenyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-({[(2-phenylpropan-2-yl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(3-fluorophenyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-{{6-({[(4-fluorophenyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-({[(4,4,4-trifluorobutyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-{{6-({[(oxan-4-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(3,3-difluorocyclobutyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(cyclopropylmethyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 4-oxo-N-{{6-({[(3,3,3-trifluoropropyl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(cyclohexylamino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 4-oxo-N-{{6-({[(3-(trifluoromethyl)bicyclo[1.1.1]pentan-1-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(oxan-2-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-({[(3-phenyloxetan-3-yl)amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-{{6-({[(oxan-3-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(1-fluorocyclohexyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-{{6-({[(3-cyclopropylphenyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-[(6-[(3,3-dimethylbutyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{[6-[(2-(trifluoromethoxy)ethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-{[6-[(2-(oxolan-2-yl)methyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(2-methanesulfonyl)ethyl]amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-[(3-phenylpyrrolidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-
- 10 a]pyrimidine-2-carboxamide;
- N-[(6-[(1-cyclohexylcyclopropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{[6-[(1,3-thiazol-5-yl)methyl]amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 tert-butyl 3-[(2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido]methyl)imidazo[1,2-a]pyridin-6-yl)methyl]amino]methyl]piperidine-1-carboxylate;
- N-{[6-[(4,4-difluorocyclohexyl)methyl]amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- tert-butyl 2-[(2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido]methyl)imidazo[1,2-
- 20 a]pyridin-6-yl)methyl]amino]methyl]piperidine-1-carboxylate;
- N-[(6-[(2-cyclopropylethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-[(piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 4-oxo-N-({6-[(1-(2,2,2-trifluoroethyl)-1H-pyrazol-3-yl)methyl]amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{[6-[(1-methylcyclohexyl)methyl]amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{[6-[(2-(pyridin-3-yl)ethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-
- 30 pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{[6-[(1,4-dioxan-2-yl)methyl]amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(cyclopropylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-[(6-[(3,3-difluorocyclobutyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-[[6-([[(oxetan-3-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-[[6-([[(1R,2R)-2-(trifluoromethyl)cyclopropyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-[[6-([[(2,2-dimethylpropyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-([[(cyclohexylmethyl)(methyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-([[(4,4-difluorocyclohexyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-[[6-([[(bicyclo[1.1.1]pentan-1-yl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-([6-([[(2S)-oxolan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 4-oxo-N-([6-([[(2R)-oxolan-2-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-([[(2,2-difluoroethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-[[6-([[(oxolan-3-yl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-[[6-([[(1-methylcyclopropyl)methyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-[[6-([[(oxolan-3-yl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 methyl 3-methyl-2-[[2-([4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl]formamido)methyl]imidazo[1,2-a]pyridin-6-yl)methyl]amino]butanoate;
 N-[[6-([[(oxan-3-yl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-[[6-([[(2S)-3,3,3-trifluoro-2-hydroxypropyl]amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-([6-([[(cyclobutylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-([6-([[(tert-butylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-[[6-([[(2-fluoroethyl)amino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-({6-[(4,4-difluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-[(4-phenylpiperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-({6-[(1,2,3,4-tetrahydroisoquinolin-2-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(diethylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-[(pyrrolidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-
- 10 a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-{{3-(pyridin-2-yl)azetidin-1-yl}}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-{{(dicyclopropylmethyl)amino}}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-[(6-{{(cyclopropylmethyl)(methyl)amino}}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(4-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-{{4-(trifluoromethyl)piperidin-1-yl}}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-
- 20 pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(3-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-{{((spiro[2.2]pentan-1-yl)methyl)amino}}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-({6-[(3,3-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-{{3-(trifluoromethyl)piperidin-1-yl}}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-{{((5,5-dimethyloxolan-2-yl)methyl)amino}}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-
- 30 oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(4-fluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-{{(3-methoxypropyl)amino}}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-[(6-{{(1-methylcyclohexyl)amino}}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-{{6-({[(4,4-dimethyloxolan-2-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(1-methylcyclopentyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 4-oxo-N-{{6-({[(propylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(3,3-dimethyloxolan-2-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2-methylpropyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-
- 10 a]pyrimidine-2-carboxamide;
- N-{{6-({[(2-(tert-butoxy)ethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(4-chlorophenyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-{{6-({[(2-(oxan-2-yl)ethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(4-benzylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-({[(4-phenoxy)piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4H-
- 20 pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2,2-difluorocyclopropyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2,2-dimethylcyclopropyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-{{6-({[(2-methyloxolan-2-yl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(4-tert-butylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(4-tert-butylcyclohexyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-
- 30 pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(2-cyclopentylethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-({[(4-(2,2-dimethylpropanoyl)piperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-{{6-({[(4-acetylpiperazin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-({6-({7-azabicyclo[2.2.1]heptan-7-yl)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-({6-[(2,2-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[(6-[(2,3,3-trimethylbutan-2-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(5-fluoropyridin-2-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-({6-[(1,1'-bi(cyclopropane))-1-yl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(1-fluorocyclopentyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-({6-[(2,6-dimethylmorpholin-4-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- methyl 1-({2-[(4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)formamido]methyl}imidazo[1,2-a]pyridin-6-yl)methyl)piperidine-3-carboxylate;
- N-[(6-[(2-fluoro-2-methylpropyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-[(6-[(1-cyclohexylethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[(6-[(2-cyclopropylethyl)(methyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-[(6-[(2,2-dimethylpropyl)(methyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(1-fluorocyclobutyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(4-fluoro-4-methylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-({6-[(3,3-difluoropiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(1-hydroxycyclohexyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-[(6-[(cyclopentylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-[[6-({[(3,3-difluorocyclopentyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(cyclobutylmethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-[[6-({[2-(3,3-difluorocyclobutyl)ethyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(2-fluorocyclobutyl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(2S)-3,3-dimethylbutan-2-yl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 N-[[6-({6-azaspiro[2.5]octan-6-yl)methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-({6-({[(1r,3r)-3-fluorocyclobutyl]methyl)amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 4-oxo-N-({6-[(2-phenylethyl)amino]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[2-(benzylamino)ethyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[2-(cyclohexylamino)ethyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 4-oxo-N-({6-[(phenylformamido)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(cyclohexylformamido)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 4-oxo-N-{{6-({[(piperidin-3-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-{{6-({[(piperidin-2-yl)methyl]amino}methyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-({[(azetidin-3-yl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-({6-[(cyclohexylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
- N-[[6-({[(2-cyclopropylethyl)amino]methyl)imidazo[1,2-a]pyridin-2-yl)methyl]-4-oxo-4H-chromene-2-carboxamide;
- 35 4-oxo-N-({6-[(piperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl)-4H-chromene-2-carboxamide;

