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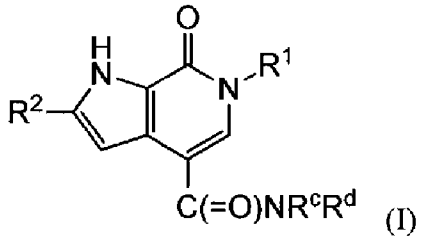
(54) Title: BROMODOMAIN INHIBITORS AND USES THEREOF



(I)

(57) Abstract: The present invention relates to compounds of formula (I): [INSERT FORMULA (1)] and to salts thereof, wherein R^1, R^2, R^c, and R^d have any of the values defined in the specification, and compositions and uses thereof. The compounds are useful as inhibitors of bromodomains. Also included are pharmaceutical compositions comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof, and methods of using such compounds and salts in the treatment of various bromodomain-mediated disorders.

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BROMODOMAIN INHIBITORS AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATION

This patent application claims the benefit of priority of U.S. application serial No. 62/077,711, filed November 10, 2014, which application is herein incorporated by reference.

TECHNICAL FIELD OF THE INVENTION

The present invention relates to compounds useful as inhibitors of bromodomains.

BACKGROUND OF THE INVENTION

Chromatin is a complex combination of DNA and protein that makes up chromosomes. It is found inside the nuclei of eukaryotic cells and is divided between heterochromatin (condensed) and euchromatin (extended) forms. The major components of chromatin are DNA and proteins. Histones are the chief protein components of chromatin, acting as spools around which DNA winds. The functions of chromatin are to package DNA into a smaller volume to fit in the cell, to strengthen the DNA to allow mitosis and meiosis, and to serve as a mechanism to control expression and DNA replication. The chromatin structure is controlled by a series of post-translational modifications to histone proteins, notably histones H3 and H4, and most commonly within the "histone tails" which extend beyond the core nucleosome structure. Histone tails tend to be free for protein-protein interaction and are also the portion of the histone most prone to post-translational modification. These modifications include acetylation, methylation, phosphorylation, ubiquitinylation, and SUMOylation. These epigenetic marks are written and erased by specific enzymes that place the tags on specific residues within the histone tail, thereby forming an epigenetic code, which is then interpreted by the cell to allow gene specific regulation of chromatin structure and thereby transcription.

Of all classes of proteins, histones are amongst the most susceptible to post-translational modification. Histone modifications are dynamic, as they can be added or removed in response to specific stimuli, and these modifications direct both structural changes to chromatin and alterations in gene transcription. Distinct classes of enzymes, namely histone acetyltransferases (HATs) and histone deacetylases (HDACs), acetylate or de-acetylate specific histone lysine residues (Struhl K., *Genes Dev.*, 1989, *12*, 5, 599-606).

Bromodomains, which are approximately 110 amino acids long, are found in a large number of chromatin-associated proteins and have been identified in approximately 70 human proteins, often adjacent to other protein motifs (Jeanmougin F., et al., *Trends Biochem. Sci.*, 1997, *22*, 5, 151-153; and Tamkun J.W., et al., *Cell*, 1992, *7*, 3, 561-572). Interactions between bromodomains and modified histones may be an important mechanism underlying chromatin

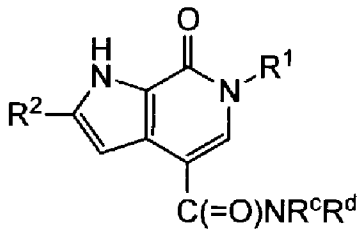
structural changes and gene regulation. Bromodomain-containing proteins have been implicated in disease processes including cancer, inflammation and viral replication. See, e.g., Prinjha *et al.*, *Trends Pharm. Sci.*, 33(3):146-153 (2012) and Muller *et al.*, *Expert Rev.*, 13(29):1-20 (September 2011).

Cell-type specificity and proper tissue functionality requires the tight control of distinct transcriptional programs that are intimately influenced by their environment. Alterations to this transcriptional homeostasis are directly associated with numerous disease states, most notably cancer, immuno-inflammation, neurological disorders, and metabolic diseases. Bromodomains reside within key chromatin modifying complexes that serve to control distinctive disease-associated transcriptional pathways. This is highlighted by the observation that mutations in bromodomain-containing proteins are linked to cancer, as well as immune and neurologic dysfunction. Moreover, recent findings have demonstrated that small molecule inhibition of the bromodomains of BRD4 may have clinical utility in diverse human diseases, ranging from auto-immunity to cardiac hypertrophy. This is possible because the underlying mechanism resides in transcriptional regulation. Hence, the selective inhibition of bromodomains across the family creates varied opportunities as novel therapeutic agents in human dysfunction.

There is a need for treatments for cancer, immunological disorders, and other bromodomain related diseases.

SUMMARY OF THE INVENTION

One aspect includes a compound of formula (I):



(I)

or a salt thereof, wherein:

R^1 is H, C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, or carbocyclyl, wherein each C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, and carbocyclyl of R^1 is optionally substituted with one or more groups R^a;

R^2 is H, C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, or C_{3-8}cycloalkyl, wherein each C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, and C_{3-8}cycloalkyl of R^2 is optionally substituted with one or more groups R^b; and

each R^a is independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^v)_2$, $-S(O)-N(R^v)_2$, $-S(O)_2-N(R^v)_2$, $-O-R^v$, $-S-R^v$, $-O-C(O)-R^v$, $-O-C(O)-O-R^v$, $-C(O)-R^v$, $-C(O)-O-R^v$,

-S(O)-R^v, -S(O)$_2$-R^v, -O-C(O)-N(R^v)$_2$, -N(R^v)-C(O)-OR^v, -N(R^v)-C(O)-N(R^v)$_2$, -N(R^v)-C(O)-R^v, -N(R^v)-S(O)-R^v, -N(R^v)-S(O)$_2$-R^v, -N(R^v)-S(O)-N(R^v)$_2$, and -N(R^v)-S(O)$_2$-N(R^v)$_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl, is optionally substituted with one or more groups independently selected from oxo, halo, -NO_2, -N(R^v)$_2$, -CN, -C(O)-N(R^v)$_2$, -S(O)-N(R^v)$_2$, -S(O)$_2$-N(R^v)$_2$, -O-R^v, -S-R^v, -O-C(O)-R^v, -C(O)-R^v, -C(O)-O-R^v, -S(O)-R^v, -S(O)$_2$-R^v, -C(O)-N(R^v)$_2$, -N(R^v)-C(O)-R^v, -N(R^v)-S(O)-R^v, -N(R^v)-S(O)$_2$-R^v and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^b is independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -N(R^w)$_2$, -CN, -C(O)-N(R^w)$_2$, -S(O)-N(R^w)$_2$, -S(O)$_2$-N(R^w)$_2$, -O-R^w, -S-R^w, -O-C(O)-R^w, -O-C(O)-O-R^w, -C(O)-R^w, -C(O)-O-R^w, -S(O)-R^w, -S(O)$_2$-R^w, -O-C(O)-N(R^w)$_2$, -N(R^w)-C(O)-OR^w, -N(R^w)-C(O)-N(R^w)$_2$, -N(R^w)-C(O)-R^w, -N(R^w)-S(O)-R^w, -N(R^w)-S(O)$_2$-R^w, -N(R^w)-S(O)-N(R^w)$_2$, and -N(R^w)-S(O)$_2$-N(R^w)$_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, -NO_2, -N(R^w)$_2$, -CN, -C(O)-N(R^w)$_2$, -S(O)-N(R^w)$_2$, -S(O)$_2$-N(R^w)$_2$, -O-R^w, -S-R^w, -O-C(O)-R^w, -C(O)-R^w, -C(O)-O-R^w, -S(O)-R^w, -S(O)$_2$-R^w, -C(O)-N(R^w)$_2$, -N(R^w)-C(O)-R^w, -N(R^w)-S(O)-R^w, -N(R^w)-S(O)$_2$-R^w and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^c and R^d is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -N(R^v)$_2$, -CN, -C(O)-N(R^h)$_2$, -S(O)-N(R^h)$_2$, -S(O)$_2$-N(R^h)$_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -S(O)$_2$-R^h, -O-C(O)-N(R^h)$_2$, -N(R^h)-C(O)-OR^h, -N(R^h)-C(O)-N(R^h)$_2$, -N(R^h)-C(O)-R^h, -N(R^h)-S(O)-R^h, -N(R^h)-S(O)$_2$-R^h, -N(R^h)-S(O)-N(R^h)$_2$, and -N(R^h)-S(O)$_2$-N(R^h)$_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl of the substituent groups, is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, -NO_2, -N(R^h)$_2$, -CN, -C(O)-N(R^h)$_2$, -S(O)-N(R^h)$_2$, -S(O)$_2$-N(R^h)$_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -S(O)$_2$-R^h, -C(O)-N(R^h)$_2$, -N(R^h)-C(O)-R^h, -N(R^h)-S(O)-R^h, N(R^h)-S(O)$_2$-R^h, and C_{1-6}alkyl, which heterocyclyl, carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, -O-R^h, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo, and C_{1-6}alkyl;

or R^c and R^d are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from C_{1-6}alkyl , carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, which C_{1-6}alkyl , carbocyclyl, and heterocyclyl are optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl;

each R^h is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, carbocyclyl, heterocyclyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^h are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, halo and C_{1-3}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^v is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^v are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, halo and C_{1-3}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; and

each R^w is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^w are taken together with the nitrogen to

which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, halo and C_{1-3}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

Another aspect includes a composition comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

Another aspect includes a method for treating a bromodomain-mediated disorder in an animal (e.g., a mammal such as a human) comprising administering a compound of formula (I) or a pharmaceutically acceptable salt thereof to the animal.

Another aspect includes a compound of formula (I) or a pharmaceutically acceptable salt thereof for use in medical therapy.

Another aspect includes a compound of formula (I) or a pharmaceutically acceptable salt thereof for the prophylactic or therapeutic treatment of a bromodomain-mediated disorder.

Another aspect includes the use of a compound of formula (I) or a pharmaceutically acceptable salt thereof to prepare a medicament for treating a bromodomain-mediated disorder in an animal (e.g., a mammal such as a human).

Another aspect includes compounds for the study of bromodomains.

Another aspect includes synthetic intermediates and synthetic processes disclosed herein that are useful for preparing a compound of formula (I) or a salt thereof.

DETAILED DESCRIPTION

Compounds and Definitions

Definitions and terms are described in more detail below. Chemical elements are identified in accordance with the Periodic Table of the Elements, CAS version, *Handbook of Chemistry and Physics*, 75th Ed.

Unless otherwise stated, compounds of formula I include enantiomeric, diastereomeric and geometric (or conformational) isomeric forms of a given structure. For example, the R and S configurations for each asymmetric center, Z and E double bond isomers, Z and E conformational isomers, single stereochemical isomers, as well as enantiomeric, diastereomeric, and geometric (or conformational) mixtures are included. Unless otherwise stated, all tautomeric forms of structures depicted herein are included. Additionally, unless otherwise stated, structures depicted herein are also meant to include compounds that differ only in the presence of one or more isotopically enriched atoms. For example, compounds of formula I, wherein the independent replacement or enrichment of one or more hydrogen by deuterium or tritium, carbon by ^{13}C- or ^{14}C carbon, nitrogen by a ^{15}N nitrogen, sulfur by a ^{33}S, ^{34}S or ^{36}S

sulfur, or oxygen by a ^{17}O or ^{18}O oxygen are included. Such compounds are useful, for example, as analytical tools, as probes in biological assays, or as therapeutic agents.

Where a particular enantiomer is described, it may, in certain embodiments be provided substantially free of the corresponding enantiomer, and may also be referred to as "optically enriched." "Optically–enriched," as used herein, means that the mixture of enantiomers is made up of a significantly greater proportion of one enantiomer, and may be described by enantiomeric excess (ee %). In certain embodiments, the mixture of enantiomers is made up of at least about 90% by weight of a given enantiomer (about 90% ee). In other embodiments, the mixture of enantiomers is made up of at least about 95%, 98% or 99% by weight of a given enantiomer (about 95%, 98% or 99% ee). Enantiomers and diastereomers may be isolated from racemic mixtures by any method known to those skilled in the art, including recrystallization from solvents in which one stereoisomer is more soluble than the other, chiral high pressure liquid chromatography (HPLC), supercritical fluid chromatography (SFC), the formation and crystallization of chiral salts, which are then separated by any of the above methods, or prepared by asymmetric syntheses and optionally further enriched. *See*, for example, Jacques et al., *Enantiomers, Racemates and Resolutions* (Wiley Interscience, New York, 1981); Wilen, et al., *Tetrahedron* 33:2725 (1977); Eliel, E.L. *Stereochemistry of Carbon Compounds* (McGraw–Hill, NY, 1962); Wilen, S.H. *Tables of Resolving Agents and Optical Resolutions* p. 268 (E.L. Eliel, Ed., Univ. of Notre Dame Press, Notre Dame, IN 1972).

The term "heteroatom" means any atom independently selected from an atom other than carbon or hydrogen, for example, one or more of oxygen, sulfur, nitrogen, phosphorus or silicon (including any oxidized form of nitrogen, sulfur, phosphorus or silicon; and the quaternized form of any nitrogen).

The terms "halo" and "halogen" as used herein refer to an atom selected from fluorine (fluoro, –F), chlorine (chloro, –Cl), bromine (bromo, –Br) and iodine (iodo, –I).

The term "oxo" refers to =O or $(=O)_2$.

The term "unsaturated", as used herein, means that a moiety has one or more units of unsaturation.

The term "carbocyclyl" used alone or as part of a larger moiety, refers to a saturated, partially unsaturated, or aromatic ring system having 3 to 20 carbon atoms. In one embodiment, carbocyclyl includes 3 to 12 carbon atoms (C_3-C_{12}). In another embodiment, carbocyclyl includes C_3-C_8, C_3-C_{10} or C_5-C_{10}. In other embodiment, carbocyclyl, as a monocycle, includes C_3-C_8, C_3-C_6 or C_5-C_6. In another embodiment, carbocyclyl, as a bicycle, includes C_7-C_{12}. In another embodiment, carbocyclyl, as a spiro system, includes C_5-C_{12}. Examples of monocyclic carbocyclyls include cyclopropyl, cyclobutyl, cyclopentyl, 1-cyclopent-1-enyl, 1-cyclopent-2-

enyl, 1-cyclopent-3-enyl, cyclohexyl, perdeuteriocyclohexyl, 1-cyclohex-1-enyl, 1-cyclohex-2-enyl, 1-cyclohex-3-enyl, cyclohexadienyl, cycloheptyl, cyclooctyl, cyclononyl, cyclodecyl, cycloundecyl, phenyl, and cyclododecyl; bicyclic carbocyclyls having 7 to 12 ring atoms include [4,3], [4,4], [4,5], [5,5], [5,6] or [6,6] ring systems, for example bicyclo[2.2.1]heptane, bicyclo[2.2.2]octane, naphthalene, and bicyclo[3.2.2]nonane; and spiro carbocyclyls include spiro[2.2]pentane, spiro[2.3]hexane, spiro[2.4]heptane, spiro[2.5]octane and spiro[4.5]decane. The term carbocyclyl includes aryl ring systems as defined herein. The term carbocycyl also includes cycloalkyl rings (e.g. saturated or partially unsaturated mono-, bi-, or spiro-carbocycles).

The term "alkyl," as used herein, refers to a saturated linear or branched-chain monovalent hydrocarbon radical. In one embodiment, the alkyl radical is one to eighteen carbon atoms (C_1-C_{18}). In other embodiments, the alkyl radical is C_0-C_6, C_0-C_5, C_0-C_3, C_1-C_{12}, C_1-C_{10}, C_1-C_8, C_1-C_6, C_1-C_5, C_1-C_4 or C_1-C_3. C_0 alkyl refers to a bond. Examples of alkyl groups include methyl (Me, $-CH_3$), ethyl (Et, $-CH_2CH_3$), 1-propyl (n-Pr, n-propyl, $-CH_2CH_2CH_3$), 2-propyl (i-Pr, i-propyl, $-CH(CH_3)_2$), 1-butyl (n-Bu, n-butyl, $-CH_2CH_2CH_2CH_3$), 2-methyl-1-propyl (i-Bu, i-butyl, $-CH_2CH(CH_3)_2$), 2-butyl (s-Bu, s-butyl, $-CH(CH_3)CH_2CH_3$), 2-methyl-2-propyl (t-Bu, t-butyl, $-C(CH_3)_3$), 1-pentyl (n-pentyl, $-CH_2CH_2CH_2CH_2CH_3$), 2-pentyl ($-CH(CH_3)CH_2CH_2CH_3$), 3-pentyl ($-CH(CH_2CH_3)_2$), 2-methyl-2-butyl ($-C(CH_3)_2CH_2CH_3$), 3-methyl-2-butyl ($-CH(CH_3)CH(CH_3)_2$), 3-methyl-1-butyl ($-CH_2CH_2CH(CH_3)_2$), 2-methyl-1-butyl ($-CH_2CH(CH_3)CH_2CH_3$), 1-hexyl ($-CH_2CH_2CH_2CH_2CH_2CH_3$), 2-hexyl ($-CH(CH_3)CH_2CH_2CH_2CH_3$), 3-hexyl ($-CH(CH_2CH_3)(CH_2CH_2CH_3)$), 2-methyl-2-pentyl ($-C(CH_3)_2CH_2CH_2CH_3$), 3-methyl-2-pentyl ($-CH(CH_3)CH(CH_3)CH_2CH_3$), 4-methyl-2-pentyl ($-CH(CH_3)CH_2CH(CH_3)_2$), 3-methyl-3-pentyl ($-C(CH_3)(CH_2CH_3)_2$), 2-methyl-3-pentyl ($-CH(CH_2CH_3)CH(CH_3)_2$), 2,3-dimethyl-2-butyl ($-C(CH_3)_2CH(CH_3)_2$), 3,3-dimethyl-2-butyl ($-CH(CH_3)C(CH_3)_3$, heptyl, octyl, nonyl, decyl, undecyl and dodecyl.

The term "alkenyl," as used herein, denotes a linear or branched-chain monovalent hydrocarbon radical with at least one carbon-carbon double bond. An alkenyl includes radicals having "cis" and "trans" orientations, or alternatively, "E" and "Z" orientations. In one example, the alkenyl radical is two to eighteen carbon atoms (C_2-C_{18}). In other examples, the alkenyl radical is C_2-C_{12}, C_2-C_{10}, C_2-C_8, C_2-C_6 or C_2-C_3. Examples include, but are not limited to, ethenyl or vinyl ($-CH=CH_2$), prop-1-enyl ($-CH=CHCH_3$), prop-2-enyl ($-CH_2CH=CH_2$), 2-methylprop-1-enyl, but-1-enyl, but-2-enyl, but-3-enyl, buta-1,3-dienyl, 2-methylbuta-1,3-diene, hex-1-enyl, hex-2-enyl, hex-3-enyl, hex-4-enyl and hexa-1,3-dienyl.

The term "alkynyl," as used herein, refers to a linear or branched monovalent hydrocarbon radical with at least one carbon-carbon triple bond. In one example, the alkynyl

radical is two to eighteen carbon atoms (C_2-C_{18}). In other examples, the alkynyl radical is C_2-C_{12}, C_2-C_{10}, C_2-C_8, C_2-C_6 or C_2-C_3. Examples include, but are not limited to, ethynyl (-C≡CH), prop-1-ynyl (-C≡CCH$_3$), prop-2-ynyl (propargyl, -CH$_2$C≡CH), but-1-ynyl, but-2-ynyl and but-3-ynyl.

The term "alkoxy" refers to a linear or branched monovalent radical represented by the formula -OR in which R is alkyl, alkenyl, alkynyl or carbocycyl. Alkoxy groups include methoxy, ethoxy, propoxy, isopropoxy, and cyclopropoxy.

The term "haloalkyl," as used herein, refers to an alkyl as defined herein that is substituted with one or more (e.g. 1, 2, 3, or 4) halo groups.

The term "aryl" used alone or as part of a larger moiety as in "arylalkyl", "arylalkoxy", or "aryloxyalkyl", refers to a monocyclic, bicyclic or tricyclic, carbon ring system, that includes fused rings, wherein at least one ring in the system is aromatic. The term "aryl" may be used interchangeably with the term "aryl ring". In one embodiment, aryl includes groups having 6-18 carbon atoms. In another embodiment, aryl includes groups having 6-10 carbon atoms. Examples of aryl groups include phenyl, naphthyl, anthracyl, biphenyl, phenanthrenyl, naphthacenyl, 1,2,3,4-tetrahydronaphthalenyl, 1H-indenyl, 2,3-dihydro-1H-indenyl, and the like, which may be substituted or independently substituted byone or more substituents described herein. A particular aryl is phenyl. In another embodiment aryl includes an aryl ring fused to one or more carbocyclic rings, such as indanyl, naphthimidyl, or tetrahydronaphthyl, and the like, where the radical or point of attachment is on an aromatic ring.

The term "heteroaryl" used alone or as part of a larger moiety, e.g., "heteroarylalkyl", or "heteroarylalkoxy", refers to a monocyclic, bicyclic or tricyclic ring system having 5 to 14 ring atoms, wherein at least one ring is aromatic and contains at least one heteroatom. In one embodiment, heteroaryl includes 4-6 membered monocyclic aromatic groups where one or more ring atoms is nitrogen, sulfur or oxygen that is independently optionally substituted. In another embodiment, heteroaryl includes 5-6 membered monocyclic aromatic groups where one or more ring atoms is nitrogen, sulfur or oxygen that is independently optionally substituted. Example heteroaryl groups include thienyl, furyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, triazolyl, thiadiazolyl, oxadiazolyl, tetrazolyl, thiatriazolyl, oxatriazolyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazinyl, tetrazinyl, tetrazolo[1,5-b]pyridazinyl, imidazol[1,2-a]pyrimidinyl, purinyl, benzoxazolyl, benzofuryl, benzothiazolyl, benzothiadiazolyl, benzotriazolyl, benzoimidazolyl, indolyl, 1,3-thiazol-2-yl, 1,3,4-triazol-5-yl, 1,3-oxazol-2-yl, 1,3,4-oxadiazol-5-yl, 1,2,4-oxadiazol-5-yl, 1,3,4-thiadiazol-5-yl, 1H-tetrazol-5-yl, 1,2,3-triazol-5-yl, and pyrid-2-yl N-oxide. The terms "heteroaryl" also includes groups in which a heteroaryl is fused to one or more aryl, carbocyclyl, or heterocyclyl rings, where the radical or point of

attachment is on the heteroaryl ring. Nonlimiting examples include indolyl, isoindolyl, benzothienyl, benzofuranyl, dibenzofuranyl, indazolyl, benzimidazolyl, benzthiazolyl, quinolyl, isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, 4*H*-quinolizinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, phenoxazinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl and pyrido[2,3-b]-1,4-oxazin-3(4H)-one. A heteroaryl group may be mono-, bi- or tri-cyclic.

As used herein, the term "heterocyclyl" refers to a "carbocyclyl" as defined herein, wherein one or more (*e.g.* 1, 2, 3, or 4) carbon atoms have been replaced with a heteroatom (*e.g.* O, N, or S). In some embodiments, a heterocyclyl refers to a saturated ring system, such as a 3 to 12 membered saturated heterocyclyl ring system. In some embodiments, a heterocyclyl refers to a heteroaryl ring system, such as a 5 to 14 membered heteroaryl ring system. A heterocyclyl can optionally be substituted with one or more substituents independently selected from those defined herein.

In one example, heterocyclyl includes 3-12 ring atoms and includes monocycles, bicycles, tricycles and spiro ring systems, wherein the ring atoms are carbon, and one to five ring atoms is a heteroatom selected from nitrogen, sulfur or oxygen, which is independently optionally substituted by one or more groups. In one example, heterocyclyl includes 1 to 4 heteroatoms. In another example, heterocyclyl includes 3- to 7-membered monocycles having one or more heteroatoms selected from nitrogen, sulfur or oxygen. In another example, heterocyclyl includes 4- to 6-membered monocycles having one or more heteroatoms selected from nitrogen, sulfur or oxygen. In another example, heterocyclyl includes 3-membered monocycles. In another example, heterocyclyl includes 4-membered monocycles. In another example, heterocyclyl includes 5-6 membered monocycles. In one example, the heterocyclyl group includes 0 to 3 double bonds. Any nitrogen or sulfur heteroatom may optionally be oxidized (e.g. NO, SO, SO_2), and any nitrogen heteroatom may optionally be quaternized (e.g. $[NR_4]^+Cl^-$, $[NR_4]^+OH^-$). Example heterocyclyls include oxiranyl, aziridinyl, thiiranyl, azetidinyl, oxetanyl, thietanyl, 1,2-dithietanyl, 1,3-dithietanyl, pyrrolidinyl, dihydro-1H-pyrrolyl, dihydrofuranyl, tetrahydrofuranyl, dihydrothienyl, tetrahydrothienyl, imidazolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, 1,1-dioxo-thiomorpholinyl, dihydropyranyl, tetrahydropyranyl, hexahydrothiopyranyl, hexahydropyrimidinyl, oxazinanyl, thiazinanyl, thioxanyl, homopiperazinyl, homopiperidinyl, azepanyl, oxepanyl, thiepanyl, oxazepinyl, oxazepanyl, diazepanyl, 1,4-diazepanyl, diazepinyl, thiazepinyl, thiazepanyl, tetrahydrothiopyranyl, oxazolidinyl, thiazolidinyl, isothiazolidinyl, 1,1-dioxoisothiazolidinonyl, oxazolidinonyl, imidazolidinonyl, 4,5,6,7-tetrahydro[2H]indazolyl, tetrahydrobenzoimidazolyl, 4,5,6,7-tetrahydrobenzo[d]imidazolyl, 1,6-dihydroimidazol[4,5-d]pyrrolo[2,3-b]pyridinyl,

thiazinyl, oxazinyl, thiadiazinyl, oxadiazinyl, dithiazinyl, dioxazinyl, oxathiazinyl, thiatriazinyl, oxatriazinyl, dithiadiazinyl, imidazolinyl, dihydropyrimidyl, tetrahydropyrimidyl, 1-pyrrolinyl, 2-pyrrolinyl, 3-pyrrolinyl, indolinyl, thiapyranyl, 2H-pyranyl, 4H-pyranyl, dioxanyl, 1,3-dioxolanyl, pyrazolinyl, pyrazolidinyl, dithianyl, dithiolanyl, pyrimidinonyl, pyrimidindionyl, pyrimidin-2,4-dionyl, piperazinonyl, piperazindionyl, pyrazolidinylimidazolinyl, 3-azabicyclo[3.1.0]hexanyl, 3,6-diazabicyclo[3.1.1]heptanyl, 6-azabicyclo[3.1.1]heptanyl, 3-azabicyclo[3.1.1]heptanyl, 3-azabicyclo[4.1.0]heptanyl, azabicyclo[2.2.2]hexanyl, 2-azabicyclo[3.2.1]octanyl, 8-azabicyclo[3.2.1]octanyl, 2-azabicyclo[2.2.2]octanyl, 8-azabicyclo[2.2.2]octanyl, 7-oxabicyclo[2.2.1]heptane, azaspiro[3.5]nonanyl, azaspiro[2.5]octanyl, azaspiro[4.5]decanyl, 1-azaspiro[4.5]decan-2-only, azaspiro[5.5]undecanyl, tetrahydroindolyl, octahydroindolyl, tetrahydroisoindolyl, tetrahydroindazolyl, 1,1-dioxohexahydrothiopyranyl. Examples of 5-membered heterocyclyls containing a sulfur or oxygen atom and one to three nitrogen atoms are thiazolyl, including thiazol-2-yl and thiazol-2-yl N-oxide, thiadiazolyl, including 1,3,4-thiadiazol-5-yl and 1,2,4-thiadiazol-5-yl, oxazolyl, for example oxazol-2-yl, and oxadiazolyl, such as 1,3,4-oxadiazol-5-yl, and 1,2,4-oxadiazol-5-yl. Example 5-membered ring heterocyclyls containing 2 to 4 nitrogen atoms include imidazolyl, such as imidazol-2-yl; triazolyl, such as 1,3,4-triazol-5-yl; 1,2,3-triazol-5-yl, 1,2,4-triazol-5-yl, and tetrazolyl, such as 1H-tetrazol-5-yl. Example benzo-fused 5-membered heterocyclyls are benzoxazol-2-yl, benzthiazol-2-yl and benzimidazol-2-yl. Example 6-membered heterocyclyls contain one to three nitrogen atoms and optionally a sulfur or oxygen atom, for example pyridyl, such as pyrid-2-yl, pyrid-3-yl, and pyrid-4-yl; pyrimidyl, such as pyrimid-2-yl and pyrimid-4-yl; triazinyl, such as 1,3,4-triazin-2-yl and 1,3,5-triazin-4-yl; pyridazinyl, in particular pyridazin-3-yl, and pyrazinyl. The pyridine N-oxides and pyridazine N-oxides and the pyridyl, pyrimid-2-yl, pyrimid-4-yl, pyridazinyl and the 1,3,4-triazin-2-yl groups, are other example heterocyclyl groups.

As used herein, the term "partially unsaturated" refers to a ring moiety that includes at least one double or triple bond between ring atoms but the ring moiety is not aromatic.

As used herein, the term "inhibitor" refers to a compound that binds to and inhibits a bromodomain with measurable affinity and activity. In certain embodiments, an inhibitor has an IC_{50} or binding constant of less about 50 μM, less than about 1 μM, less than about 500 nM, less than about 100 nM, or less than about 10 nM.

The terms "measurable affinity" and "measurably inhibit," as used herein, refer to a measurable reduction in activity of a bromodomain between: (i) a sample comprising a compound of formula I or composition thereof and such bromodomain, and (ii) an equivalent

sample comprising such bromodomain, in the absence of said compound, or composition thereof.

"Pharmaceutically acceptable salts" include both acid and base addition salts. It is to be understood that when a compound or Example herein is shown as a specific salt, the corresponding free-base, as well as other salts of the corresponding free-base (including pharmaceutically acceptable salts of the corresponding free-base) are contemplated.

"Pharmaceutically acceptable acid addition salt" refers to those salts which retain the biological effectiveness and properties of the free bases and which are not biologically or otherwise undesirable, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, carbonic acid, phosphoric acid and the like, and organic acids may be selected from aliphatic, cycloaliphatic, aromatic, araliphatic, heterocyclic, carboxylic, and sulfonic classes of organic acids such as formic acid, acetic acid, propionic acid, glycolic acid, gluconic acid, lactic acid, pyruvic acid, oxalic acid, malic acid, maleic acid, maloneic acid, succinic acid, fumaric acid, tartaric acid, citric acid, aspartic acid, ascorbic acid, glutamic acid, anthranilic acid, benzoic acid, cinnamic acid, mandelic acid, embonic acid, phenylacetic acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, salicyclic acid and the like.

"Pharmaceutically acceptable base addition salts" include those derived from inorganic bases such as sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Particularly base addition salts are the ammonium, potassium, sodium, calcium and magnesium salts. Salts derived from pharmaceutically acceptable organic nontoxic bases includes salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, ethanolamine, 2-diethylaminoethanol, tromethamine, dicyclohexylamine, lysine, arginine, histidine, caffeine, procaine, hydrabamine, choline, betaine, ethylenediamine, glucosamine, methylglucamine, theobromine, purines, piperazine, piperidine, N-ethylpiperidine, polyamine resins and the like. Particular organic non-toxic bases are isopropylamine, diethylamine, ethanolamine, tromethamine, dicyclohexylamine, choline, and caffeine.

The term "tautomer" or "tautomeric form" refers to structural isomers of different energies which are interconvertible via a low energy barrier. For example, proton tautomers (also known as prototropic tautomers) include interconversions via migration of a proton, such as keto-enol and imine-enamine isomerizations. Valence tautomers include interconversions by reorganization of some of the bonding electrons.

A "solvate" refers to an association or complex of one or more solvent molecules and a compound of the present invention. Examples of solvents include water, isopropanol, ethanol, methanol, DMSO, ethyl acetate, acetic acid and ethanolamine. The term "hydrate" refers to the complex where the solvent molecule is water.

"Therapeutically effective amount" refers to an amount of a compound of the present invention that (i) treats the particular disease, condition or disorder, (ii) attenuates, ameliorates or eliminates one or more symptoms of the particular disease, condition, or disorder, or (iii) prevents or delays the onset of one or more symptoms of the particular disease, condition or disorder described herein. In the case of cancer, the therapeutically effective amount of the drug may reduce the number of cancer cells; reduce the tumor size; inhibit (i.e., slow to some extent and preferably stop) cancer cell infiltration into peripheral organs; inhibit (i.e., slow to some extent and preferably stop) tumor metastasis; inhibit, to some extent, tumor growth; and/or relieve to some extent one or more of the symptoms associated with the cancer. For cancer therapy, efficacy can, for example, be measured by assessing the time to disease progression (TTP) and/or determining the response rate (RR). In the case of immunological disorders, the therapeutic effective amount is an amount sufficient to decrease or alleviate an allergic disorder, the symptoms of an autoimmune and/or inflammatory disease, or the symptoms of an acute inflammatory reaction (e.g. asthma). In some embodiments, a therapeutically effective amount is an amount of a chemical entity described herein sufficient to significantly decrease the activity or number of drug tolerant or drug tolerant persisting cancer cells.

"Treatment" (and variations such as "treat" or "treating") refers to clinical intervention in an attempt to alter the natural course of the individual or cell being treated, and can be performed either for prophylaxis or during the course of clinical pathology. Desirable effects of treatment include one or more of preventing occurrence or recurrence of disease, alleviation of symptoms, diminishment of any direct or indirect pathological consequences of the disease, stabilized (*i.e.*, not worsening) state of disease, preventing metastasis, decreasing the rate of disease progression, amelioration or palliation of the disease state, prolonging survival as compared to expected survival if not receiving treatment and remission or improved prognosis. In certain embodiments, a compound of formula I is used to delay development of a disease or disorder or to slow the progression of a disease or disorder. Those individuals in need of treatment include those already with the condition or disorder as well as those prone to have the condition or disorder, (for example, through a genetic mutation or aberrant expression of a gene or protein) or those in which the condition or disorder is to be prevented.

As used herein, "a" or "an" means one or more, unless clearly indicated otherwise.

As used herein, "another" means at least a second or more.

Exemplary Values

It is to be understood that two or more of the following embodiments may be combined.

One embodiment provides a compound of formula I or a salt thereof, wherein:

R^1 is H, C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, or carbocyclyl, wherein each C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, and carbocyclyl of R^1 is optionally substituted with one or more groups R^a;

R^2 is H, C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, or C_{3-8}cycloalkyl, wherein each C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, and C_{3-8}cycloalkyl of R^2 is optionally substituted with one or more groups R^b; and

each R^a is independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^v)_2$, $-S(O)-N(R^v)_2$, $-S(O)_2-N(R^v)_2$, $-O-R^v$, $-S-R^v$, $-O-C(O)-R^v$, $-O-C(O)-O-R^v$, $-C(O)-R^v$, $-C(O)-O-R^v$, $-S(O)-R^v$, $-S(O)_2-R^v$, $-O-C(O)-N(R^v)_2$, $-N(R^v)-C(O)-OR^v$, $-N(R^v)-C(O)-N(R^v)_2$, $-N(R^v)-C(O)-R^v$, $-N(R^v)-S(O)-R^v$, $-N(R^v)-S(O)_2-R^v$, $-N(R^v)-S(O)-N(R^v)_2$, and $-N(R^v)-S(O)_2-N(R^v)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl, is optionally substituted with one or more groups independently selected from oxo, halo, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^v)_2$, $-S(O)-N(R^v)_2$, $-S(O)_2-N(R^v)_2$, $-O-R^v$, $-S-R^v$, $-O-C(O)-R^v$, $-C(O)-R^v$, $-C(O)-O-R^v$, $-S(O)-R^v$, $-S(O)_2-R^v$, $-C(O)-N(R^v)_2$, $-N(R^v)-C(O)-R^v$, $-N(R^v)-S(O)-R^v$, $-N(R^v)-S(O)_2-R^v$ and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^b is independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^w)_2$, -CN, $-C(O)-N(R^w)_2$, $-S(O)-N(R^w)_2$, $-S(O)_2-N(R^w)_2$, $-O-R^w$, $-S-R^w$, $-O-C(O)-R^w$, $-O-C(O)-O-R^w$, $-C(O)-R^w$, $-C(O)-O-R^w$, $-S(O)-R^w$, $-S(O)_2-R^w$, $-O-C(O)-N(R^w)_2$, $-N(R^w)-C(O)-OR^w$, $-N(R^w)-C(O)-N(R^w)_2$, $-N(R^w)-C(O)-R^w$, $-N(R^w)-S(O)-R^w$, $-N(R^w)-S(O)_2-R^w$, $-N(R^w)-S(O)-N(R^w)_2$, and $-N(R^w)-S(O)_2-N(R^w)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, $-NO_2$, $-N(R^w)_2$, -CN, $-C(O)-N(R^w)_2$, $-S(O)-N(R^w)_2$, $-S(O)_2-N(R^w)_2$, $-O-R^w$, $-S-R^w$, $-O-C(O)-R^w$, $-C(O)-R^w$, $-C(O)-O-R^w$, $-S(O)-R^w$, $-S(O)_2-R^w$, $-C(O)-N(R^w)_2$, $-N(R^w)-C(O)-R^w$, $-N(R^w)-S(O)-R^w$, $-N(R^w)-S(O)_2-R^w$ and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^c and R^d is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more substituent groups

independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl of the substituent groups, is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $N(R^h)-S(O)_2-R^h$, and C_{1-6}alkyl, which heterocyclyl, carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, $-O-R^h$, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo, and C_{1-6}alkyl;

or R^c and R^d are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from C_{1-6}alkyl , carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, which C_{1-6}alkyl , carbocyclyl, and heterocyclyl are optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl;

each R^h is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, carbocyclyl, heterocyclyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^h are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, halo and C_{1-3}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^v is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^v are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, halo and C_{1-3}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; and

each R^w is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^w are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, halo and C_{1-3}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

One embodiment provides a compound of formula I or a salt thereof, wherein:

R^1 is H, C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, or carbocyclyl, wherein each C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, and carbocyclyl of R^1 is optionally substituted with one or more groups R^a;

R^2 is H, C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, or C_{3-8}cycloalkyl, wherein each C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, and C_{3-8}cycloalkyl of R^2 is optionally substituted with one or more groups R^b; and

each R^a is independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^v)_2$, $-S(O)-N(R^v)_2$, $-S(O)_2-N(R^v)_2$, $-O-R^v$, $-S-R^v$, $-O-C(O)-R^v$, $-O-C(O)-O-R^v$, $-C(O)-R^v$, $-C(O)-O-R^v$, $-S(O)-R^v$, $-S(O)_2-R^v$, $-O-C(O)-N(R^v)_2$, $-N(R^v)-C(O)-OR^v$, $-N(R^v)-C(O)-N(R^v)_2$, $-N(R^v)-C(O)-R^v$, $-N(R^v)-S(O)-R^v$, $-N(R^v)-S(O)_2-R^v$, $-N(R^v)-S(O)-N(R^v)_2$, and $-N(R^v)-S(O)_2-N(R^v)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl, is optionally substituted with one or more groups independently selected from oxo, halo, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^v)_2$, $-S(O)-N(R^v)_2$, $-S(O)_2-N(R^v)_2$, $-O-R^v$, $-S-R^v$, $-O-C(O)-R^v$, $-C(O)-R^v$, $-C(O)-O-R^v$, $-S(O)-R^v$, $-S(O)_2-R^v$, $-C(O)-N(R^v)_2$, $-N(R^v)-C(O)-R^v$, $-N(R^v)-S(O)-R^v$, $-N(R^v)-S(O)_2-R^v$ and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^b is independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^w)_2$, -CN, $-C(O)-N(R^w)_2$, $-S(O)-N(R^w)_2$, $-S(O)_2-N(R^w)_2$, $-O-R^w$, $-S-R^w$, $-O-C(O)-R^w$, $-O-C(O)-O-R^w$, $-C(O)-R^w$, $-C(O)-O-R^w$, $-S(O)-R^w$, $-S(O)_2-R^w$, $-O-C(O)-N(R^w)_2$, $-N(R^w)-C(O)-OR^w$, $-N(R^w)-C(O)-N(R^w)_2$, $-N(R^w)-C(O)-R^w$, $-N(R^w)-S(O)-R^w$, $-N(R^w)-S(O)_2-R^w$, $-N(R^w)-S(O)-N(R^w)_2$, and $-N(R^w)-S(O)_2-N(R^w)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, $-NO_2$, $-N(R^w)_2$, -CN, $-C(O)-N(R^w)_2$, $-S(O)-N(R^w)_2$, $-S(O)_2-N(R^w)_2$, $-O-R^w$, $-S-R^w$, $-O-C(O)-R^w$, $-C(O)-R^w$, $-C(O)-O-R^w$, $-S(O)-R^w$, $-S(O)_2-R^w$, $-C(O)-N(R^w)_2$, $-N(R^w)-C(O)-R^w$, $-N(R^w)-S(O)-R^w$, $-N(R^w)-S(O)_2-R^w$ and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^c and R^d is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl of the substituent groups, is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $N(R^h)-S(O)_2-R^h$, and C_{1-6}alkyl, which carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, $-O-R^h$, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo, and C_{1-6}alkyl;

or R^c and R^d are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from

C_{1-6}alkyl , carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, which C_{1-6}alkyl , carbocyclyl, and heterocyclyl are optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl;

each R^h is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, carbocyclyl, heterocyclyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^h are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, halo and C_{1-3}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^v is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^v are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, halo and C_{1-3}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; and

each R^w is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^w are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, halo and C_{1-3}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

In certain embodiments R^1 is C_{1-12}alkyl or C_{2-12}alkenyl, wherein each C_{1-12}alkyl and C_{2-12}alkenyl is optionally substituted with one or more groups R^a.

In certain embodiments R^1 is C_{1-6}alkyl or C_{2-6}alkenyl, wherein each C_{1-6}alkyl and C_{2-6}alkenyl is optionally substituted with one or more groups R^a.

In certain embodiments R^1 is C_{1-6}alkyl or C_{2-6}alkenyl, wherein each C_{1-6}alkyl and C_{2-6}alkenyl is optionally substituted with one or more groups independently selected from carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-N(R^v)_2$, -CN, $-C(O)-N(R^v)_2$, $-O-R^v$, $-O-C(O)-R^v$, $-C(O)-R^v$, and $-C(O)-O-R^v$.

In certain embodiments R^1 is C_{1-6}alkyl or C_{2-6}alkenyl, wherein each C_{1-6}alkyl and C_{2-6}alkenyl is optionally substituted with one or more groups independently selected from carbocyclyl, -F, -Cl, $-O-R^v$, $-O-C(O)-R^v$, $-C(O)-R^v$, and $-C(O)-O-R^v$.

In certain embodiments R^1 is C_{1-6}alkyl or C_{2-6}alkenyl, wherein each C_{1-6}alkyl and C_{2-6}alkenyl is optionally substituted with one or more groups independently selected from C_{3-6}cycloalkyl.

In certain embodiments R^1 is methyl, butyl, 2-propenyl, 2-buten-1-yl, 3-buten-1-yl or 2-cyclopropylethyl.

In certain embodiments R^2 is H or C_{1-12}alkyl wherein each C_{1-12}alkyl is optionally substituted with one or more groups R^b.

In certain embodiments R^2 is H or C_{1-6}alkyl wherein each C_{1-12}alkyl is optionally substituted with one or more groups R^b.

In certain embodiments R^2 is H or C_{1-6}alkyl wherein each C_{1-12}alkyl is optionally substituted with one or more carbocyclyl, -F, -Cl, $-O-R^w$, $-O-C(O)-R^w$, $-C(O)-R^w$, $-C(O)-O-R^w$.

In certain embodiments R^2 is H or methyl.

In certain embodiments R^2 is H.

In certain embodiments R^c is hydrogen, C_{1-6}alkyl, or carbocyclyl, wherein each C_{1-6}alkyl and carbocyclyl is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl of the substituent groups, is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $N(R^h)-S(O)_2-R^h$, and C_{1-6}alkyl, which heterocyclyl, carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, $-O-R^h$, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

In certain embodiments R^c is hydrogen, C_{1-6}alkyl, or carbocyclyl, wherein each C_{1-6}alkyl and carbocyclyl is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $N(R^h)-S(O)_2-R^h$, and C_{1-6}alkyl, which carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, $-O-R^h$, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

In certain embodiments R^c is hydrogen, C_{1-6}alkyl, or C_{3-8}cycloalkyl, wherein each C_{1-6}alkyl and C_{3-8}cycloalkyl is optionally substituted with one or more substituent groups independently selected from $-O-R^h$.

In certain embodiments R^c is hydrogen, methyl, ethyl, cyclopropyl, cyclobutyl, or 2-methoxyethyl.

In certain embodiments R^c is hydrogen.

In certain embodiments R^c is methyl, ethyl, cyclopropyl, cyclobutyl, or 2-methoxyethyl.