- N-{{6-({[(4-chlorophenyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-chromene-2-carboxamide;
- N-{{6-[(benzylamino)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-chromene-2-carboxamide;
- 5 N-{{6-({[(1-methylcyclohexyl)methyl]amino)methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-chromene-2-carboxamide;
- N-{{6-({[(2,2-dimethylpropyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-chromene-2-carboxamide;
- 4-oxo-N-{{7-({[(2-phenylethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4H-pyrido[1,2-
- 10 a]pyrimidine-2-carboxamide;
- N-{{7-({[(cyclohexylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{7-({[(cyclopropylmethyl)amino]methyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-{{6-{{1-[(cyclohexylmethyl)amino]cyclopropyl}imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-{{6-(2-amino-3-phenylpropyl)imidazo[1,2-a]pyridin-2-yl)methyl}-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- (cyclohexylmethyl)[(2-{{4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl}methyl}imidazo[1,2-a]pyridin-
- 20 6-yl)methyl]amine;
- N-(cyclohexylmethyl)-2-{{4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl}methyl}imidazo[1,2-a]pyridine-6-carboxamide;
- (2,2-dimethylpropyl)[(2-{{4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl}methyl}imidazo[1,2-a]pyridin-6-yl)methyl]amine;
- 25 4-{{1-{{6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl}-1H-indazole;
- [(2-{{4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl}methyl}imidazo[1,2-a]pyridin-6-yl)methyl][(3,3-difluorocyclobutyl)methyl]amine;
- [(2-{{4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl}methyl}imidazo[1,2-a]pyridin-6-
- 30 yl)methyl](2,2-dimethylpropyl)amine;
- [(2-{{4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl}methyl}imidazo[1,2-a]pyridin-6-yl)methyl](cyclohexylmethyl)amine;
- 6-bromo-4-{{1-{{6-[(4,4-dimethylpiperidin-1-yl)methyl]imidazo[1,2-a]pyridin-2-yl)methyl}-1H-1,2,3-triazol-4-yl}-1H-indazole;
- 35 (2-{{4-(6-bromo-1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl}methyl}imidazo[1,2-a]pyridin-6-yl)methanol;

- (2,2-dimethylpropyl)[(2-{[4-(1H-indazol-5-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)methyl]amine;
- ((cyclohexylmethyl)[1-(2-{[4-(1H-indazol-4-yl)-1H-1,2,3-triazol-1-yl]methyl}imidazo[1,2-a]pyridin-6-yl)ethyl]amine;
- 5 (2,2-dimethylpropyl)({2-[(4-{1H-pyrazolo[3,4-c]pyridin-4-yl}-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl)methyl)amine;
- {2-[(4-{1H-pyrazolo[3,4-c]pyridin-4-yl}-1H-1,2,3-triazol-1-yl)methyl]imidazo[1,2-a]pyridin-6-yl}methanol;
- N-({6-[(3R,5S)-5-tert-butylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-
- 10 pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(3S,5R)-5-tert-butylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-1H-indazole-4-carboxamide;
- N-({6-[(3S,5R)-5-cyclohexylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-chromene-2-carboxamide;
- N-({6-[4-(2,2-dimethylpropyl)morpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-
- 20 pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-({6-[(3S,5R)-5-methylmorpholin-3-yl]imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide; and
- N-({6-(9-methoxy-2,3,4,5-tetrahydro-1,4-benzoxazepin-3-yl)imidazo[1,2-a]pyridin-2-yl)methyl)-4-oxo-4H-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazol-6-ol;
- 4-[1-[[6-[[[(1-hydroxycyclobutyl)methylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazol-6-ol;
- 1-[[[2-[[4-(5-methoxy-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-
- 30 yl]methylamino]methyl]cyclobutanol;
- 1-[[[2-[[4-(6-methoxy-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol;
- N-(cyclobutylmethyl)-1-[2-[[4-(6-methoxy-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine;
- 35 N-(cyclobutylmethyl)-1-[2-[[4-(5-methoxy-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine;
- 4-[1-[(6-methylimidazo[1,2-a]pyridin-2-yl)methyl]triazol-4-yl]-1H-indazol-3-amine