In certain embodiments R^d is C_{1-6}alkyl, carbocyclyl or heterocyclyl,wherein each C_{1-6}alkyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $N(R^h)-S(O)_2-R^h$, and C_{1-6}alkyl, which heterocyclyl, carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, $-O-R^h$,

heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

In certain embodiments R^d is C_{1-6}alkyl, carbocyclyl or heterocyclyl,wherein each C_{1-6}alkyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $N(R^h)-S(O)_2-R^h$, and C_{1-6}alkyl, which carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, cyano, $-O-R^h$, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

In certain embodiments R^d is C_{1-6}alkyl that is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $N(R^h)-S(O)_2-R^h$, and C_{1-6}alkyl, which heterocyclyl, carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, $-O-R^h$, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

In certain embodiments R^d is C_{1-6}alkyl that is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, -

$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, $-NO_2$, $-N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, N(R^h)-$S(O)_2$-R^h, and C_{1-6}alkyl, which carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, cyano, -O-R^h, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

In certain embodiments R^d is carbocyclyl that is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, $-NO_2$, $-N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, N(R^h)-$S(O)_2$-R^h, and C_{1-6}alkyl, which heterocyclyl, carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, -O-R^h, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

In certain embodiments R^d is carbocyclyl that is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, $-NO_2$, $-N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, N(R^h)-$S(O)_2$-R^h, and C_{1-6}alkyl, which carbocyclyl and

C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, -O-R^h, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

In certain embodiments R^d is heterocyclyl that is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^v)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, -NO_2, -$N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, $N(R^h)$-$S(O)_2$-R^h, and C_{1-6}alkyl, which heterocyclyl, carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, -O-R^h, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

In certain embodiments R^d is heterocyclyl that is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^v)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, -NO_2, -$N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, $N(R^h)$-$S(O)_2$-R^h, and C_{1-6}alkyl, which carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, -O-R^h, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

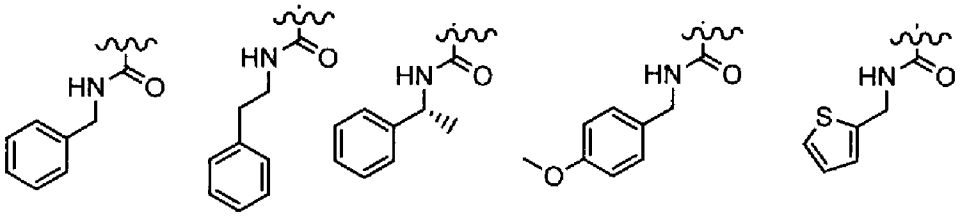
In certain embodiments R^c and R^d are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^v)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -

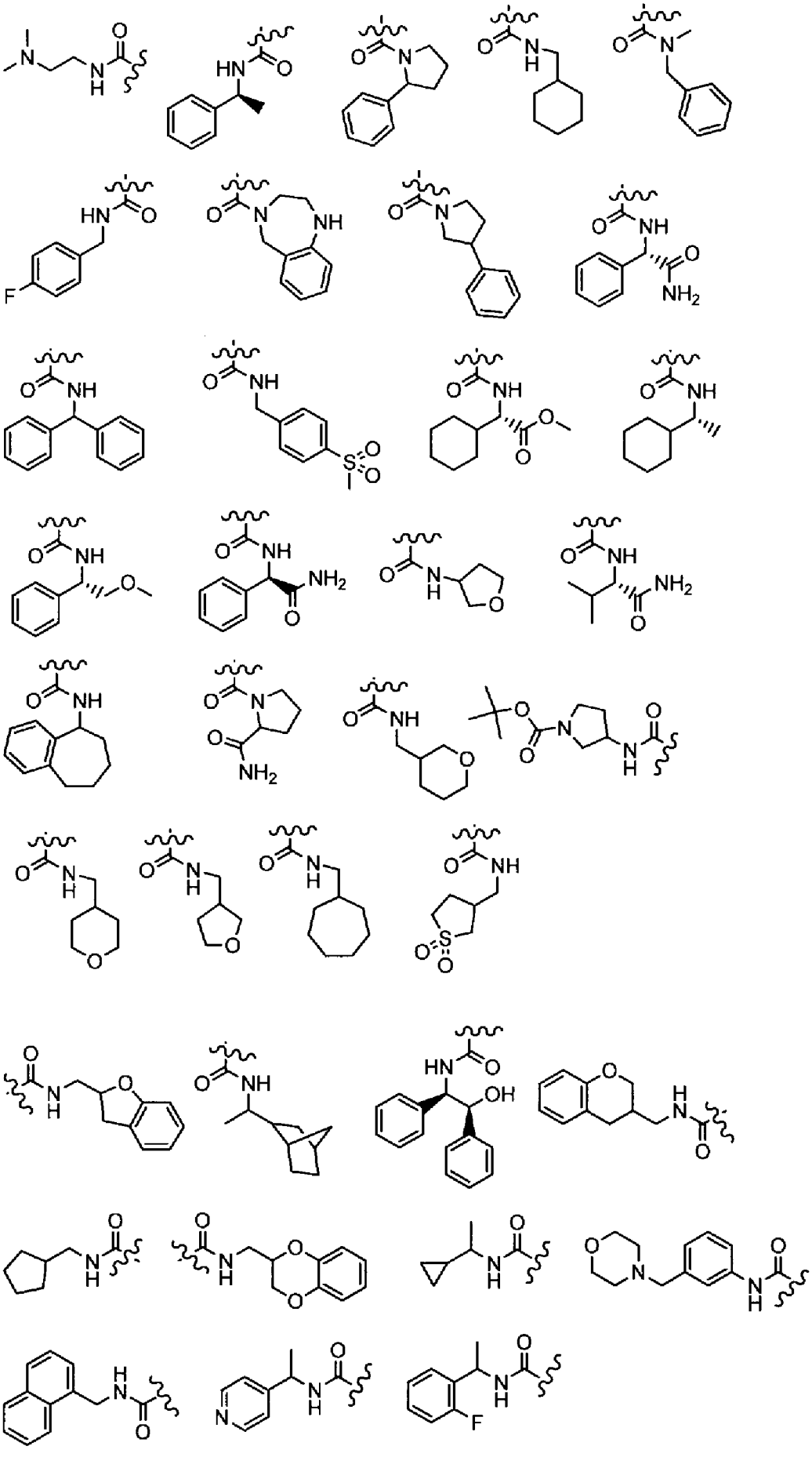
O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from C_{1-6}alkyl , carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, which C_{1-6}alkyl , carbocyclyl, and heterocyclyl are optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

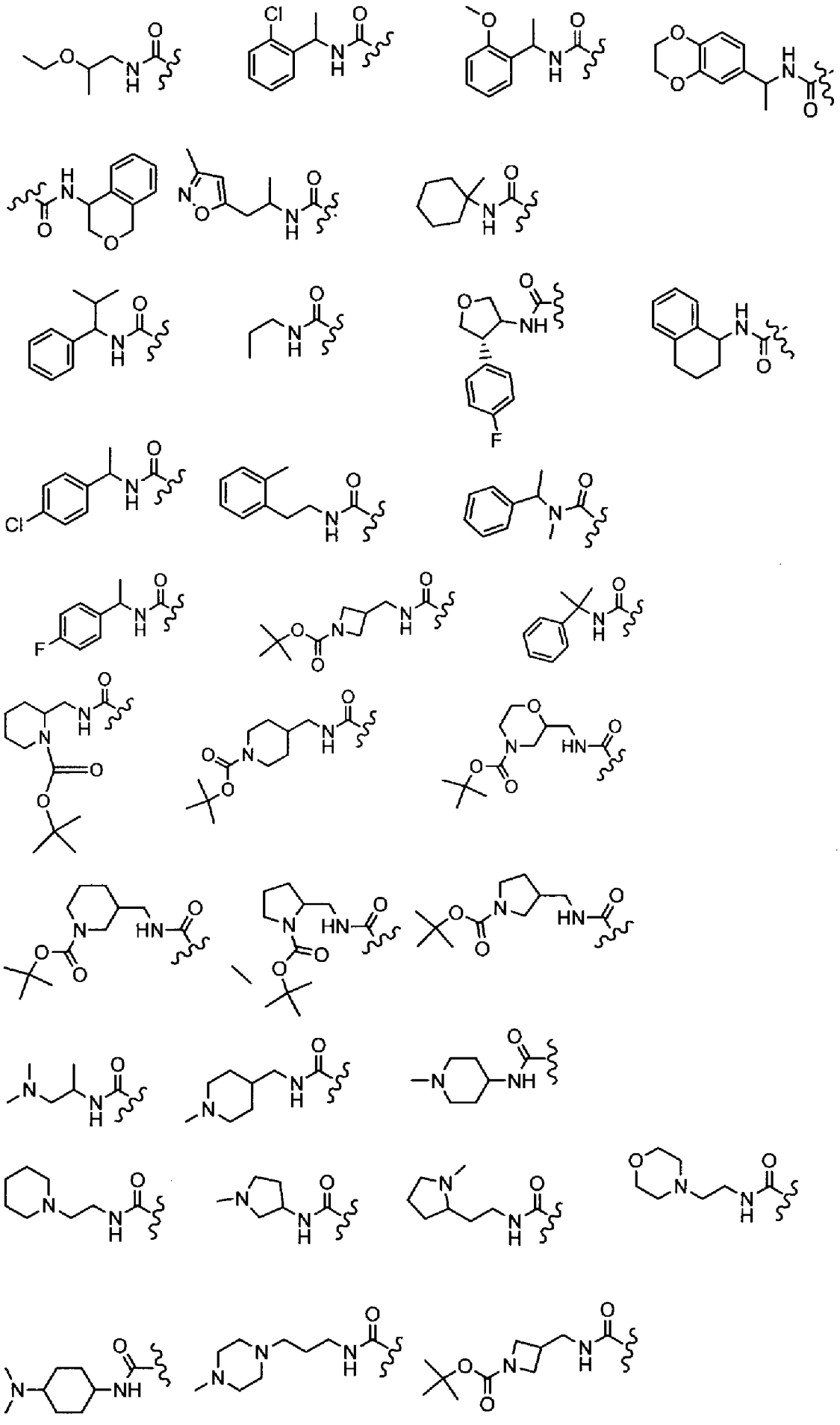
In certain embodiments R^c and R^d are taken together with the nitrogen to which they are attached to form a 5-6 membered monocyclic heterocyclyl or a 8-12 membered bicyclic heterocyclyl, wherein the monocyclic or bicyclic heterocyclyl is optionally substituted with one or more groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^v)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from C_{1-6}alkyl , carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, which C_{1-6}alkyl , carbocyclyl, and heterocyclyl are optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

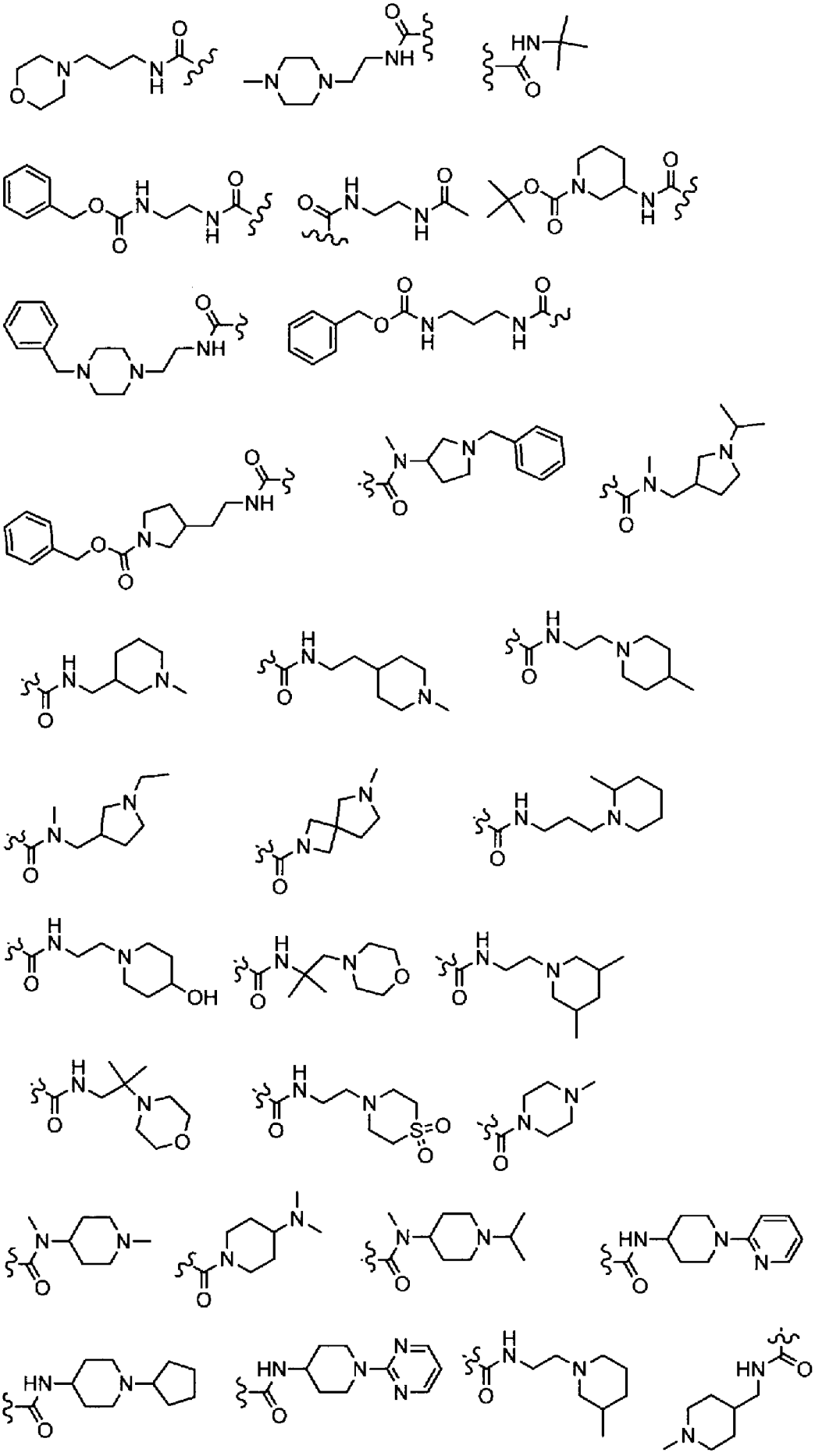
In certain embodiments the compound is a compound as described in the Examples herein, or a freebase or salt thereof.

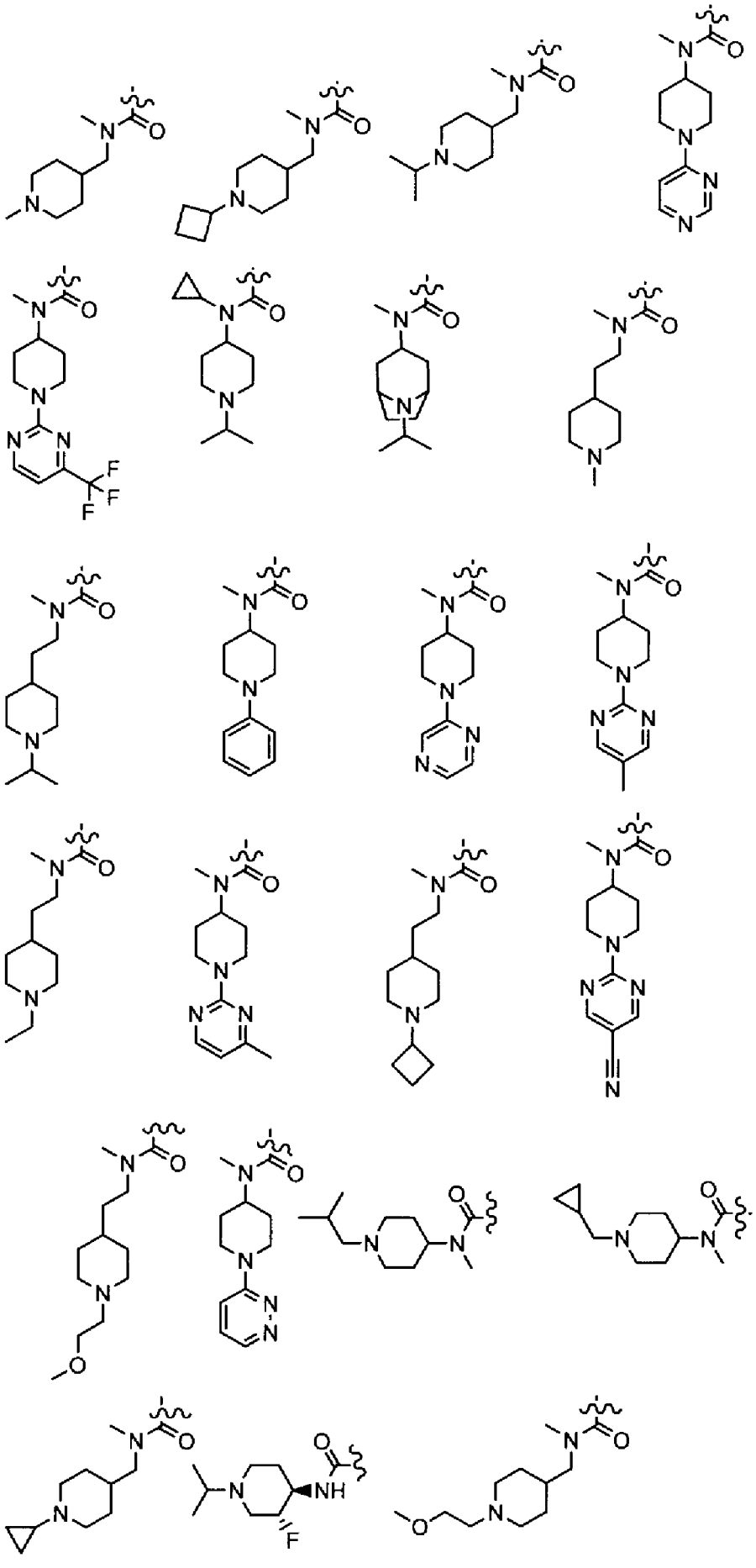
In certain embodiments –C(=O)NR^cR^d is selected from:

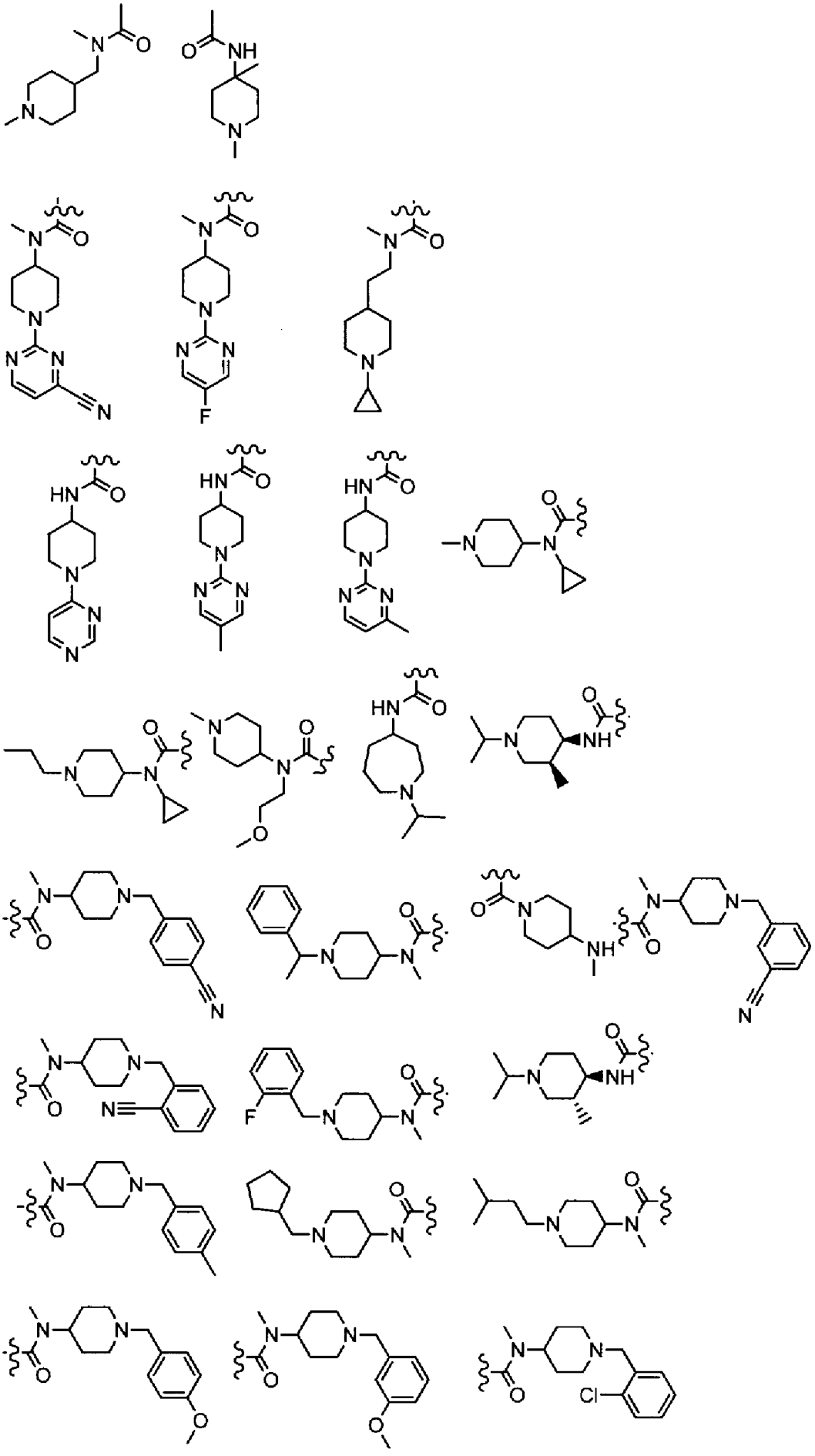


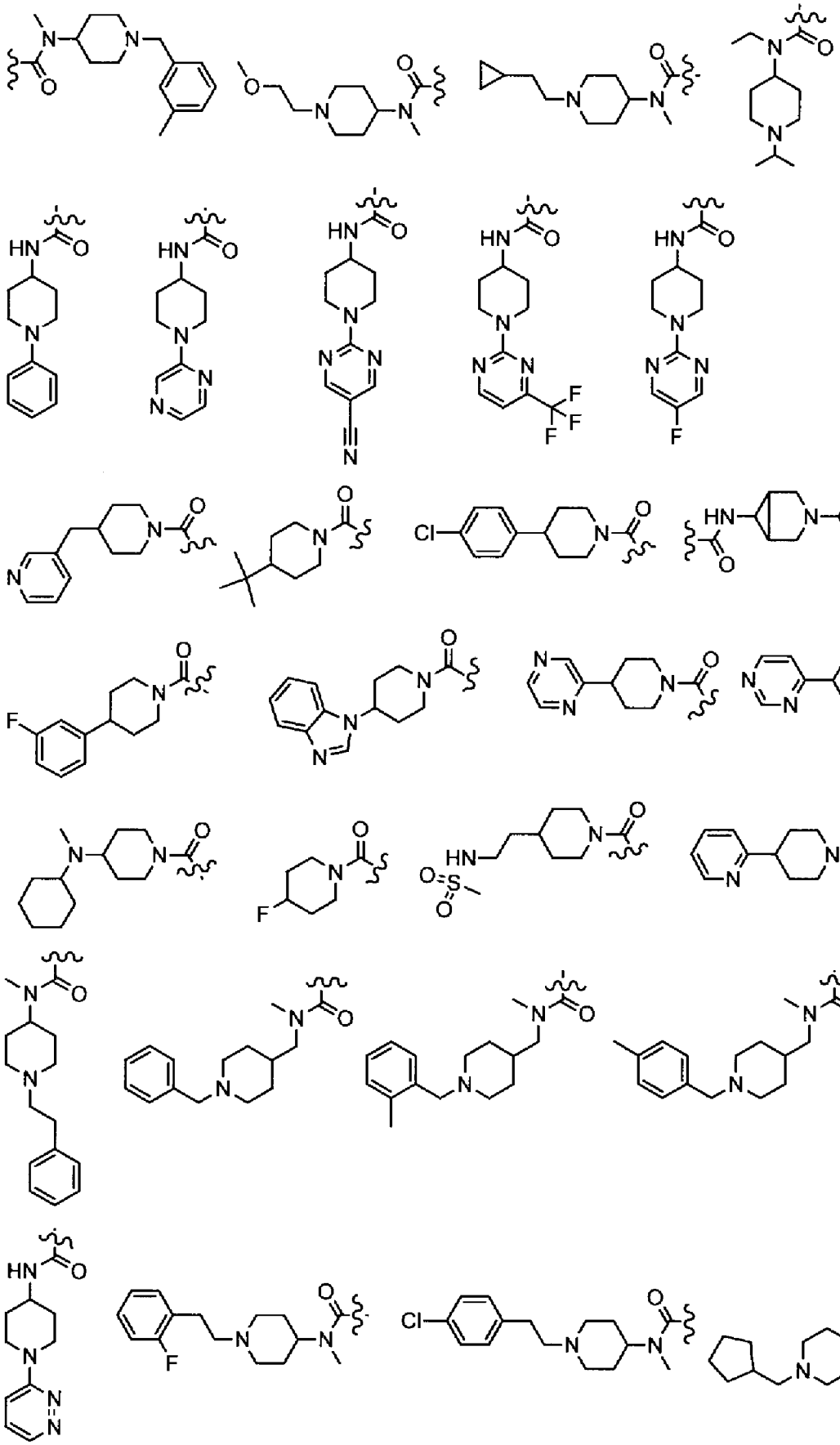


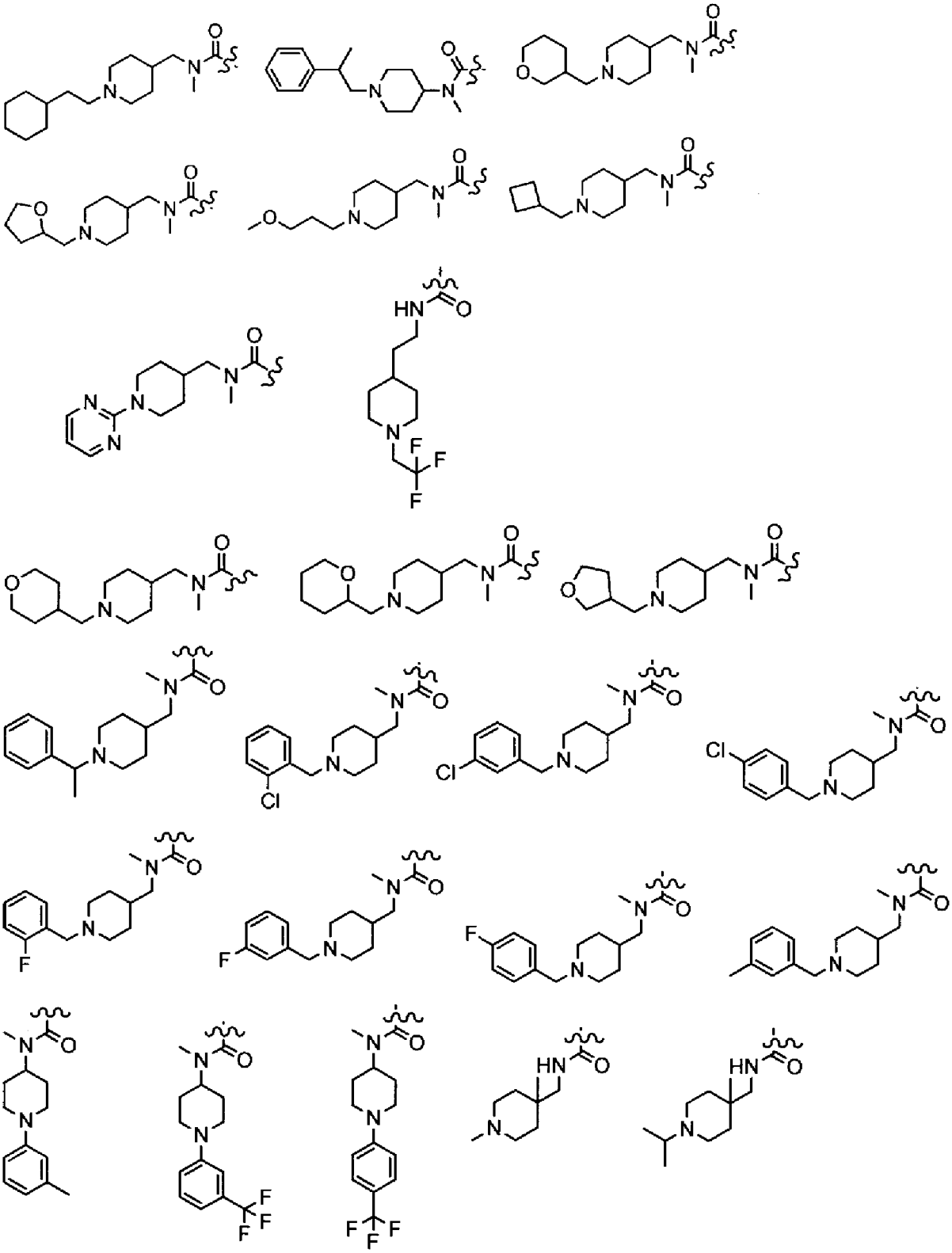


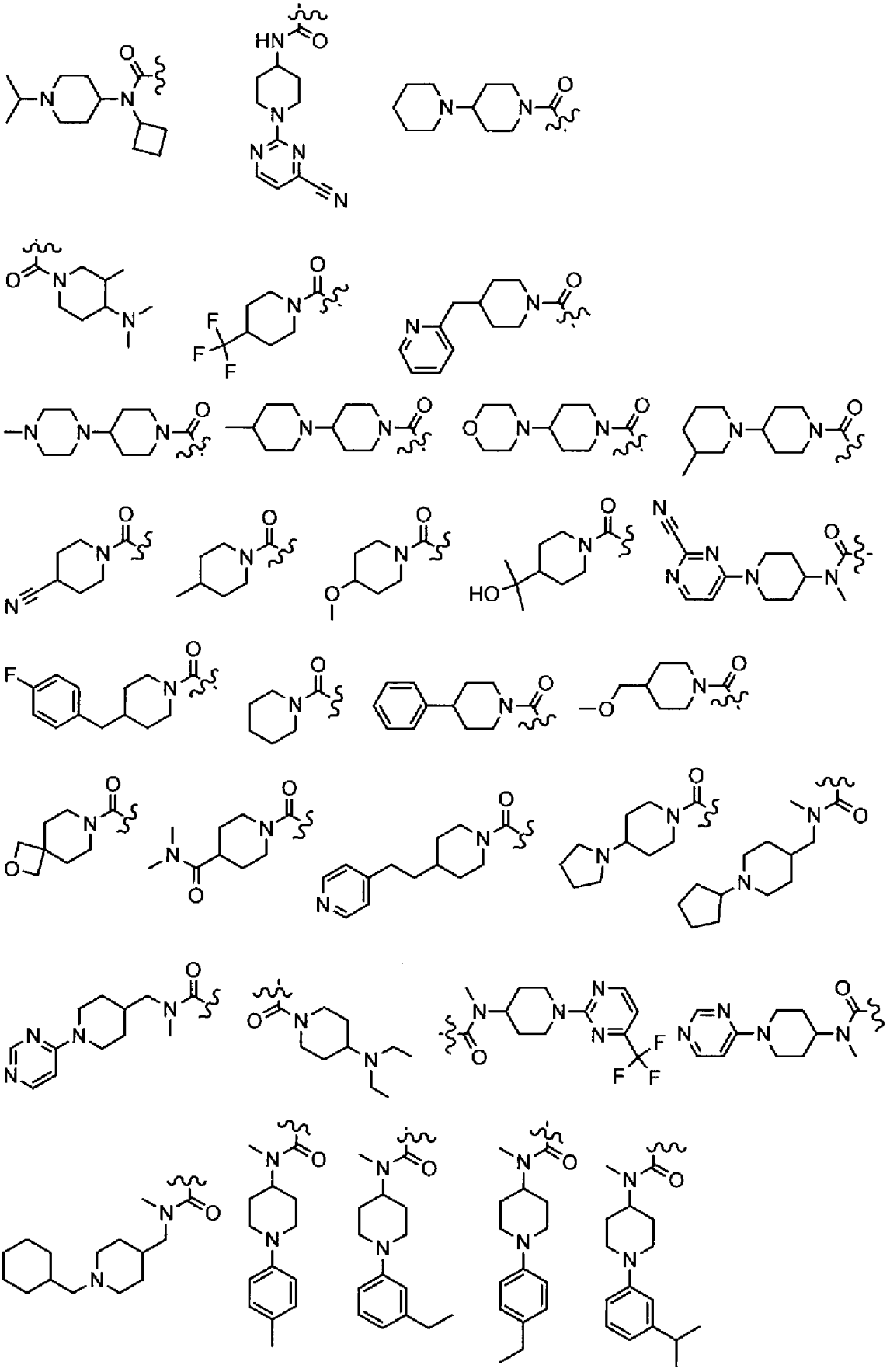


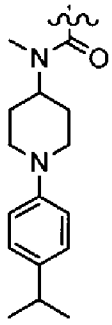
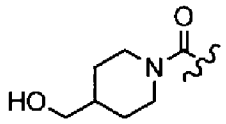
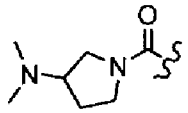
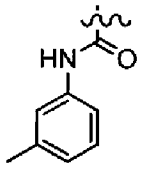
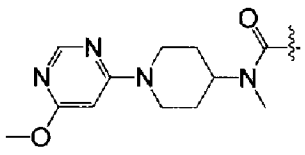
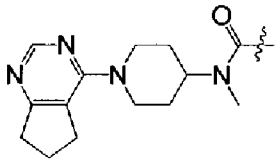
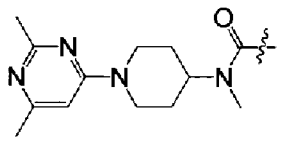
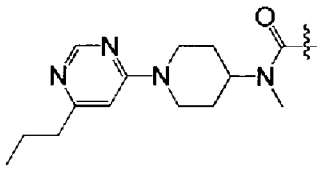
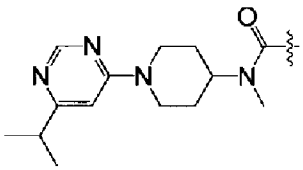
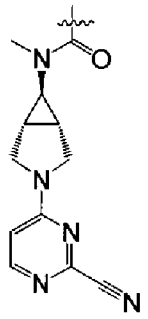
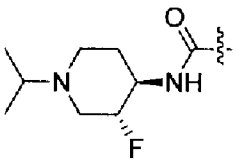
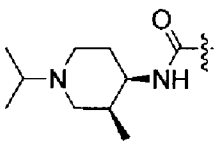
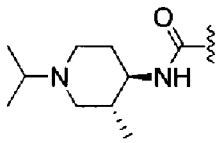
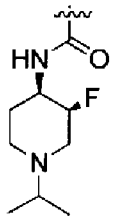
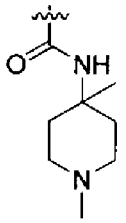
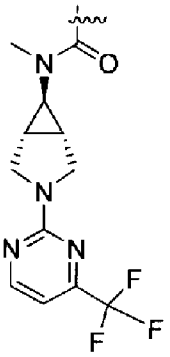








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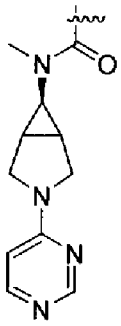

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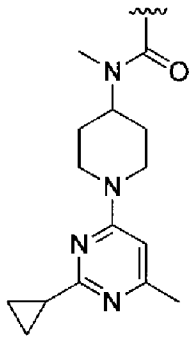
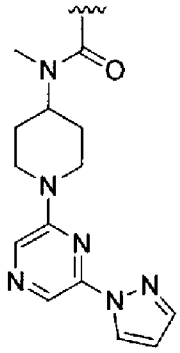
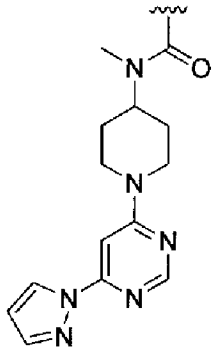
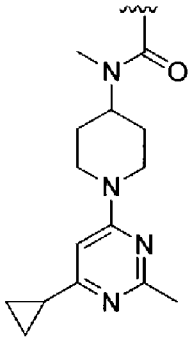
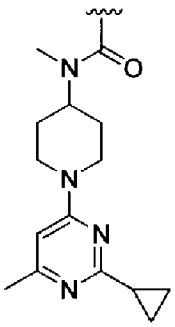
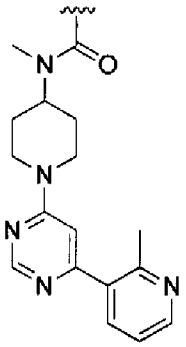
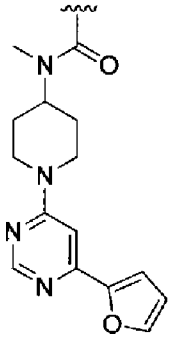
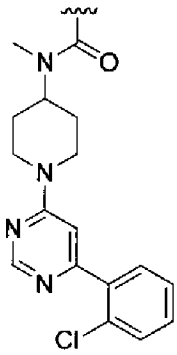
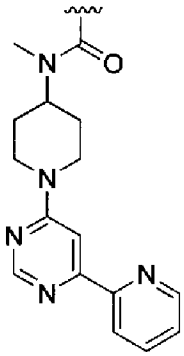
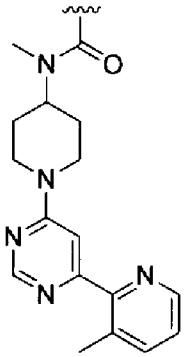
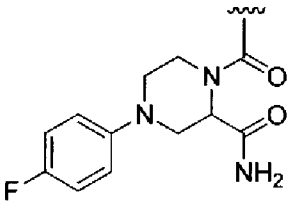
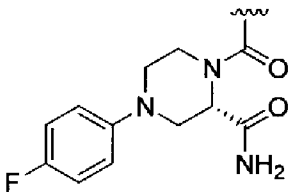
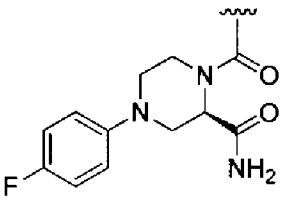
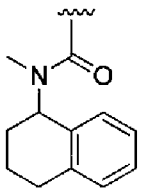
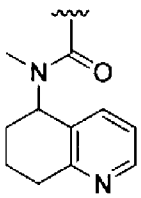
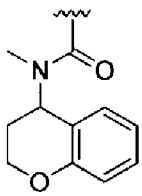
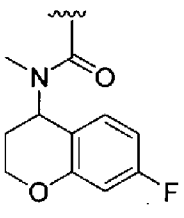
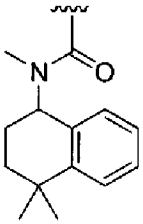
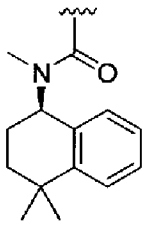
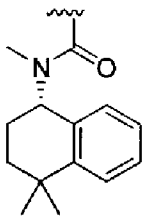
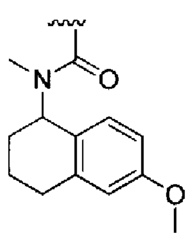
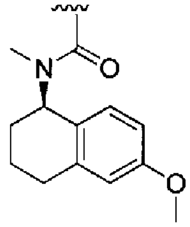
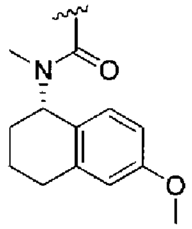
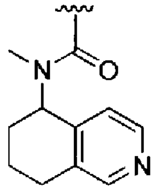
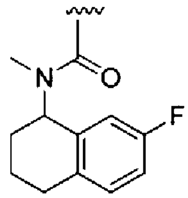
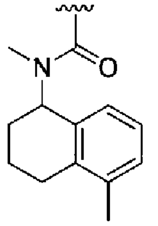
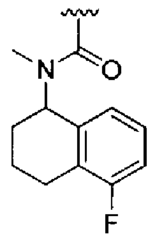
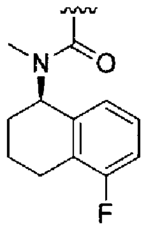
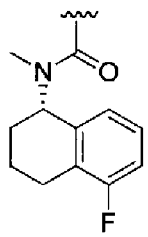
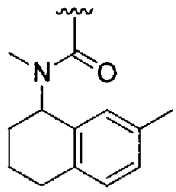
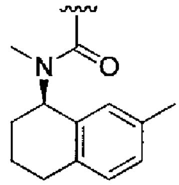
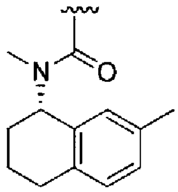
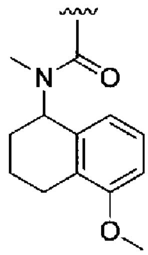
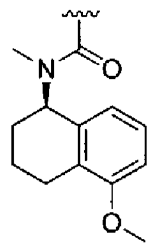
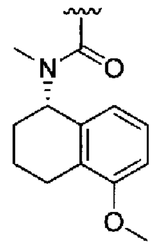
In certain embodiments $-C(=O)NR^cR^d$ is selected from:

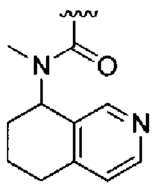
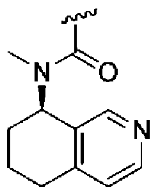
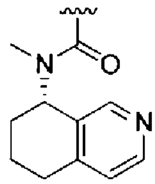





















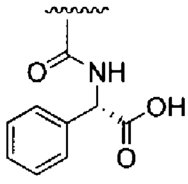
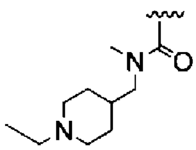
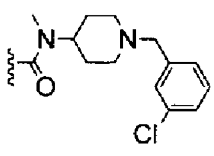
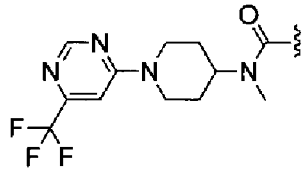
  

   and 

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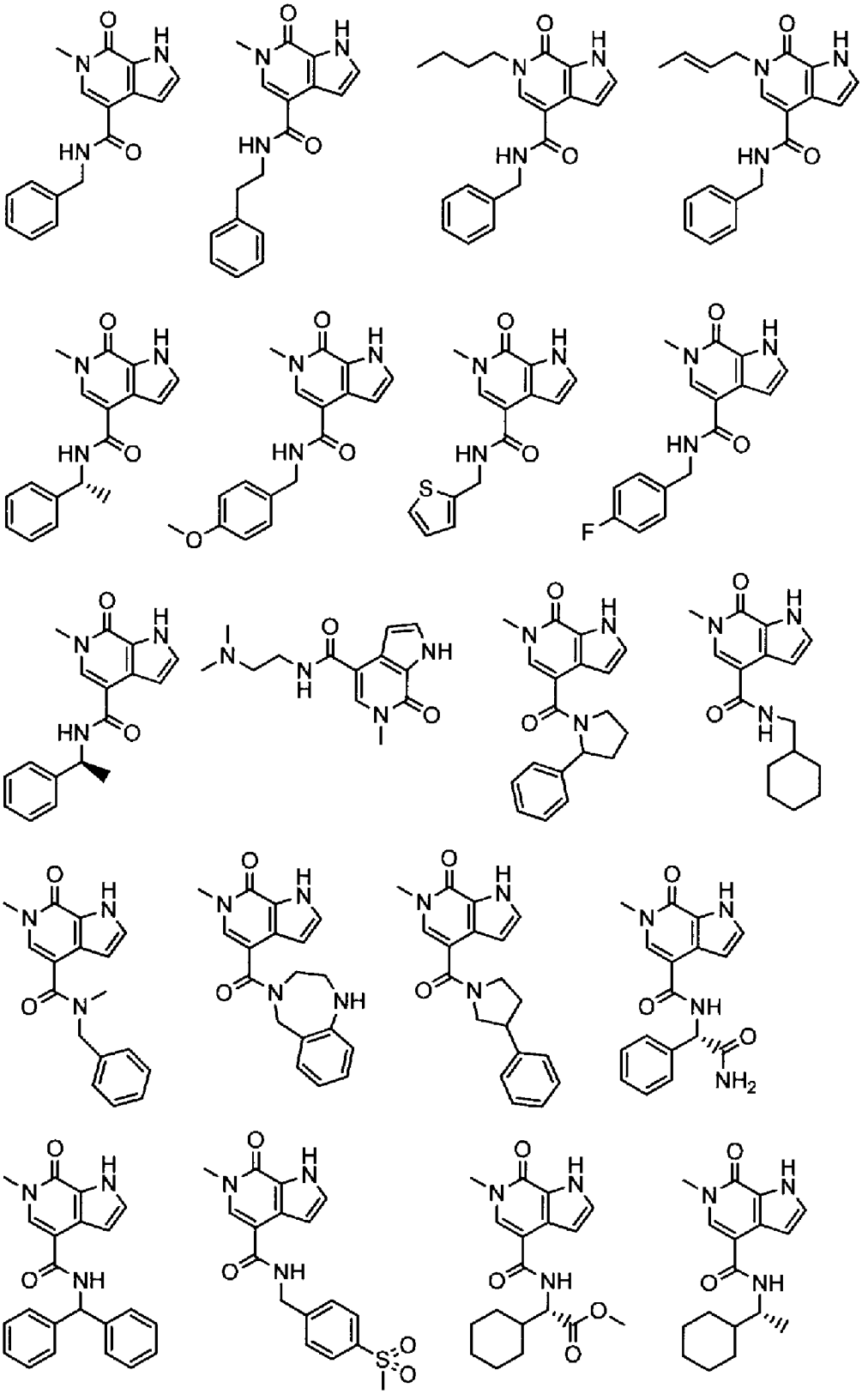