- N-[[6-[[[(1-methoxycyclobutyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-[(1,4-oxazepan-3-yl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-[[6-[[[(2-cyano-2-methyl-propyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-[[[(3-fluoro-1-bicyclo[1.1.1]pentanyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 4-oxo-N-[[6-[(spiro[3.3]heptan-2-yl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]pyrido[1,2-a]pyrimidine-2-carboxamide;
- 10 4-oxo-N-[[6-[(spiro[2.3]hexan-5-yl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-[(1-bicyclo[1.1.1]pentanyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 15 4-oxo-N-[[6-[(spiro[2.3]hexan-2-yl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-[[[(2-methoxy-2-methyl-propyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-[[[(1-methylcyclobutyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 20 N-[[6-(butylaminomethyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-[[[(1-hydroxycyclopentyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 25 N-[[6-[(2-methylbutylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-[(2-cyclobutylethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-[[[(2-hydroxy-2-methyl-propyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 30 N-[[6-[[[(1-hydroxycyclobutyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-[(2-hydroxybutylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 35 N-[[6-[[[(3-methylcyclobutyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;

- N-[[6-[[[(3,3-dimethylcyclobutyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-[(2,2-dimethylbutylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 5 N-[[6-[[[(2S)-2-methylbutyl]amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 1-[[[2-[[4-(6-bromo-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclohexanol;
- 1-[[[2-[[4-(6-bromo-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol;
- 10 1-[2-[[4-(6-bromo-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]-N-(cyclobutylmethyl)methanamine;
- 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazole-6-carboxylic acid;
- 15 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazole-6-carboxamide;
- 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-N,N-dimethyl-1H-indazole-6-carboxamide;
- [4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-indazol-6-yl]-morpholino-methanone;
- 20 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-N-(2-hydroxyethyl)-1H-indazole-6-carboxamide;
- 1-[2-[[4-(6-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]-N-(cyclobutylmethyl)methanamine;
- 25 1-[[[2-[[4-(6-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol;
- N-[[2-[[4-(6-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methyl]-2,2-dimethyl-propan-1-amine;
- N-(cyclobutylmethyl)-1-[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine;
- 30 1-[[[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclohexanol;
- N-(cyclohexylmethyl)-1-[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine;
- 35 1-[[[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol;

- 1-[[[2-[[4-(7-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclopentanamine;
- N-[[6-[(4,4-dimethyl-1-piperidyl)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-5-fluoro-4-oxo-chromene-2-carboxamide;
- 5 N-(cyclobutylmethyl)-1-[2-[[4-(6-morpholino-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine;
- 6-[2-(2-aminoethoxy)ethoxy]-N-[[6-[(4,4-dimethyl-1-piperidyl)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-1H-indazole-4-carboxamide;
- N-[[6-[1-(cyclobutylmethylamino)-2-phenyl-ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-
- 10 pyrido[1,2-a]pyrimidine-2-carboxamide;
- N-[[6-[1-[bis(cyclobutylmethyl)amino]-2-phenyl-ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
- 1-[2-[[4-(7-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]-N-(cyclobutylmethyl)methanamine;
- 15 1-[[[2-[[4-(7-chloro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol;
- [2-[[4-(6-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanol
- N-(cyclobutylmethyl)-1-[2-[[4-(6-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine;
- 20 1-[[[2-[[4-(6-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol;
- N-(cyclohexylmethyl)-1-[2-[[4-(6-fluoro-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine;
- N-[[2-[[4-(6-cyclopropyl-1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methyl]-
- 25 2,2-dimethyl-propan-1-amine;
- N-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-1H-indazole-4-carboxamide;
- N-(cyclobutylmethyl)-1-[2-[[4-(1H-pyrazolo[4,3-c]pyridin-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine;
- 30 N-(cyclohexylmethyl)-1-[2-[[4-(1H-pyrazolo[4,3-c]pyridin-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine;
- 1-[[[2-[[4-(1H-pyrazolo[4,3-c]pyridin-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclobutanol;
- N-(cyclobutylmethyl)-1-[2-[[4-(1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-
- 35 yl]methanamine;
- 1-[[[2-[[4-(1H-indazol-4-yl)triazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-yl]methylamino]methyl]cyclohexanol;