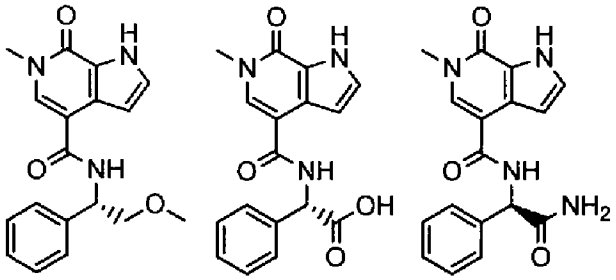
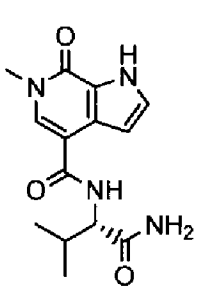
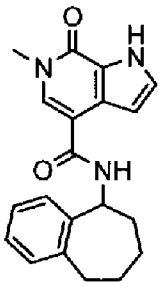
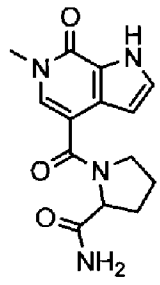
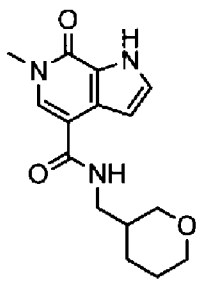
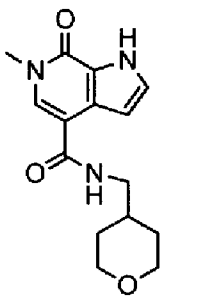
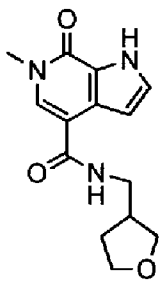
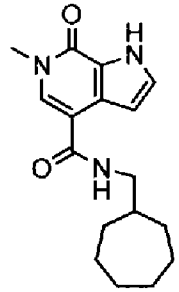
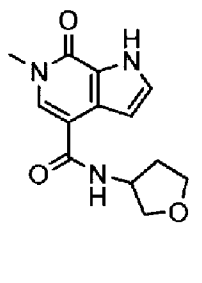
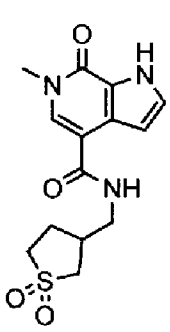
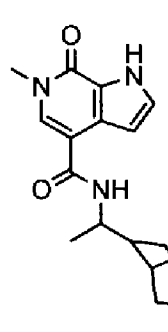
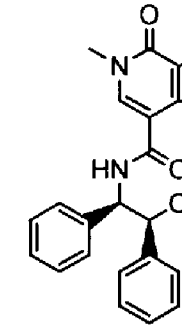

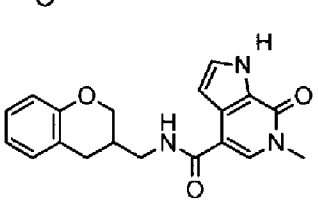
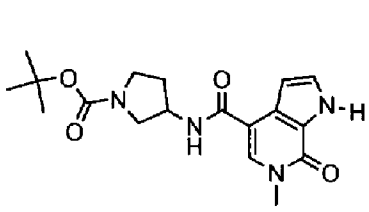
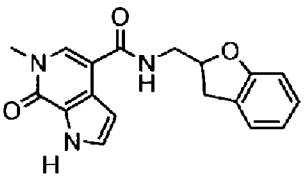
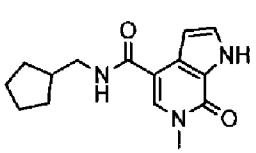
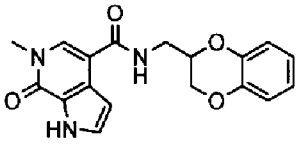
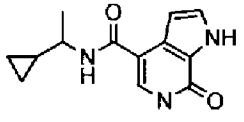

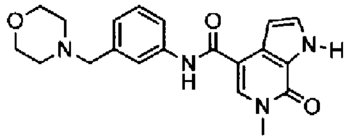
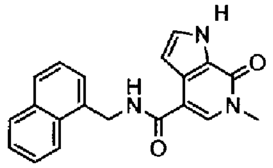
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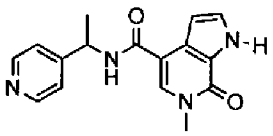
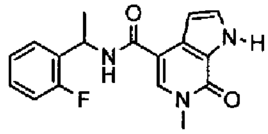
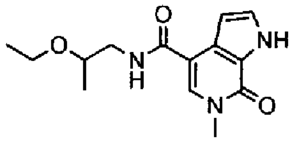
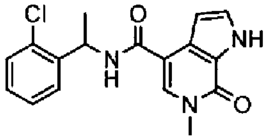
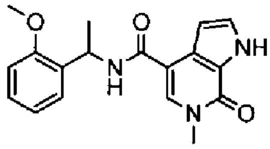
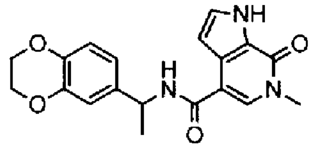
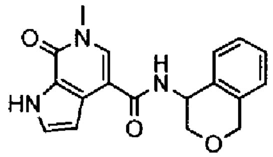
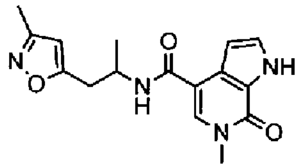
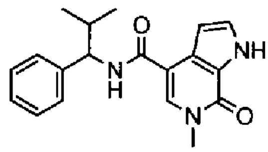
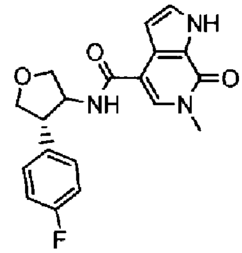
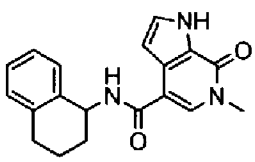
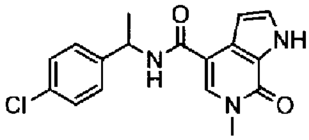
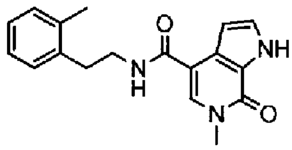
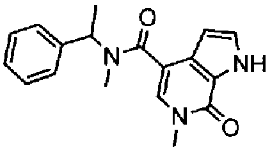
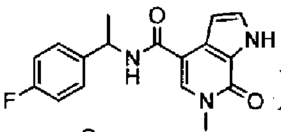
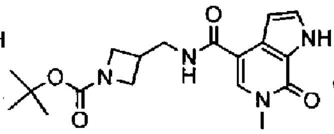
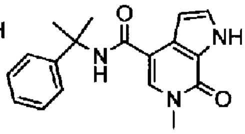



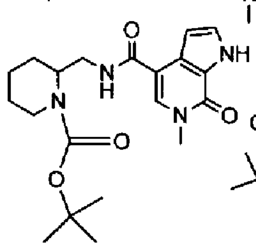
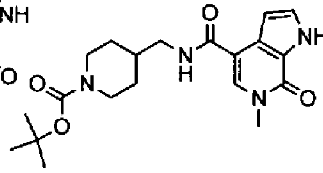
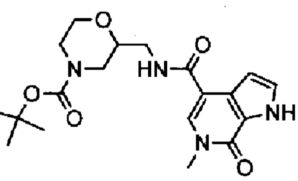




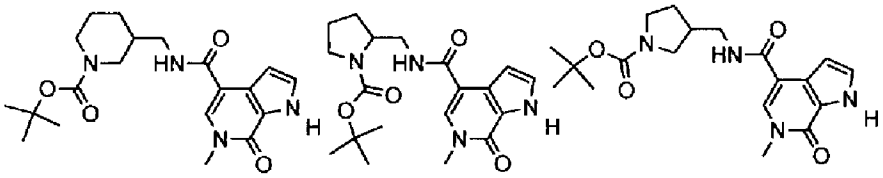
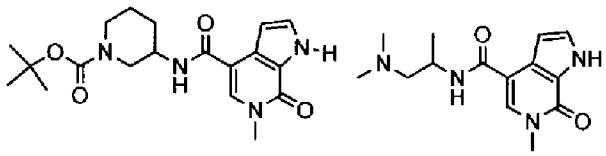




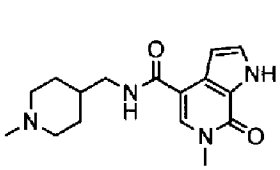
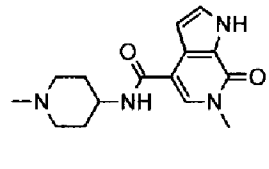
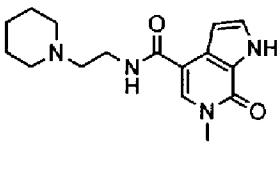
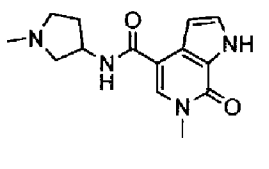
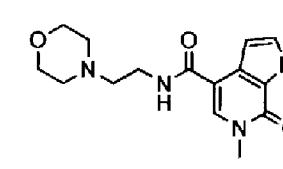
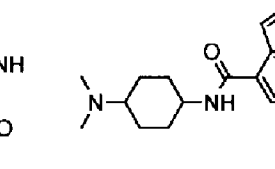
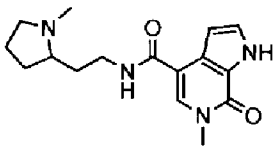




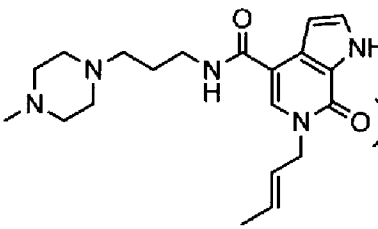
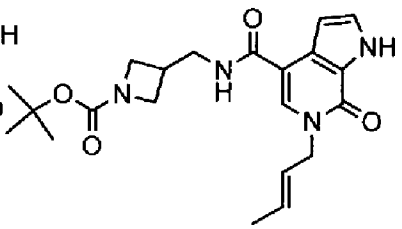
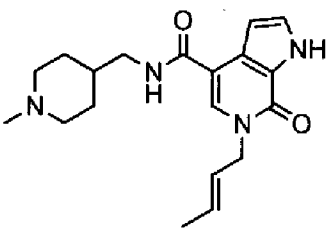
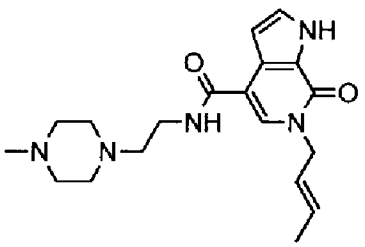
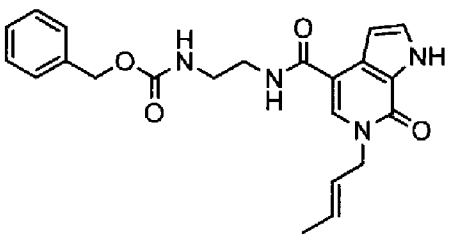
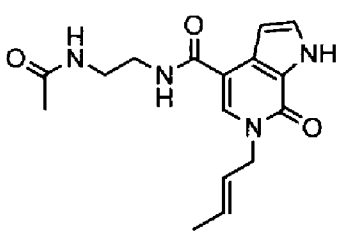
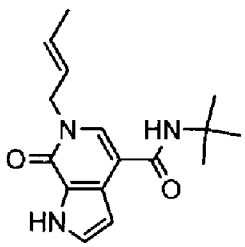




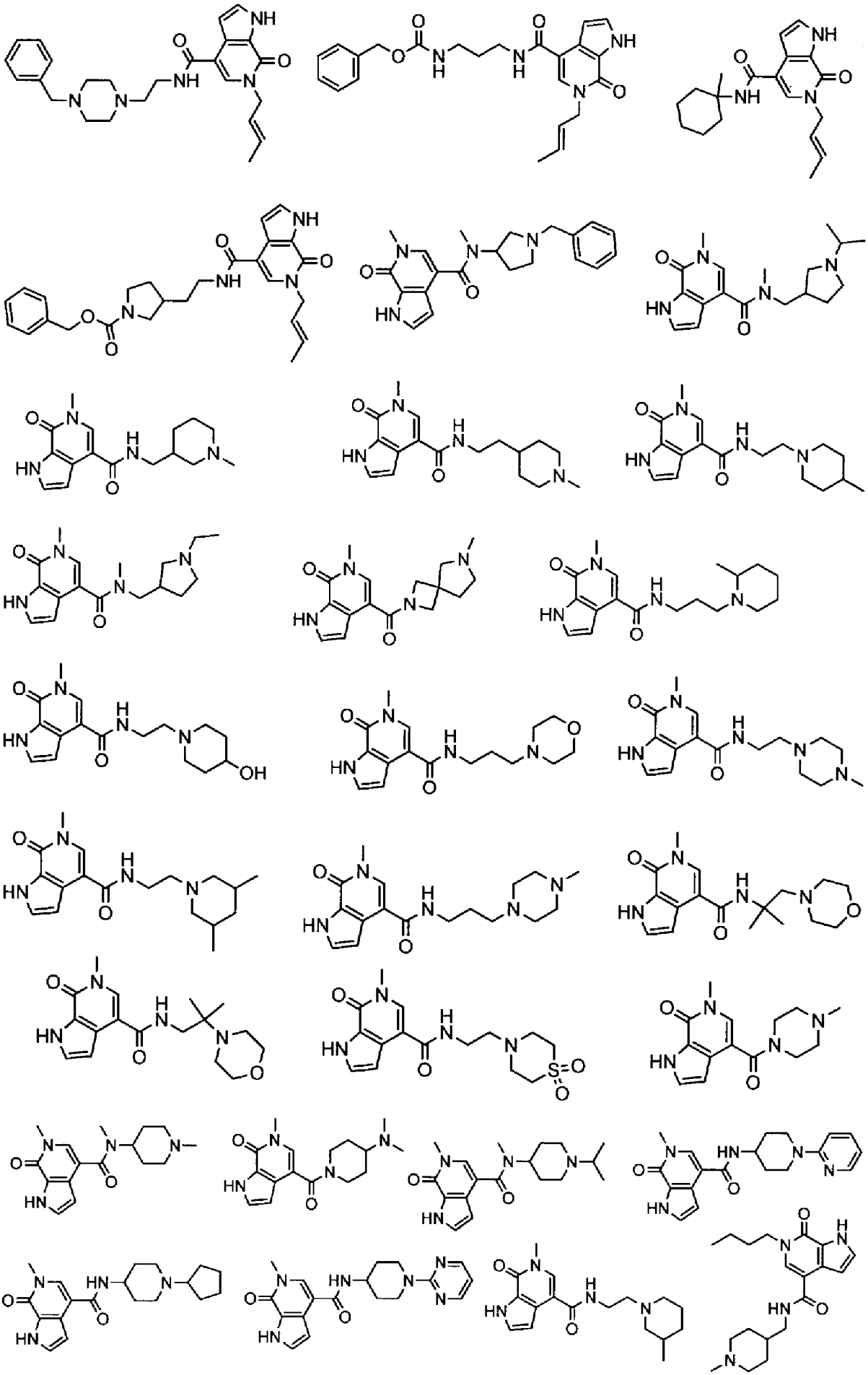




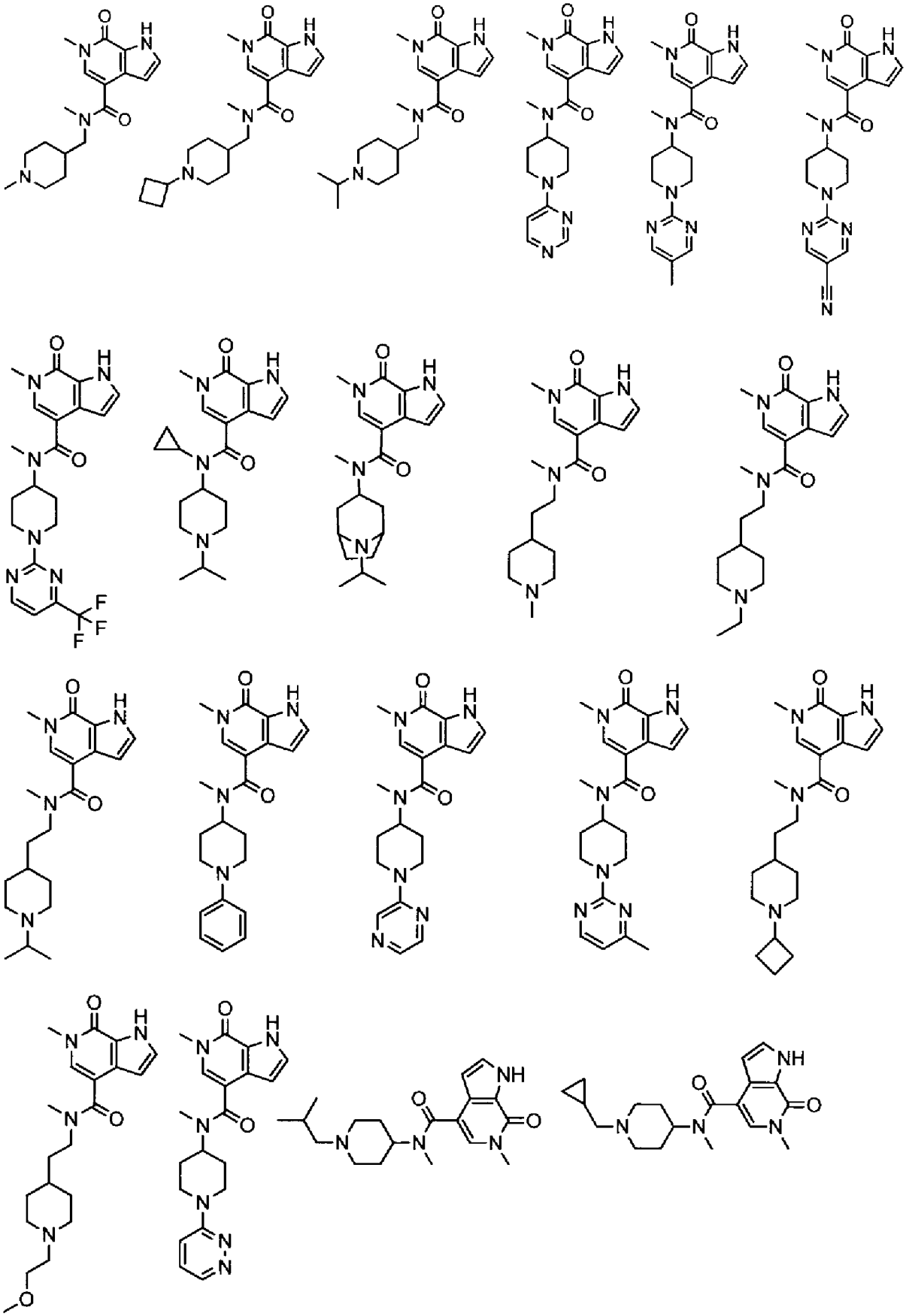




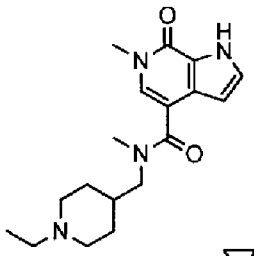
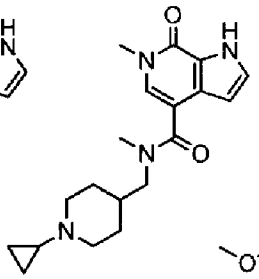
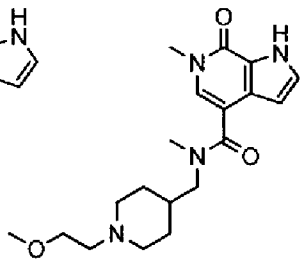
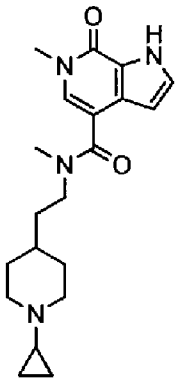
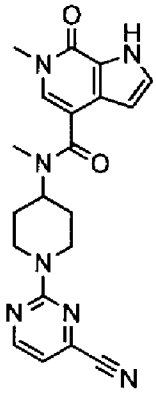
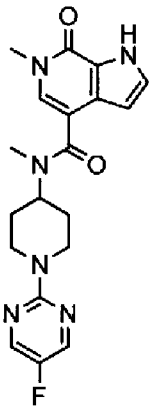
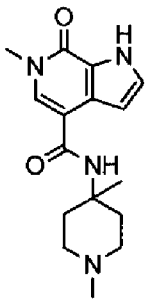
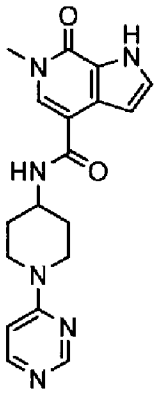
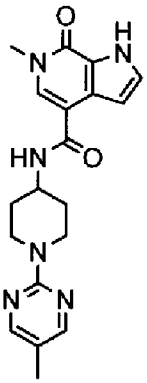
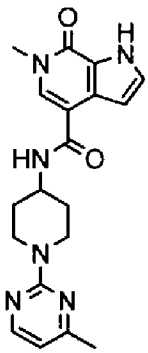
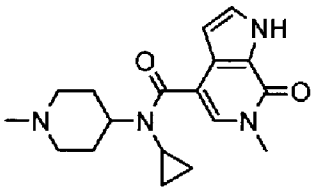
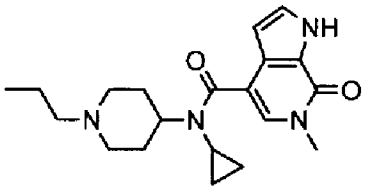
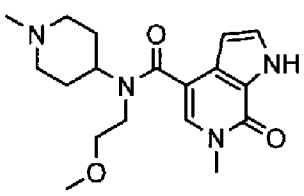
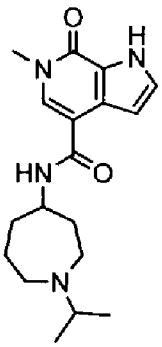
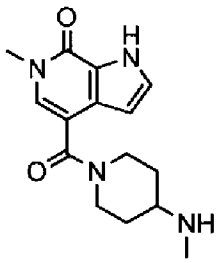
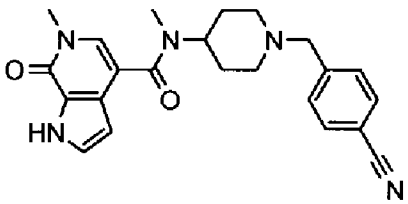
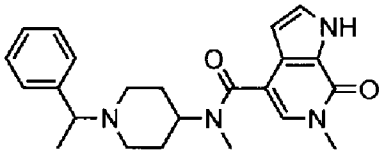
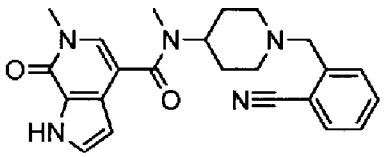
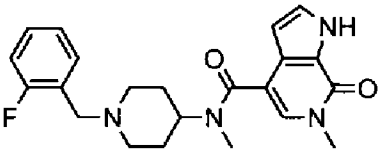
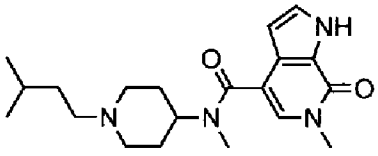