- 2-[[4-(1H-indazol-4-yl)imidazol-1-yl]methyl]-6-methyl-imidazo[1,2-a]pyridine;
 N-[[6-[2-cyano-1-(cyclobutylmethylamino)ethyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-
 pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-(6-methylmorpholin-3-yl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-
 5 a]pyrimidine-2-carboxamide;
 N-[[6-(7-bromo-9-methoxy-2,3,4,5-tetrahydro-1,4-benzoxazepin-3-yl)imidazo[1,2-a]pyridin-2-
 yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
 4-oxo-N-[(6-piperazin-2-yl)imidazo[1,2-a]pyridin-2-yl]methyl]pyrido[1,2-a]pyrimidine-2-
 carboxamide;
 10 N-[[6-(6-cyclohexyl-4-oxo-2-piperidyl)imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-
 a]pyrimidine-2-carboxamide;
 1-[2-(1H-indazol-4-yl)thiazol-5-yl]-1-(6-methylimidazo[1,2-a]pyridin-2-yl)ethanol;
 2-[[1-(1H-indazol-4-yl)triazol-4-yl]methyl]imidazo[1,2-a]pyridine;
 N-[(3,3-difluorocyclobutyl)methyl]-1-[2-[[1-(1H-indazol-4-yl)triazol-4-yl]methyl]imidazo[1,2-
 15 a]pyridin-6-yl]methanamine;
 4-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-yl]-1H-
 indazole-6-carbonitrile;
 N-(cyclobutylmethyl)-1-[2-[[4-(1H-indazol-4-yl)imidazol-1-yl]methyl]imidazo[1,2-a]pyridin-6-
 yl]methanamine;
 20 N-[[6-[[acetyl(cyclobutylmethyl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-
 pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-(cyclobutylmethyl)-1-[2-[[3-(1H-indazol-4-yl)-1,2,4-triazol-1-yl]methyl]imidazo[1,2-a]pyridin-
 6-yl]methanamine;
 2-[1-[[6-[(cyclobutylmethylamino)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]triazol-4-
 25 yl]pyrido[1,2-a]pyrimidin-4-one;
 N-[[6-[(2-bicyclo[2.2.1]hept-5-enyl)methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-
 oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-[[[(1R,2R,4S)-norbornan-2-yl]methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-
 oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
 30 N-[[6-[[[(1R,2S,4S)-norbornan-2-yl]methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-
 oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-(2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-
 pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-(2-azabicyclo[2.2.1]heptan-2-yl)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-
 35 pyrido[1,2-a]pyrimidine-2-carboxamide;
 N-[[6-(2-azabicyclo[2.2.2]octan-2-yl)methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-
 pyrido[1,2-a]pyrimidine-2-carboxamide;

N-[[6-[[[(2,2-difluorospiro[3.3]heptan-6-yl)amino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]-4-oxo-pyrido[1,2-a]pyrimidine-2-carboxamide;

4-oxo-N-[[6-[[[rac-(1S,2S,4S)-7-oxabicyclo[2.2.1]hept-5-en-2-yl]methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]pyrido[1,2-a]pyrimidine-2-

5 carboxamide;

4-oxo-N-[[6-[[[rac-(1S,2R,4S)-7-oxabicyclo[2.2.1]hept-5-en-2-yl]methylamino]methyl]imidazo[1,2-a]pyridin-2-yl]methyl]pyrido[1,2-a]pyrimidine-2-carboxamide; and

N-[(1-methoxycyclobutyl)methyl]-1-[2-[[4-(6-methoxy-1H-indazol-4-yl)triazol-1-

10 yl]methyl]imidazo[1,2-a]pyridin-6-yl]methanamine.

35. A pharmaceutical composition comprising a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable excipients.

15

36. A compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35, for use in therapy.

37. A compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35, for use in the treatment of a proliferative condition.

20

38. A compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35, for use in the treatment of cancer.

25

39. A compound according to any one of claims 1 to 34 or a pharmaceutically acceptable salt there, or a pharmaceutical composition according to claim 35, for use in the treatment of leukaemia.

30

40. A compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35, for use in the treatment of AML leukaemia or chronic myeloid leukaemia.

35

41. A compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35, for use in the inhibition of METTL3 activity.

42. A compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35, for use in the treatment of an autoimmune disease, a neurological disease, an inflammatory disease or an infectious disease.

43. Use of a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a proliferative condition.

44. Use of a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cancer.

45. Use of a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of leukaemia.

46. Use of a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of AML leukaemia or chronic myeloid leukaemia.

47. Use of a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of an autoimmune disease, a neurological disease, an inflammatory disease or an infectious disease.

48. Use of a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the inhibition of METTL3 activity.

49. A method of treating a proliferative disorder, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35.

50. A method of treating cancer, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to any one of claims

1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35.

51. A method of treating leukaemia, said method comprising administering to a subject in
5 need thereof a therapeutically effective amount of a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35.
52. A method of treating AML leukaemia or chronic myeloid leukaemia, said method
10 comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35.
53. A method of treating an autoimmune disease, a neurological disease, an inflammatory
15 disease or an infectious disease, said method comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35.
- 20 54. A method of inhibiting METTL3 activity *in vitro* or *in vivo*, said method comprising contacting a cell with an effective amount of a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35.
- 25 55. A method of inhibiting metastasis *in vitro* or *in vivo*, said method comprising contacting a cell with an effective amount of a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition according to claim 35.
- 30 56. A combination comprising a compound according to any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, with one or more additional therapeutic agents.

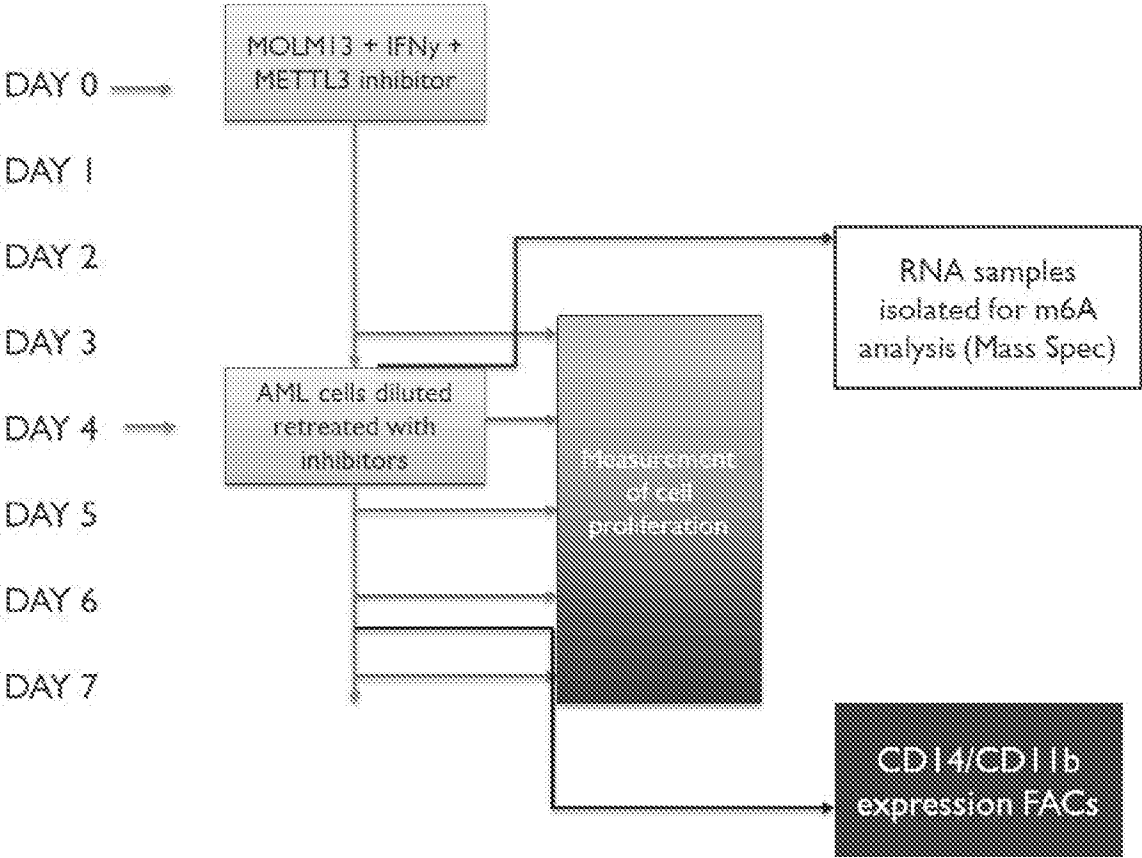
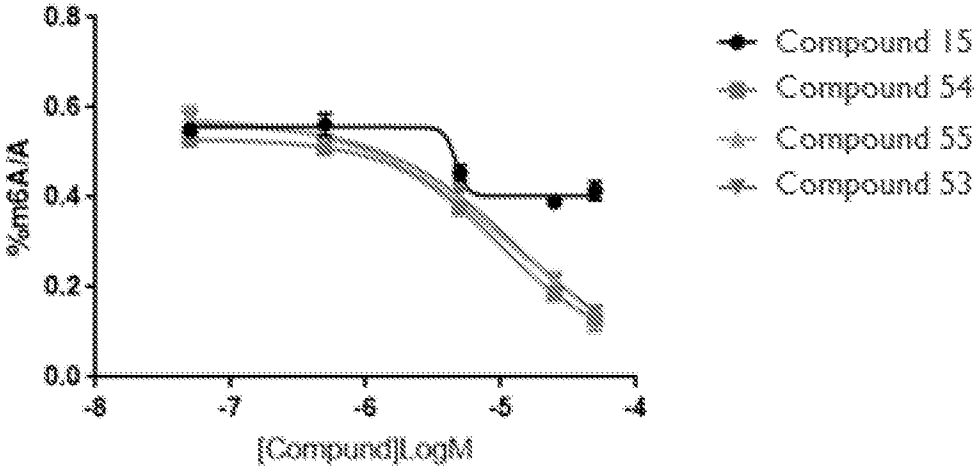