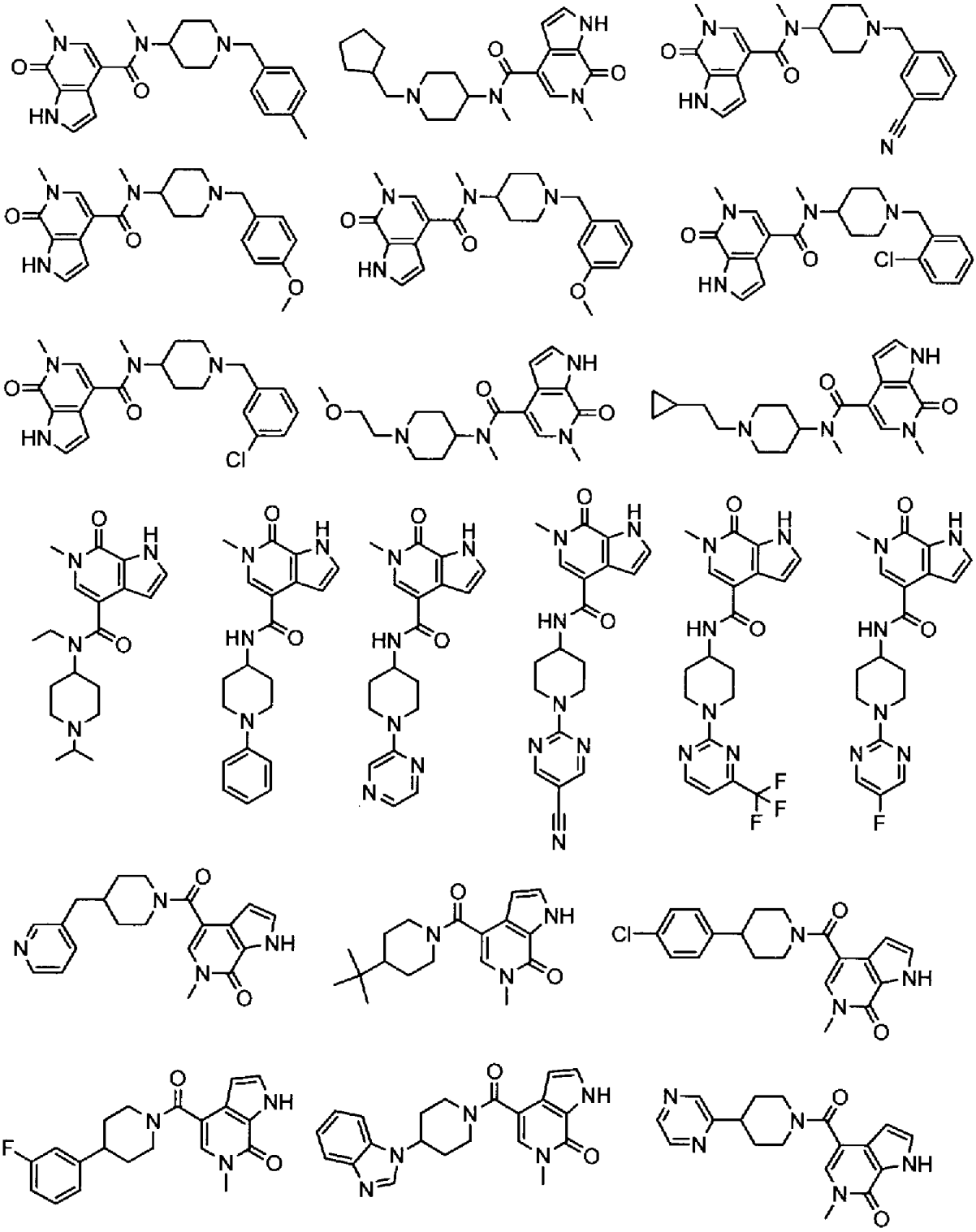








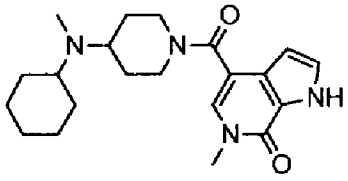
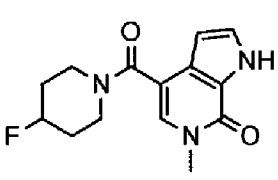
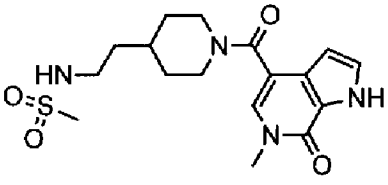
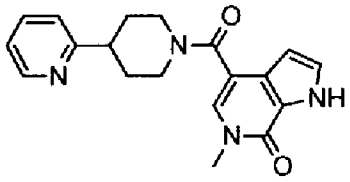
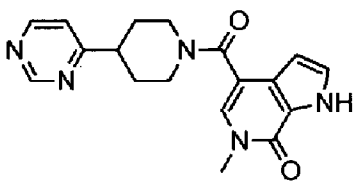
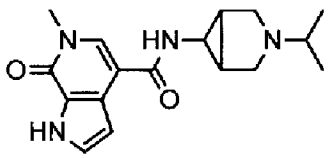
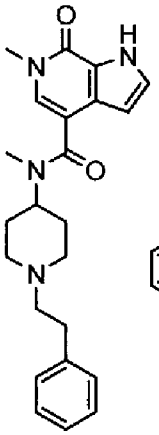
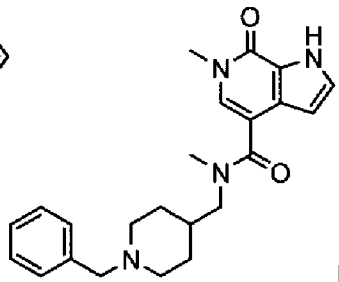
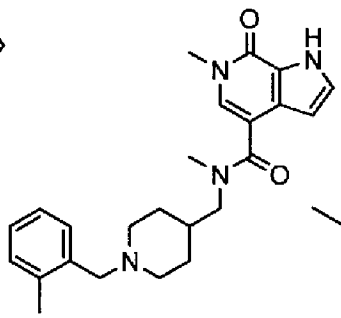
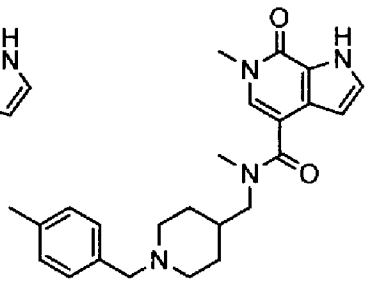
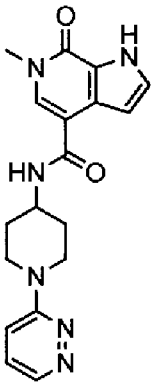
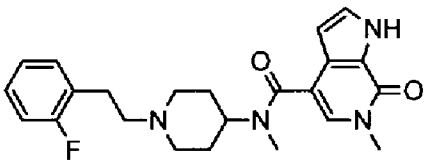
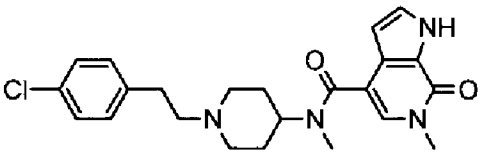
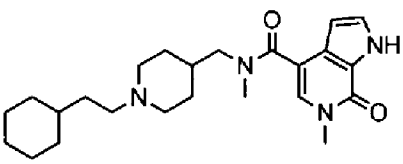
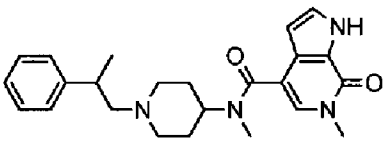
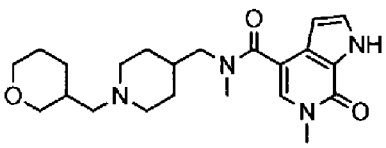
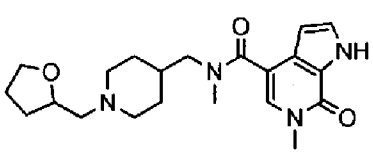
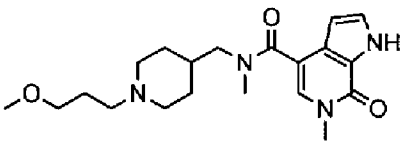
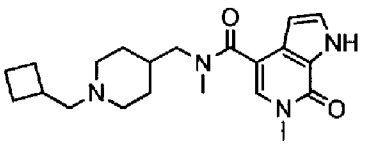








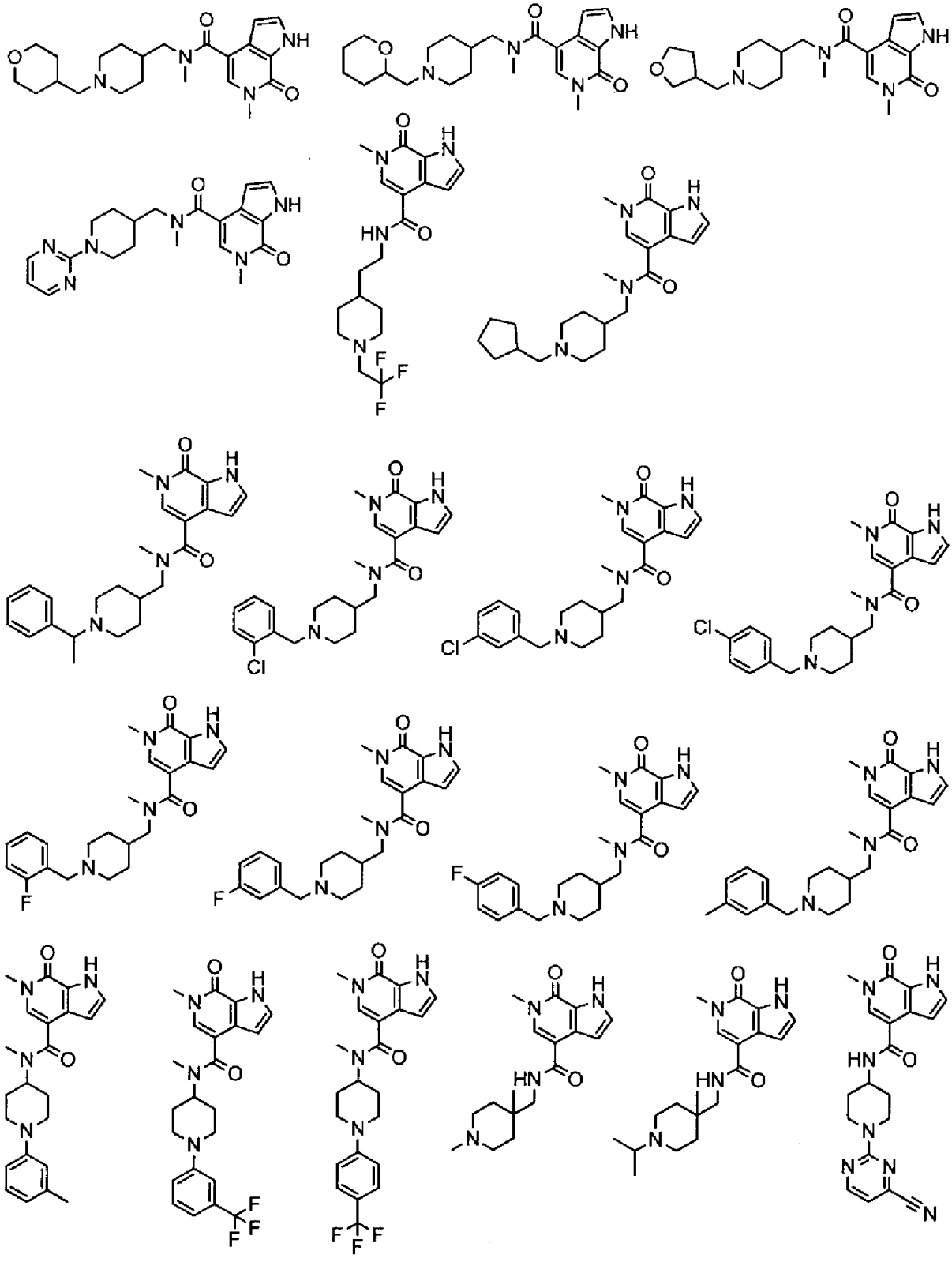


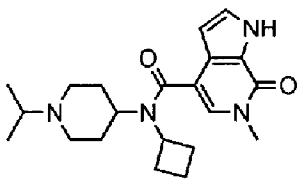
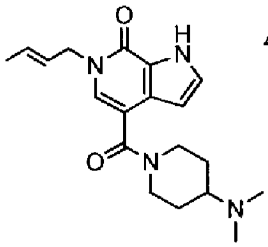
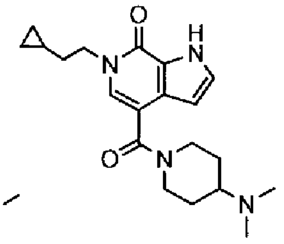
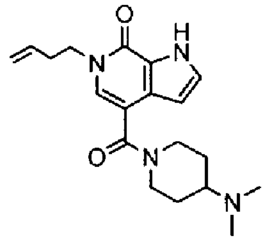
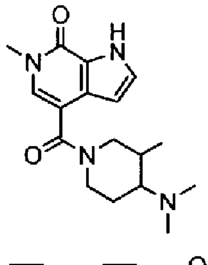
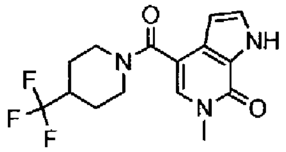
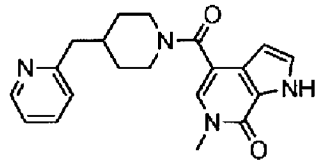
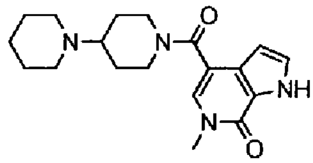
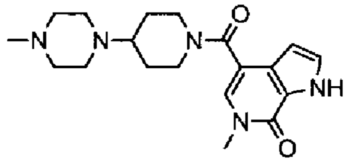
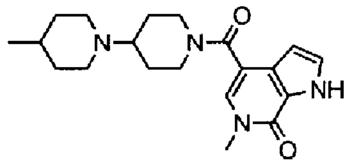
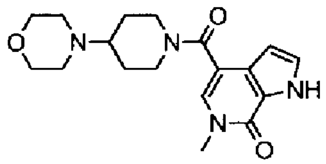
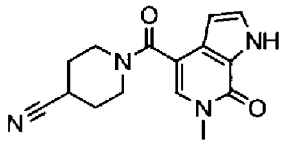
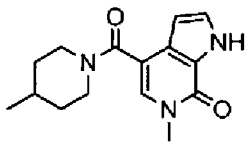
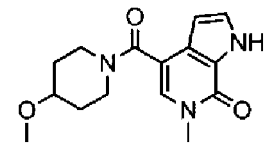
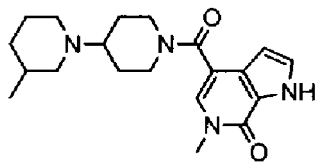
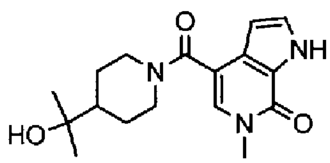
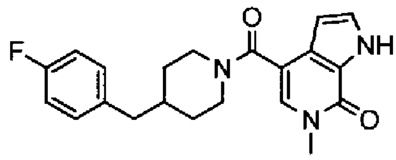
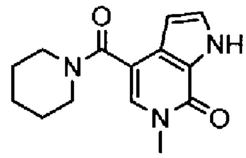
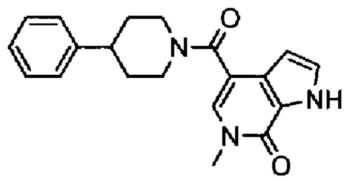
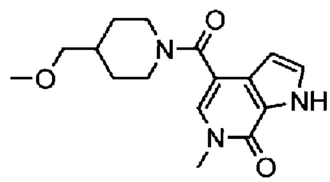
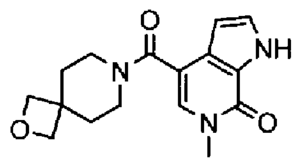


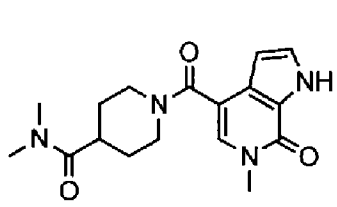
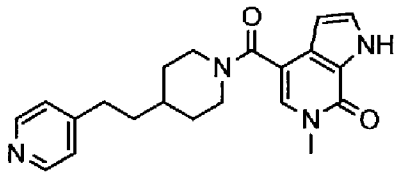
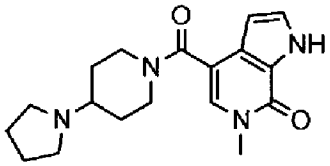
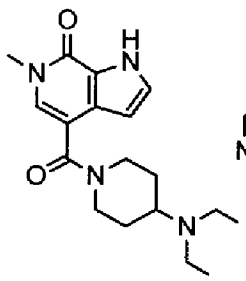
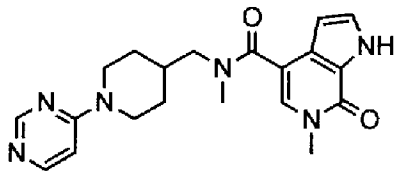
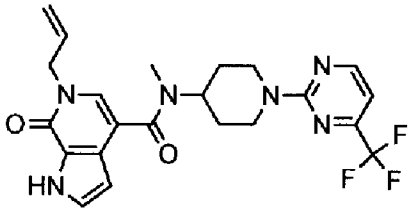
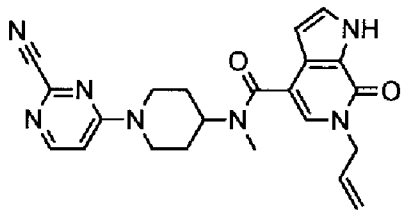
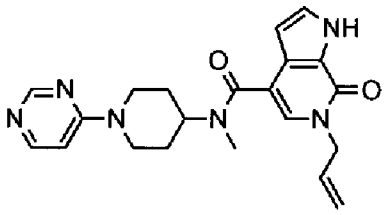
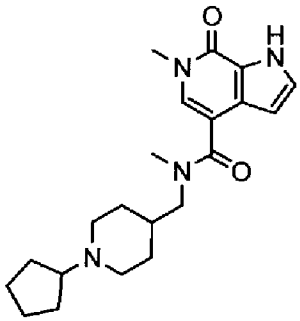
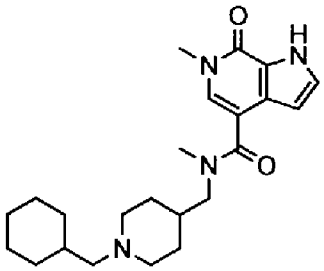
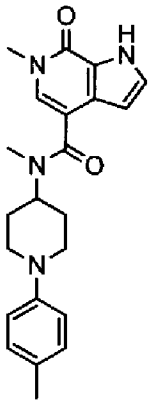
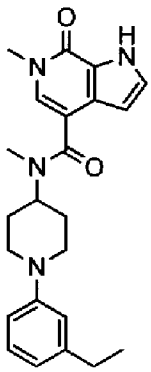
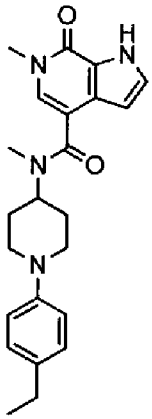
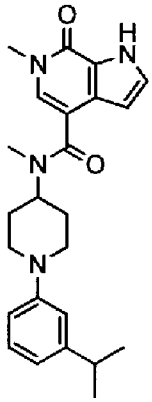
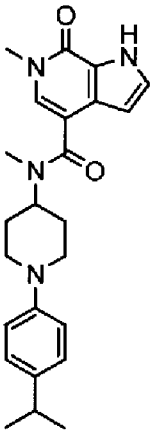
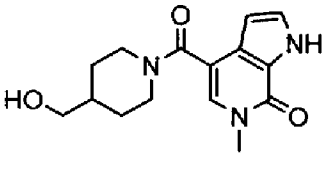
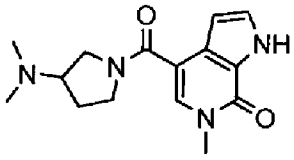
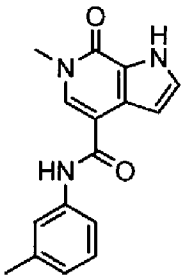





















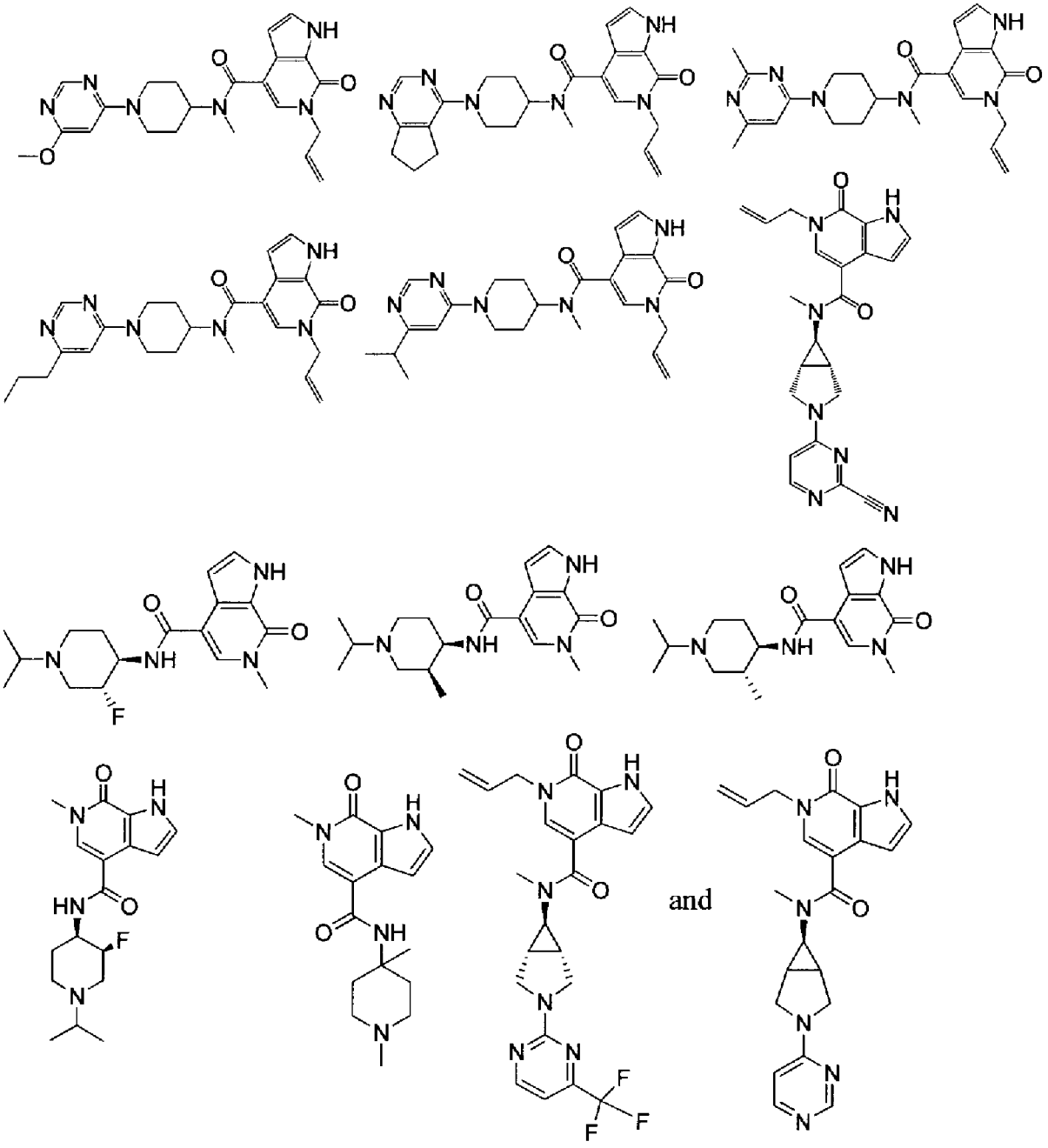




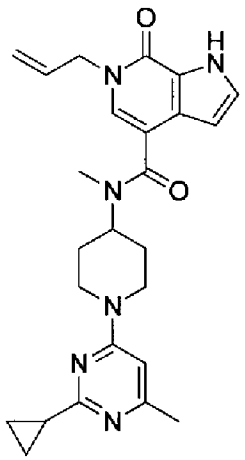
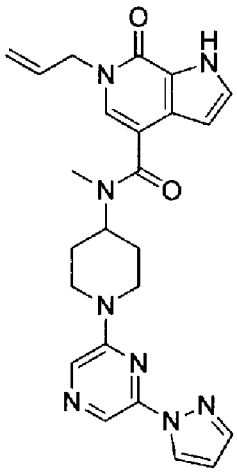
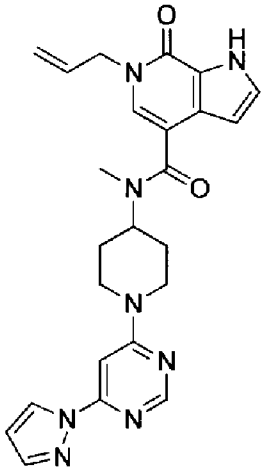
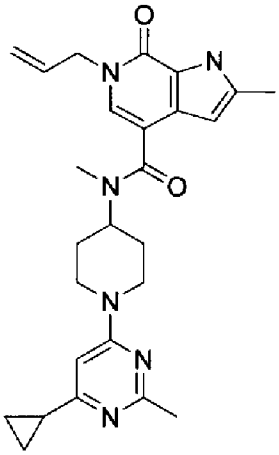
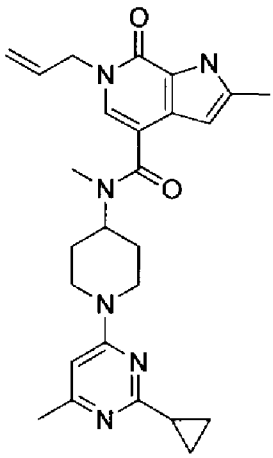
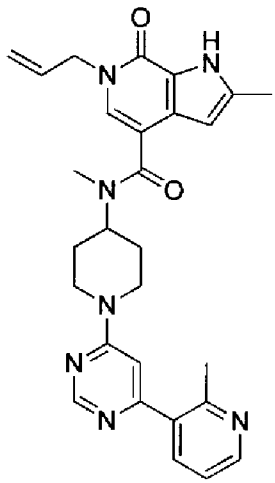
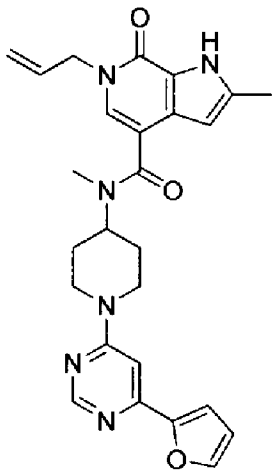
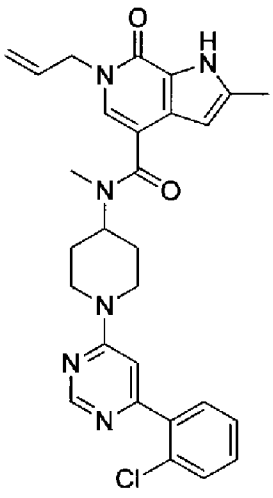
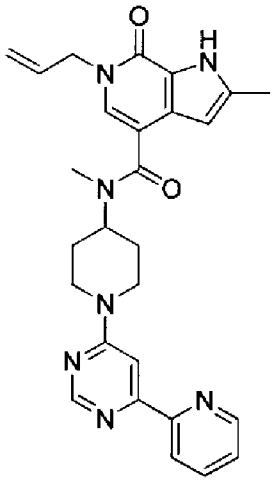



















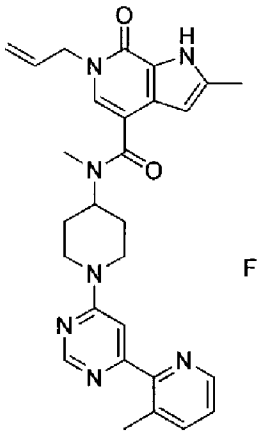


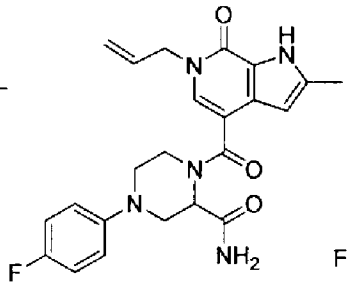
and

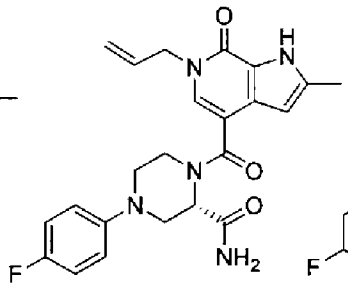
and salts thereof.

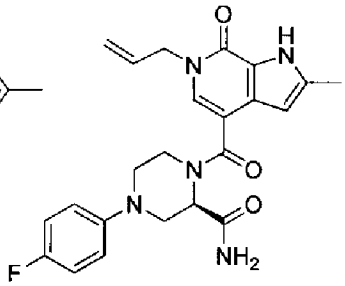
In certain embodiments the compound is selected from:

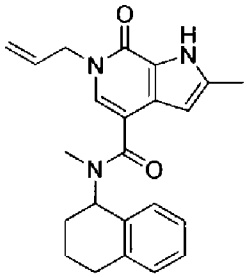










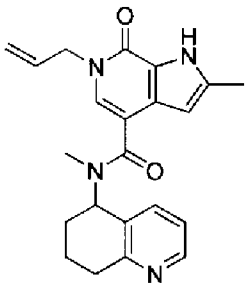


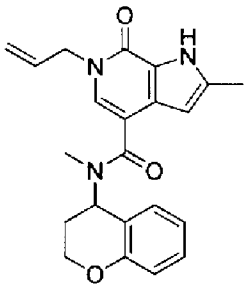


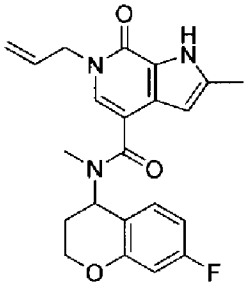


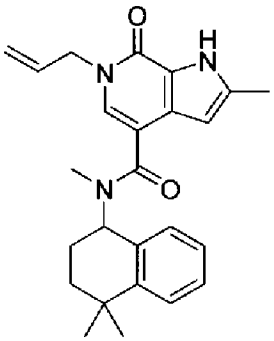


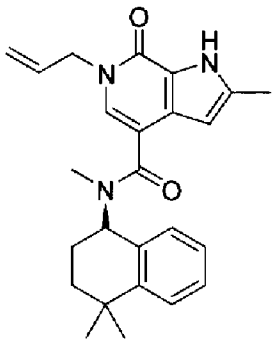


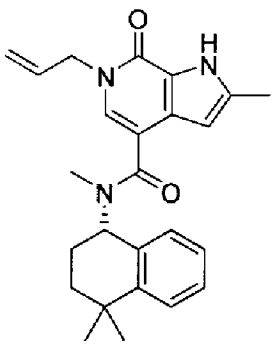


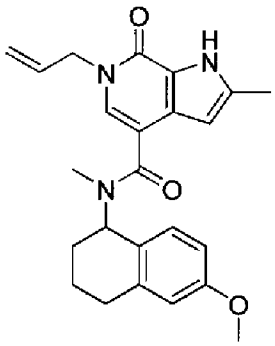


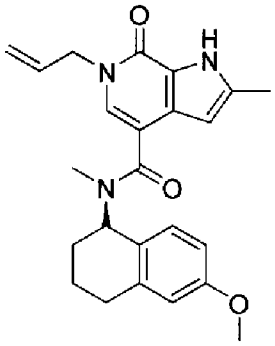


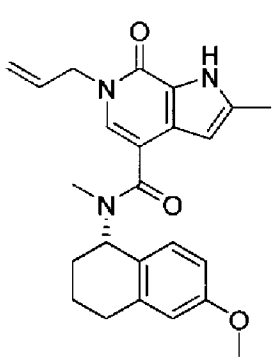


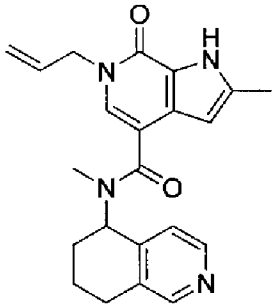
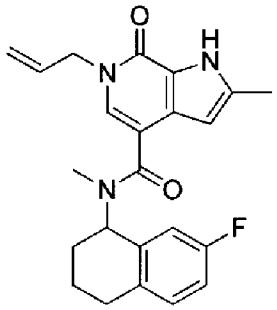
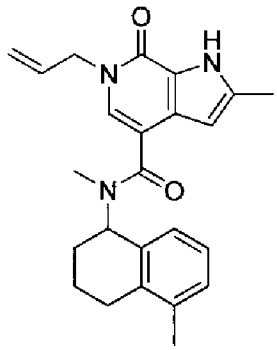
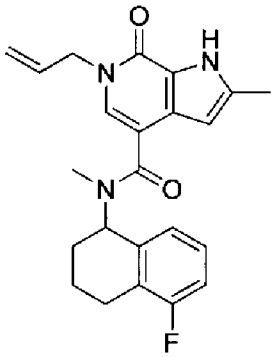
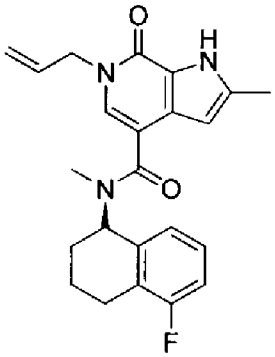
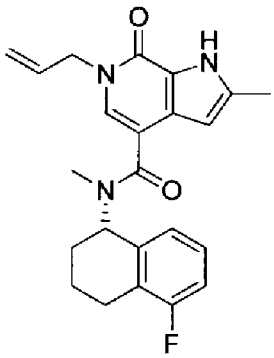
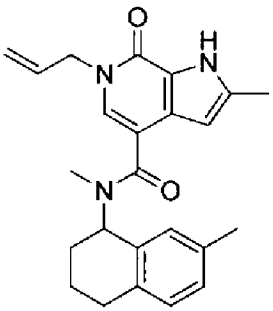
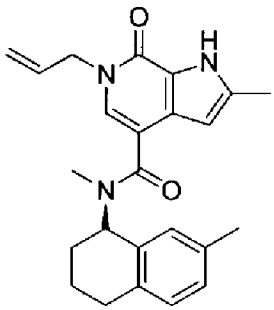
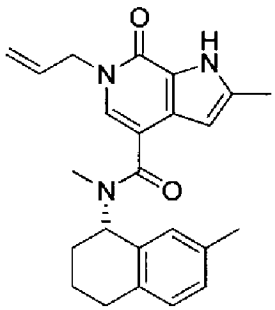
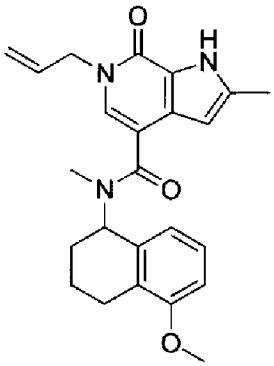
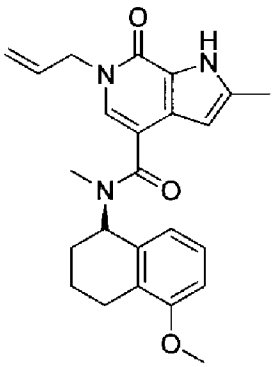
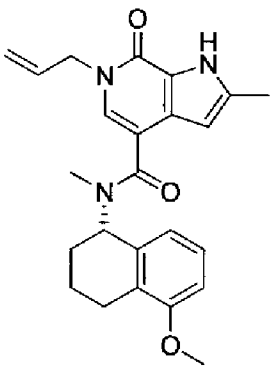
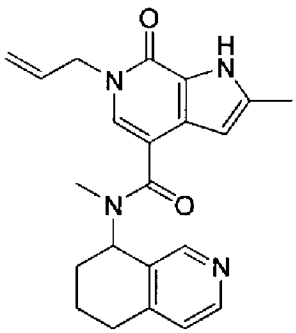
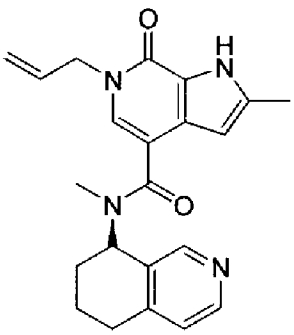
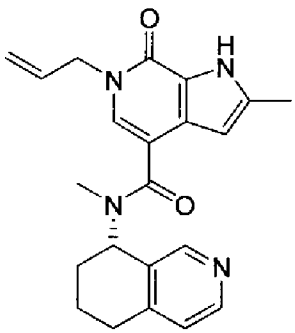


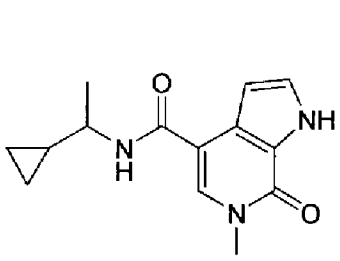




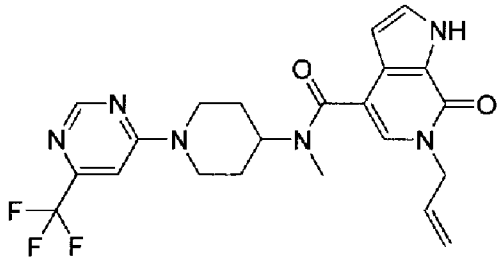






and



and salts thereof.

In certain embodiments the invention provides compound **1000** as described in Examples 292 and 294, and salts thereof. The invention also provides a method for evaluating a compound's ability to inhibit TAF1-BD2 by monitoring the engagement of compound **1000** with a TAF1-BD2 target as described in Example 265.

In certain embodiments the invention provides compound **1001** as described in Examples 293 and 294, and salts thereof. The invention also provides a method for evaluating a compound's ability to inhibit CECR2 by monitoring the engagement of compound **1001** with a CECR2 target as described in Example 265

Uses, Formulation and Administration

Pharmaceutically acceptable compositions

Another aspect includes a pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof. In one embodiment, the composition further comprises a pharmaceutically acceptable carrier, adjuvant, or vehicle. In another embodiment, the composition further comprises an amount of the compound effective to measurably inhibit a bromodomain. In certain embodiments, the composition is formulated for administration to a patient in need thereof.

The term "patient" or "individual" as used herein, refers to an animal, such as a mammal, such as a human. In one embodiment, patient or individual refers to a human.

The term "pharmaceutically acceptable carrier, adjuvant, or vehicle" refers to a non-toxic carrier, adjuvant, or vehicle that does not destroy the pharmacological activity of the compound with which it is formulated. Pharmaceutically acceptable carriers, adjuvants or vehicles that may be used in the compositions of this invention include, but are not limited to, ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances such as phosphates, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, water, salts or electrolytes, such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, zinc salts, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances,

polyethylene glycol, sodium carboxymethylcellulose, polyacrylates, waxes, polyethylene-polyoxypropylene-block polymers, polyethylene glycol and wool fat.

Compositions comprising a compound of formula I or salt thereof may be administered orally, parenterally, by inhalation spray, topically, transdermally, rectally, nasally, buccally, sublingually, vaginally, intraperitoneal, intrapulmonary, intradermal, epidural or via an implanted reservoir. The term "parenteral" as used herein includes subcutaneous, intravenous, intramuscular, intra-articular, intra-synovial, intrasternal, intrathecal, intrahepatic, intralesional and intracranial injection or infusion techniques.

In one embodiment, the composition comprising a compound of formula I or salt thereof is formulated as a solid dosage form for oral administration. Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. In certain embodiments, the solid oral dosage form comprising a compound of formula (I) or a salt thereof further comprises one or more of (i) an inert, pharmaceutically acceptable excipient or carrier, such as sodium citrate or dicalcium phosphate, and (ii) filler or extender such as starches, lactose, sucrose, glucose, mannitol, or silicic acid, (iii) binders such as carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidinone, sucrose or acacia, (iv) humectants such as glycerol, (v) disintegrating agent such as agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates or sodium carbonate, (vi) solution retarding agents such as paraffin, (vii) absorption accelerators such as quaternary ammonium salts, (viii) a wetting agent such as cetyl alcohol or glycerol monostearate, (ix) absorbent such as kaolin or bentonite clay, and (x) lubricant such as talc, calcium stearate, magnesium stearate, polyethylene glycols or sodium lauryl sulfate. In certain embodiments, the solid oral dosage form is formulated as capsules, tablets or pills. In certain embodiments, the solid oral dosage form further comprises buffering agents. In certain embodiments, such compositions for solid oral dosage forms may be formulated as fillers in soft and hard-filled gelatin capsules comprising one or more excipients such as lactose or milk sugar, polyethylene glycols and the like.

In certain embodiments, tablets, dragees, capsules, pills and granules of the compositions comprising a compound of formula I or salt thereof optionally comprise coatings or shells such as enteric coatings. They may optionally comprise opacifying agents and can also be of a composition that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally, in a delayed manner. Examples of embedding compositions include polymeric substances and waxes, which may also be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugar as well as high molecular weight polethylene glycols and the like.

In another embodiment, a composition comprises micro-encapsulated compound of formula (I) or salt thereof, and optionally, further comprises one or more excipients.

In another embodiment, compositions comprise liquid dosage formulations comprising a compound of formula I or salt thereof for oral administration, and optionally further comprise one or more of pharmaceutically acceptable emulsions, microemulsions, solutions, suspensions, syrups and elixirs. In certain embodiments, the liquid dosage form optionally, further comprise one or more of an inert diluent such as water or other solvent, a solubilizing agent, and an emulsifier such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethylformamide, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor, and sesame oils), glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols or fatty acid esters of sorbitan, and mixtures thereof. In certain embodiments, liquid oral compositions optionally further comprise one or more adjuvant, such as a wetting agent, a suspending agent, a sweetening agent, a flavoring agent and a perfuming agent.

Injectable preparations, for example, sterile injectable aqueous or oleaginous suspensions may be formulated according to the known art using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation may also be a sterile injectable solution, suspension or emulsion in a nontoxic parenterally acceptable diluent or solvent, for example, as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, U.S.P. and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil can be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid are used in the preparation of injectables.

Injectable formulations can be sterilized, for example, by filtration through a bacterial-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions which can be dissolved or dispersed in sterile water or other sterile injectable medium prior to use.

In order to prolong the effect of a compound of formula (I), it is often desirable to slow the absorption of the compound from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material with poor water solubility. The rate of absorption of the compound then depends upon its rate of dissolution that, in turn, may depend upon crystal size and crystalline form. Alternatively, delayed absorption of a parenterally administered compound form is accomplished by dissolving or suspending the compound in an oil vehicle. Injectable depot forms are made by forming microencapsule matrices of the compound in biodegradable polymers such as polylactide-

polyglycolide. Depending upon the ratio of compound to polymer and the nature of the particular polymer employed, the rate of compound release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the compound in liposomes or microemulsions that are compatible with body tissues.

In certain embodiments, the composition for rectal or vaginal administration are formulated as suppositories which can be prepared by mixing a compound of formula (I) or a salt thereof with suitable non-irritating excipients or carriers such as cocoa butter, polyethylene glycol or a suppository wax, for example those which are solid at ambient temperature but liquid at body temperature and therefore melt in the rectum or vaginal cavity and release the compound of formula (I).

Example dosage forms for topical or transdermal administration of a compound of formula (I) include ointments, pastes, creams, lotions, gels, powders, solutions, sprays, inhalants or patches. The compound of formula (I) or a salt thereof is admixed under sterile conditions with a pharmaceutically acceptable carrier, and optionally preservatives or buffers. Additional formulation examples include an ophthalmic formulation, ear drops, eye drops,. transdermal patches. Transdermal dosage forms can be made by dissolving or dispensing the compound of formula (I) or a salt thereof in medium, for example ethanol or dimethylsulfoxide. Absorption enhancers can also be used to increase the flux of the compound across the skin. The rate can be controlled by either providing a rate controlling membrane or by dispersing the compound in a polymer matrix or gel.

Nasal aerosol or inhalation formulations of a compound of formula (I) or a salt thereof may be prepared as solutions in saline, employing benzyl alcohol or other suitable preservatives, absorption promoters to enhance bioavailability, fluorocarbons, and/or other conventional solubilizing or dispersing agents.

In certain embodiments, pharmaceutical compositions may be administered with or without food. In certain embodiments, pharmaceutically acceptable compositions are administered without food. In certain embodiments, pharmaceutically acceptable compositions of this invention are administered with food.