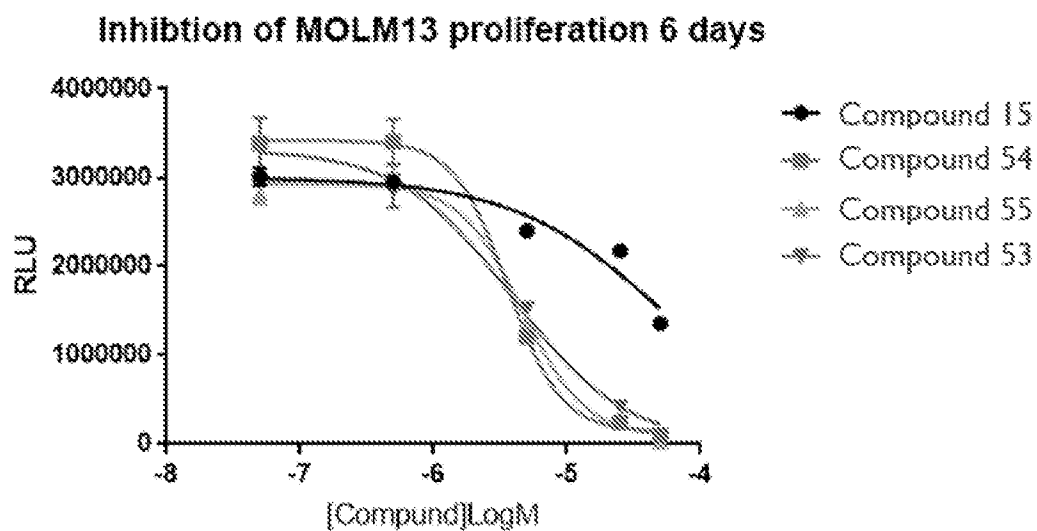
Figure 1

m6A levels in total RNA from MOLM13 (+IFN γ) day 4



	Compound 15	Compound 54	Compound 55	Compound 53
IC50		9.822e-006	1.252e-005	1.417e-005

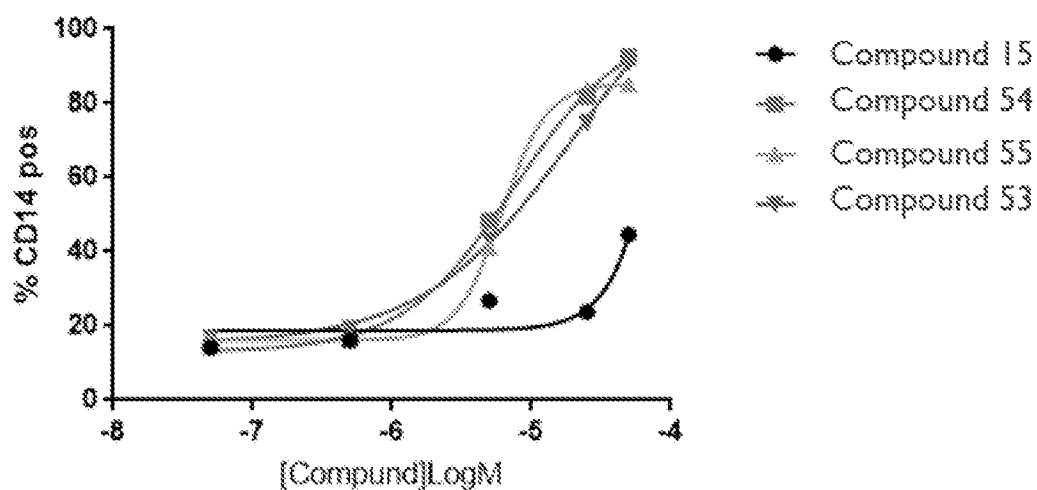
Figure 2



	Compound 15	Compound 54	Compound 55	Compound 53
IC50		3.587e-006	4.644e-006	3.903e-006

Figure 3

Inhibition of MOLM13 CD14 expression 6 days



	Compound 15	Compound 54	Compound 55	Compound 53
IC50		7.571e-006	6.181e-006	2.081e-005

Figure 4

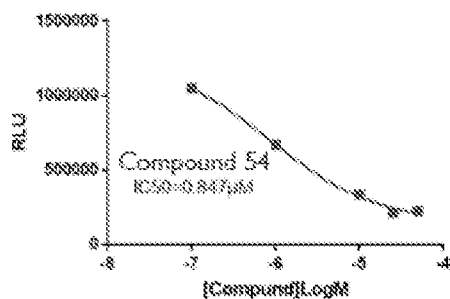
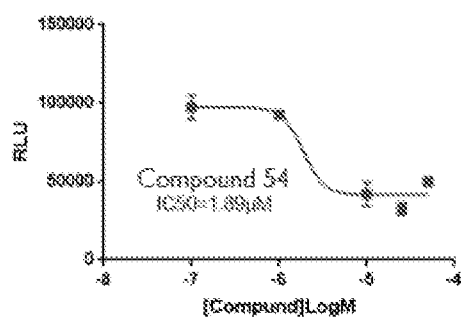
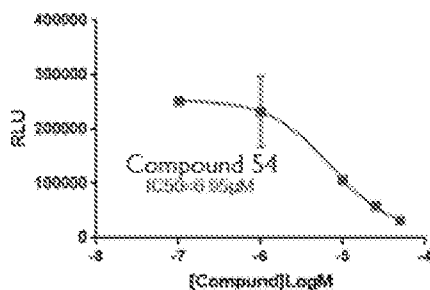
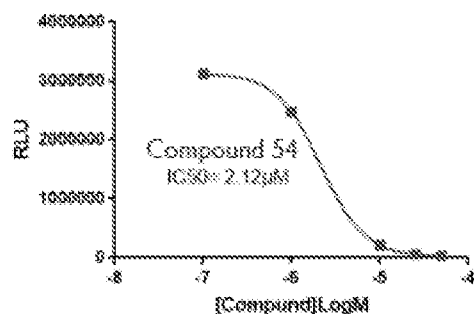
AMLInhibition of MOLM14 proliferation 7 days (IFN γ treated)Inhibition of Kasumi-1 proliferation 6 days (IFN γ treated)Inhibition of NOMO-1 proliferation 6 days (IFN γ treated)Inhibition of THP.1 proliferation 7 days (IFN γ treated)

Figure 5

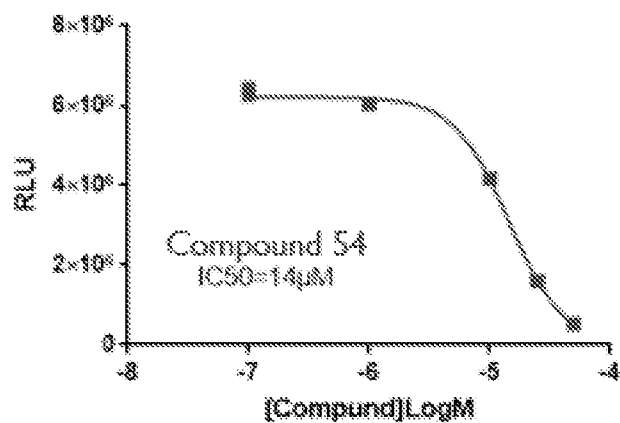
chronic myeloid leukaemiaInhibition of KCL-22 proliferation 6 days (IFN γ treated)

Figure 6

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2020/050898

A. CLASSIFICATION OF SUBJECT MATTER INV. A61P35/00 A61P35/02 C07D471/04 C07D519/00 A61P25/00 A61P29/00 A61P31/00 A61P37/00 A61K31/437 A61K31/4375 A61K31/444 A61K31/496 A61K31/5377 A61K31/553		
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) A61P C07D		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, CHEM ABS Data, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 946 031 A (BEARD COLIN C) 23 March 1976 (1976-03-23) column 5, line 53 - line 54; compounds 2-(3-pyridylcarbonylamino)-benzimidazole -----	1,2,4-8, 10,11, 15,21,33
X	YU UKHIN L ET AL: "Synthesis of phthalimides linked to quinoline derivatives by an amide bridge", RUSSIAN CHEMICAL BULLETIN, KLUWER ACADEMIC PUBLISHERS-PLENUM PUBLISHERS, NE, vol. 59, no. 5, 17 November 2010 (2010-11-17), pages 1023-1030, XP019862835, ISSN: 1573-9171, DOI: 10.1007/S11172-010-0199-8 page 1024; compound 3 ----- -/-	1,2,4-8, 11,33
☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 13 May 2020		Date of mailing of the international search report 26/05/2020
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 Brandstetter, T

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2020/050898

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1, 2, 4-12, 14-56(all partially)
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2020/050898

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/44156 A2 (GLAXO GROUP LTD [GB]; GLAXOSMITHKLINE K K [JP] ET AL.) 6 June 2002 (2002-06-06) example 93 claims 1, 66, 70 -----	1,2,4,7, 8,10,11, 21,33, 35-38, 49,50
X	US 2003/144281 A1 (CYWIN CHARLES [US] ET AL) 31 July 2003 (2003-07-31) page 5 - page 13 nicotineamide derivatives; claims 9-10, 11, 16 -----	1,2,4-8, 11,21, 33, 35-38, 49,50
X	WO 01/10380 A2 (ICAGEN INC [US]; MCNAUGHTON SMITH GRANT ANDREW [US] ET AL.) 15 February 2001 (2001-02-15) claim 1 figure 1; compounds 45-51 page 20, line 24 - line 26 -----	1-8,10, 11,33, 35,36, 42-48,53
X	US 2010/029619 A1 (UCHIKAWA OSAMU [JP] ET AL) 4 February 2010 (2010-02-04) claims 1, 13, 16 paragraph [0824] - paragraph [0827] examples 86, 87, 100, 101, 102, 105, 114 paragraph [0830] -----	1-8,10, 13,21, 33, 35-39, 41-51, 53,54,56
X	US 2009/163488 A1 (OGURO YUYA [JP] ET AL) 25 June 2009 (2009-06-25) claims 1, 21, 31 paragraph [0372] example 121 -----	1-6,10, 13,21, 33, 35-38, 41, 43-50,55
X	WO 2009/106749 A2 (SANOFI AVENTIS [FR]; PEYRONEL JEAN-FRANCOIS [FR]) 3 September 2009 (2009-09-03) claims 1, 9, 14-16, 18 ----- -/--	1-8,10, 11,13, 21,33, 35-38, 41-50, 53,54

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2020/050898

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2007/095588 A1 (NOVARTIS AG [CH]; NI ZHI-JIE [US] ET AL.) 23 August 2007 (2007-08-23) claims 1, 34, 50, 57, 59, 61 page 167; compound 123 page 170; compound 143 page 44, line 29 - line 32 -----	1-7,10, 13,21, 33, 35-38, 41-50, 53,54,56
X	ANANDA HERATH ET AL: "Continuous-flow synthesis of highly functionalized imidazo-oxadiazoles facilitated by microfluidic extraction", BEILSTEIN JOURNAL OF ORGANIC CHEMISTRY, vol. 13, 6 January 2017 (2017-01-06), pages 239-246, XP055694204, DOI: 10.3762/bjoc.13.26 entry 6; page 243; table 3 -----	1-8,10, 11,13, 21,33
X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 2 March 2018 (2018-03-02), XP002798988, Database accession no. 2183120-12-7 abstract -----	1-8,11, 13-15, 17-19,33
X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 21 February 2018 (2018-02-21), XP002798989, Database accession no. 2177960-21-1 abstract -----	1-8,11, 13-15, 17-19,33
X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 10 November 2010 (2010-11-10), XP002798990, Database accession no. 125238-76-9 abstract -----	1-8,10, 11, 13-21, 26-31,33
X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 25 February 2009 (2009-02-25), XP002798991, Database accession no. 1111584-55-4 abstract ----- -/--	1-8,10, 11,13, 15,16, 20,21, 30,33

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2020/050898

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 15 March 2006 (2006-03-15), XP002798992, Database accession no. 876940-30-6 abstract -----	1-8,10, 11, 13-17, 20-23, 29,33
X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 29 September 2004 (2004-09-29), XP002798993, Database accession no. 753467-34-4 abstract -----	1-8,10, 11, 13-17, 19-23, 29,30,33
X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 4 April 2006 (2006-04-04), XP002798994, Database accession no. 879162-99-9 abstract -----	1-8,10, 11, 13-17, 20,21, 23,33
X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 7 July 2011 (2011-07-07), XP002798995, Database accession no. 1311663-16-7 abstract -----	1-8,10, 11,13,33
X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 15 September 2010 (2010-09-15), XP002798996, Database accession no. 1241196-40-6 abstract -----	1-8,10, 11,13,33
X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 1 July 2007 (2007-07-01), XP002798997, Database accession no. 924179-82-8 abstract -----	1-8,10, 11, 13-17, 21-23, 29,30,33
A	WO 2018/169994 A1 (HOPE CITY [US]) 20 September 2018 (2018-09-20) the whole document -----	1-56

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2020/050898

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 3946031	A	23-03-1976	NONE
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Information on patent family members

International application No

PCT/GB2020/050898

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			WO 2018169994 A1	20-09-2018

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1, 2, 4-12, 14-56(all partially)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty.

E.g. D1

(2-(3-pyridylcarbonylamino)-benzimidazole in column 5, lines 53-54), D2 (compound 3 on page 1024), D3 (example 93) or D4 (nicotine amide derivatives on pages 5, 6, 9, 12, 13 and in claims 9-10) disclose compounds which fall at least within the scope of claims 1-2 and/or 4-8, 10, 11, 15, 21 and 33. D3 and D4 in addition disclose compositions comprising said compounds and their medical use in the treatment of cancer, etc. (cf. claim 66 and 70 of D3 and claims 11 and 16 of D4). At least the subject-matter of claims 1-2 and/or 4-8, 10, 11, 15, 21, 33, 35-38 and 49-50 is therefore not new.

D5 discloses compounds of formula

I (claim 1) and their medical use in the treatment of neurological conditions (page 20, lines 24-26). Compounds of formula I of D5 and the presently claimed compounds exhibit a certain overlap. Specific compound falling within this overlapping area and at least within the scope of present claims 1-8, 10, 11 and 33 have also been disclosed in D5 (compounds 45-53 in figure 1). At least the subject-matter of claims 1-8, 10, 11, 33, 35, 36, 42-48 and 53 is therefore not new.

So many documents

were retrieved that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, the search was restricted to compounds of claim 3 and subject-matter referring to them.

1.5 The search was therefore restricted to compounds of claim 3 and subject-matter referring to them.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.