Specific dosage and treatment regimen for any particular patient will depend upon a variety of factors, including age, body weight, general health, sex, diet, time of administration, rate of excretion, drug combination, the judgment of the treating physician, and the severity of the particular disease being treated. The amount of a provided compound of formula I or salt thereof in the composition will also depend upon the particular compound in the composition.

In one embodiment, the therapeutically effective amount of the compound of the invention administered parenterally per dose will be in the range of about 0.01-100 mg/kg, alternatively about 0.1 to 20 mg/kg of patient body weight per day, with the typical initial range of compound used being 0.3 to 15 mg/kg/day. In another embodiment, oral unit dosage forms, such as tablets and capsules, contain from about 5 to about 100 mg of the compound of the invention.

An example tablet oral dosage form comprises about 2 mg, 5 mg, 25mg, 50mg, 100mg, 250mg or 500mg of a compound of formula (I) or salt thereof, and further comprises about 5-30 mg anhydrous lactose, about 5-40 mg sodium croscarmellose, about 5-30mg polyvinylpyrrolidone (PVP) K30 and about 1-10 mg magnesium stearate. The process of formulating the tablet comprises mixing the powdered ingredients together and further mixing with a solution of the PVP. The resulting composition can be dried, granulated, mixed with the magnesium stearate and compressed to tablet form using conventional equipment. An example of an aerosol formulation can be prepared by dissolving about 2-500 mg of a compound of formula I or salt thereof, in a suitable buffer solution, e.g. a phosphate buffer, and adding a tonicifier, e.g. a salt such sodium chloride, if desired. The solution may be filtered, e.g. using a 0.2 micron filter, to remove impurities and contaminants.

Uses of Compounds and Pharmaceutically Acceptable Compositions

Another aspect includes the use of a compound of formula (I) or a salt thereof for the inhibition of a bromodomain (*in vitro* or *in vivo*).

Another embodiment includes a method for treating a bromodomain-mediated disorder in an animal comprising administering a compound of formula (I), or a pharmaceutically acceptable salt thereof to the animal. Bromodomain-mediated disorders include, but are not limited to those disorders described herein.

Another embodiment includes a method of increasing efficacy of a cancer treatment comprising a cytotoxic agent in an animal comprising administering to the animal an effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof.

Another embodiment includes a method of delaying or preventing development of cancer resistance to a cytotoxic agent in an animal, comprising administering to the animal a compound of formula (I) or a pharmaceutically acceptable salt thereof.

Another embodiment includes a method of extending the duration of response to a cancer therapy in an animal, comprising administering to an animal undergoing the cancer therapy a compound of formula (I) or a pharmaceutically acceptable salt thereof, wherein the duration of response to the cancer therapy when the compound of formula (I) or the pharmaceutically

acceptable salt thereof is administered is extended over the duration of response to the cancer therapy in the absence of the administration of the compound of formula (I) or the pharmaceutically acceptable salt thereof.

Another embodiment includes a method of treating cancer in an individual comprising administering to the individual (a) a compound of formula (I) or a pharmaceutically acceptable salt thereof, and (b) a cytotoxic agent. In one embodiment the cytotoxic agent is selected from anti-microtubule agents, platinum coordination complexes, alkylating agents, antibiotic agents, topoisomerase II inhibitors, antimetabolites, topoisomerase I inhibitors, hormones and hormonal analogues, signal transduction pathway inhibitors, non-receptor tyrosine kinase angiogenesis inhibitors, immunotherapeutic agents, proapoptotic agents, inhibitors of LDH-A, inhibitors of fatty acid biosynthesis, cell cycle signaling inhibitors, HDAC inhibitors, proteasome inhibitors, and inhibitors of cancer metabolism. In one embodiment the cytotoxic agent is a taxane. In one embodiment the taxane is paclitaxel or docetaxel. In one embodiment the cytotoxic agent is a platinum agent. In one embodiment the cytotoxic agent is an antagonist of EGFR. In one embodiment the antagonist of EGFR is N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine or a pharmaceutically acceptable salt thereof (*e.g.*, erlotinib). In one embodiment the cytotoxic agent is a RAF inhibitor. In one embodiment the RAF inhibitor is a BRAF or CRAF inhibitor. In one embodiment the RAF inhibitor is vemurafenib. In one embodiment the cytotoxic agent is a PI3K inhibitor.

In certain embodiments, treatment may be administered after one or more symptoms have developed. In other embodiments, treatment may be administered in the absence of symptoms. For example, treatment may be administered to a susceptible individual prior to the onset of symptoms (e.g., in light of a history of symptoms and/or in light of genetic or other susceptibility factors). Treatment may also be continued after symptoms have resolved, for example to prevent or delay their recurrence.

Bromodomain-mediated Disorders

A "bromodomain-mediated disorder" is characterized by the participation of one or more bromodomains (e.g., BRD4) in the inception, manifestation of one or more symptoms or disease markers, severity, or progression of a disorder. Bromodomains include, but are not limited to ASH1L, ATAD2, ATAD2B, BAZ1A, BAZ1B, BAZ2A, BAZ2B, BPTF, BRD1, BRD2, BRD3, BRD4, BRD7, BRD8, BRD9, BRDT, BRPF1, BRPF3, BRWD1, BRWD3, CECR2, CREBBP (aka, CBP), EP300, GCN5L2, KIAA2026, MLL, MLL4, PBRM, PCAF, PHIP, SMARCA2, SMARCA4, SP100, SP110, SP140, SP140L, TAF1, TAF1L, TRIM24, TRIM28, TRIM33, TRIM66, ZMYND8, and ZMYND11.

Bromodomain-mediated disorders include cancers, including, but not limited to acoustic neuroma, acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemia (monocytic, myeloblastic, adenocarcinoma, angiosarcoma, astrocytoma, myelomonocytic and promyelocytic), acute T-cell leukemia, basal cell carcinoma, bile duct carcinoma, bladder cancer, brain cancer, breast cancer, bronchogenic carcinoma, cervical cancer, chondrosarcoma, chordoma, choriocarcinoma, chronic leukemia, chronic lymphocytic leukemia, chronic myelocytic (granulocytic) leukemia, chronic myelogenous leukemia, colon cancer, colorectal cancer, craniopharyngioma, cystadenocarcinoma, diffuse large B-cell lymphoma, dysproliferative changes (dysplasias and metaplasias), embryonal carcinoma, endometrial cancer, endotheliosarcoma, ependymoma, epithelial carcinoma, erythroleukemia, esophageal cancer, estrogen-receptor positive breast cancer, essential thrombocythemia, Ewing's tumor, fibrosarcoma, follicular lymphoma, germ cell testicular cancer, glioma, glioblastoma, gliosarcoma, heavy chain disease, hemangioblastoma, hepatoma, hepatocellular cancer, hormone insensitive prostate cancer, leiomyosarcoma, leukemia, liposarcoma, lung cancer, lymphagioendotheliosarcoma, lymphangiosarcoma, lymphoblastic leukemia, lymphoma (Hodgkin's and non-Hodgkin's), malignancies and hyperproliferative disorders of the bladder, breast, colon, lung, ovaries, pancreas, prostate, skin and uterus, lymphoid malignancies of T-cell or B-cell origin, medullary carcinoma, medulloblastoma, melanoma, meningioma, mesothelioma, multiple myeloma, myelogenous leukemia, myeloma, myxosarcoma, neuroblastoma, NUT midline carcinoma (NMC), non-small cell lung cancer, oligodendroglioma, oral cancer, osteogenic sarcoma, ovarian cancer, pancreatic cancer, papillary adenocarcinomas, papillary carcinoma, pinealoma, polycythemia vera, prostate cancer, rectal cancer, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, sebaceous gland carcinoma, seminoma, skin cancer, small cell lung carcinoma, solid tumors (carcinomas and sarcomas), small cell lung cancer, stomach cancer, squamous cell carcinoma, synovioma, sweat gland carcinoma, thyroid cancer, Waldenstr6m's macroglobulinemia, testicular tumors, uterine cancer and Wilms' tumor.

In certain embodiments, the cancer is lung cancer, breast cancer, pancreatic cancer, colorectal cancer, and/or melanoma. In certain embodiments, the cancer is lung. In certain embodiments, the lung cancer is NSCLC. In certain embodiments, the cancer is breast cancer. In certain embodiments, the cancer is melanoma.

Bromodomain-mediated disorders also include inflammatory diseases, inflammatory conditions, and autoimmune diseases, including, but not limited to: Addison's disease, acute gout, ankylosing spondylitis, asthma, atherosclerosis, Behcet's disease, bullous skin diseases, chronic obstructive pulmonary disease (COPD), Crohn's disease,dermatitis,

eczema,giant cell arteritis, glomerulonephritis, hepatitis, hypophysitis, inflammatory bowel disease, Kawasaki disease, lupus nephritis, multiple sclerosis, myocarditis,myositis, nephritis, organ transplant rejection, osteoarthritis, pancreatitis, pericarditis, Polyarteritis nodosa, pneumonitis, primary biliary cirrhosis, psoriasis, psoriatic arthritis, rheumatoid arthritis, scleritis, sclerosing cholangitis, sepsis, systemic lupus erythematosus, Takayasu's Arteritis, toxic shock, thyroiditis, type I diabetes, ulcerative colitis, uveitis, vitiligo, vasculitis, and Wegener's granulomatosis.

Bromodomain-mediated disorders also include AIDS; chronic kidney diseases, including, but are not limited to diabetic nephropathy, hypertensive nephropathy, HIV-associated nephropathy, glomerulonephritis, lupus nephritis, IgA nephropathy, focal segmental glomerulosclerosis, membranous glomerulonephritis, minimal change disease, polycystic kidney disease and tubular interstitial nephritis; acute kidney injury or disease or condition including, but are not limited to ischemia- reperfusion induced, cardiac and major surgery induced, percutaneous coronary intervention induced, radio-contrast agent induced, sepsis induced, pneumonia induced, and drug toxicity induced; obesity; dyslipidemia; hypercholesterolemia; Alzheimer's disease; metabolic syndrome; hepatic steatosis; type II diabetes; insulin resistance; and diabetic retinopathy.

Bromodomain inhibitors may also be used to provide male contraception.

Co-Administration of Compounds and Other Agents

The compounds of formula (I) or salts thereof may be employed alone or in combination with other agents for treatment. For example, the second agent of the pharmaceutical combination formulation or dosing regimen may have complementary activities to the compound of formula (I) such that they do not adversely affect each other. The compounds may be administered together in a unitary pharmaceutical composition or separately. In one embodiment a compound or a pharmaceutically acceptable salt can be co-administered with a cytotoxic agent to treat proliferative diseases and cancer.

The term "co-administering" refers to either simultaneous administration, or any manner of separate sequential administration, of a compound of formula (I) or a salt thereof, and a further active pharmaceutical ingredient or ingredients, including cytotoxic agents and radiation treatment. If the administration is not simultaneous, the compounds are administered in a close time proximity to each other. Furthermore, it does not matter if the compounds are administered in the same dosage form, e.g. one compound may be administered topically and another compound may be administered orally.

Typically, any agent that has activity against a disease or condition being treated may be co-administered. Examples of such agents can be found in Cancer Principles and Practice of Oncology by V.T. Devita and S. Hellman (editors), 6th edition (February 15, 2001), Lippincott Williams & Wilkins Publishers. A person of ordinary skill in the art would be able to discern which combinations of agents would be useful based on the particular characteristics of the drugs and the disease involved.

In one embodiment, the treatment method includes the co-administration of a compound of formula (I) or a pharmaceutically acceptable salt thereof and at least one cytotoxic agent. The term "cytotoxic agent" as used herein refers to a substance that inhibits or prevents a cellular function and/or causes cell death or destruction. Cytotoxic agents include, but are not limited to, radioactive isotopes (e.g., At^{211}, I^{131}, I^{125}, Y^{90}, Re^{186}, Re^{188}, Sm^{153}, Bi^{212}, P^{32}, Pb^{212} and radioactive isotopes of Lu); chemotherapeutic agents; growth inhibitory agents; enzymes and fragments thereof such as nucleolytic enzymes; and toxins such as small molecule toxins or enzymatically active toxins of bacterial, fungal, plant or animal origin, including fragments and/or variants thereof.

Exemplary cytotoxic agents can be selected from anti-microtubule agents, platinum coordination complexes, alkylating agents, antibiotic agents, topoisomerase II inhibitors, antimetabolites, topoisomerase I inhibitors, hormones and hormonal analogues, signal transduction pathway inhibitors, non-receptor tyrosine kinase angiogenesis inhibitors, immunotherapeutic agents, proapoptotic agents, inhibitors of LDH-A; inhibitors of fatty acid biosynthesis; cell cycle signaling inhibitors; HDAC inhibitors, proteasome inhibitors; and inhibitors of cancer metabolism.

"Chemotherapeutic agent" includes chemical compounds useful in the treatment of cancer. Examples of chemotherapeutic agents include erlotinib (TARCEVA®, Genentech/OSI Pharm.), bortezomib (VELCADE®, Millennium Pharm.), disulfiram , epigallocatechin gallate , salinosporamide A, carfilzomib, 17-AAG(geldanamycin), radicicol, lactate dehydrogenase A (LDH-A), fulvestrant (FASLODEX®, AstraZeneca), sunitib (SUTENT®, Pfizer/Sugen), letrozole (FEMARA®, Novartis), imatinib mesylate (GLEEVEC®., Novartis), finasunate (VATALANIB®, Novartis), oxaliplatin (ELOXATIN®, Sanofi), 5-FU (5-fluorouracil), leucovorin, Rapamycin (Sirolimus, RAPAMUNE®, Wyeth), Lapatinib (TYKERB®, GSK572016, Glaxo Smith Kline), Lonafamib (SCH 66336), sorafenib (NEXAVAR®, Bayer Labs), gefitinib (IRESSA®, AstraZeneca), AG1478, alkylating agents such as thiotepa and CYTOXAN® cyclosphosphamide; alkyl sulfonates such as busulfan, improsulfan and piposulfan; aziridines such as benzodopa, carboquone, meturedopa, and uredopa; ethylenimines and methylamelamines including altretamine, triethylenemelamine, triethylenephosphoramide,

triethylenethiophosphoramide and trimethylomelamine; acetogenins (especially bullatacin and bullatacinone); a camptothecin (including topotecan and irinotecan); bryostatin; callystatin; CC-1065 (including its adozelesin, carzelesin and bizelesin synthetic analogs); cryptophycins (particularly cryptophycin 1 and cryptophycin 8); adrenocorticosteroids (including prednisone and prednisolone); cyproterone acetate; 5α-reductases including finasteride and dutasteride); vorinostat, romidepsin, panobinostat, valproic acid, mocetinostat dolastatin; aldesleukin, talc duocarmycin (including the synthetic analogs, KW-2189 and CB1-TM1); eleutherobin; pancratistatin; a sarcodictyin; spongistatin; nitrogen mustards such as chlorambucil, chlomaphazine, chlorophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosoureas such as carmustine, chlorozotocin, fotemustine, lomustine, nimustine, and ranimnustine; antibiotics such as the enediyne antibiotics (e.g., calicheamicin, especially calicheamicin γ1I and calicheamicin ω1I (*Angew Chem. Intl. Ed. Engl.* **1994** 33:183-186); dynemicin, including dynemicin A; bisphosphonates, such as clodronate; an esperamicin; as well as neocarzinostatin chromophore and related chromoprotein enediyne antibiotic chromophores), aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, carabicin, caminomycin, carzinophilin, chromomycinis, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, ADRIAMYCIN® (doxorubicin), morpholino-doxorubicin, cyanomorpholino-doxorubicin, 2-pyrrolino-doxorubicin and deoxydoxorubicin), epirubicin, esorubicin, idarubicin, marcellomycin, mitomycins such as mitomycin C, mycophenolic acid, nogalamycin, olivomycins, peplomycin, porfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites such as methotrexate and 5-fluorouracil (5-FU); folic acid analogs such as denopterin, methotrexate, pteropterin, trimetrexate; purine analogs such as fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimidine analogs such as ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine; androgens such as calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals such as aminoglutethimide, mitotane, trilostane; folic acid replenisher such as frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; eniluracil; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elfomithine; elliptinium acetate; an epothilone; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidainine; maytansinoids such as maytansine and ansamitocins; mitoguazone; mitoxantrone; mopidamnol; nitraerine; pentostatin; phenamet; pirarubicin; losoxantrone; podophyllinic acid; 2-ethylhydrazide; procarbazine; PSK® polysaccharide complex (JHS Natural Products, Eugene, Oreg.); razoxane; rhizoxin; sizofuran;

spirogermanium; tenuazonic acid; triaziquone; 2,2',2"-trichlorotriethylamine; trichothecenes (especially T-2 toxin, verracurin A, roridin A and anguidine); urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); cyclophosphamide; thiotepa; taxoids, e.g., TAXOL (paclitaxel; Bristol-Myers Squibb Oncology, Princeton, N.J.), ABRAXANE® (Cremophor-free), albumin-engineered nanoparticle formulations of paclitaxel (American Pharmaceutical Partners, Schaumberg, Ill.), and TAXOTERE® (docetaxel, doxetaxel; Sanofi-Aventis); chloranmbucil; GEMZAR® (gemcitabine); 6-thioguanine; mercaptopurine; methotrexate; platinum analogs such as cisplatin and carboplatin; vinblastine; etoposide (VP-16); ifosfamide; mitoxantrone; vincristine; NAVELBINE® (vinorelbine); novantrone; teniposide; edatrexate; daunomycin; aminopterin; capecitabine (XELODA®); ibandronate; CPT-11; topoisomerase inhibitor RFS 2000; difluoromethylornithine (DMFO); retinoids such as retinoic acid; and pharmaceutically acceptable salts, acids and derivatives of any of the above.

Chemotherapeutic agent also includes (i) anti-hormonal agents that act to regulate or inhibit hormone action on tumors such as anti-estrogens and selective estrogen receptor modulators (SERMs), including, for example, tamoxifen (including NOLVADEX®; tamoxifen citrate), raloxifene, droloxifene, iodoxyfene , 4-hydroxytamoxifen, trioxifene, keoxifene, LY117018, onapristone, and FARESTON® (toremifine citrate); (ii) aromatase inhibitors that inhibit the enzyme aromatase, which regulates estrogen production in the adrenal glands, such as, for example, 4(5)-imidazoles, aminoglutethimide, MEGASE® (megestrol acetate), AROMASIN® (exemestane; Pfizer), formestanie, fadrozole, RIVISOR® (vorozole), FEMARA® (letrozole; Novartis), and ARIMIDEX® (anastrozole; AstraZeneca); (iii) anti-androgens such as flutamide, nilutamide, bicalutamide, leuprolide and goserelin; buserelin, tripterelin, medroxyprogesterone acetate, diethylstilbestrol, premarin, fluoxymesterone, all transretionic acid, fenretinide, as well as troxacitabine (a 1,3-dioxolane nucleoside cytosine analog); (iv) protein kinase inhibitors; (v) lipid kinase inhibitors; (vi) antisense oligonucleotides, particularly those which inhibit expression of genes in signaling pathways implicated in aberrant cell proliferation, such as, for example, PKC-alpha, Ralf and H-Ras; (vii) ribozymes such as VEGF expression inhibitors (e.g., ANGIOZYME®) and HER2 expression inhibitors; (viii) vaccines such as gene therapy vaccines, for example, ALLOVECTIN®, LEUVECTIN®, and VAXID®; PROLEUKIN®, rIL-2; a topoisomerase 1 inhibitor such as LURTOTECAN®; ABARELIX® rmRH; and (ix) pharmaceutically acceptable salts, acids and derivatives of any of the above.

Chemotherapeutic agent also includes antibodies such as alemtuzumab (Campath), bevacizumab (AVASTIN®, Genentech); cetuximab (ERBITUX®, Imclone); panitumumab (VECTIBIX®, Amgen), rituximab (RITUXAN®, Genentech/Biogen Idec), pertuzumab

(OMNITARG®, 2C4, Genentech), trastuzumab (HERCEPTIN®, Genentech), tositumomab (Bexxar, Corixia), and the antibody drug conjugate, gemtuzumab ozogamicin (MYLOTARG®, Wyeth). Additional humanized monoclonal antibodies with therapeutic potential as agents in combination with the compounds of the invention include: apolizumab, aselizumab, atlizumab, bapineuzumab, bivatuzumab mertansine, cantuzumab mertansine, cedelizumab, certolizumab pegol, cidfusituzumab, cidtuzumab, daclizumab, eculizumab, efalizumab, epratuzumab, erlizumab, felvizumab, fontolizumab, gemtuzumab ozogamicin, inotuzumab ozogamicin, ipilimumab, labetuzumab, lintuzumab, matuzumab, mepolizumab, motavizumab, motovizumab, natalizumab, nimotuzumab, nolovizumab, numavizumab, ocrelizumab, omalizumab, palivizumab, pascolizumab, pecfusituzumab, pectuzumab, pexelizumab, ralivizumab, ranibizumab, reslivizumab, reslizumab, resyvizumab, rovelizumab, ruplizumab, sibrotuzumab, siplizumab, sontuzumab, tacatuzumab tetraxetan, tadocizumab, talizumab, tefibazumab, tocilizumab, toralizumab, tucotuzumab celmoleukin, tucusituzumab, umavizumab, urtoxazumab, ustekinumab, visilizumab, and the anti–interleukin-12 (ABT-874/J695, Wyeth Research and Abbott Laboratories) which is a recombinant exclusively human-sequence, full-length $IgG_1 \lambda$ antibody genetically modified to recognize interleukin-12 p40 protein.

Chemotherapeutic agent also includes "EGFR inhibitors," which refers to compounds that bind to or otherwise interact directly with EGFR and prevent or reduce its signaling activity, and is alternatively referred to as an "EGFR antagonist." Examples of such agents include antibodies and small molecules that bind to EGFR. Examples of antibodies which bind to EGFR include MAb 579 (ATCC CRL HB 8506), MAb 455 (ATCC CRL HB8507), MAb 225 (ATCC CRL 8508), MAb 528 (ATCC CRL 8509) (see, US Patent No. 4,943, 533, Mendelsohn *et al.*) and variants thereof, such as chimerized 225 (C225 or Cetuximab; ERBUTIX®) and reshaped human 225 (H225) (see, WO 96/40210, Imclone Systems Inc.); IMC-11F8, a fully human, EGFR-targeted antibody (Imclone); antibodies that bind type II mutant EGFR (US Patent No. 5,212,290); humanized and chimeric antibodies that bind EGFR as described in US Patent No. 5,891,996; and human antibodies that bind EGFR, such as ABX-EGF or Panitumumab (see WO98/50433, Abgenix/Amgen); EMD 55900 (Stragliotto *et al. Eur. J. Cancer* 32A:636-640 (1996)); EMD7200 (matuzumab) a humanized EGFR antibody directed against EGFR that competes with both EGF and TGF-alpha for EGFR binding (EMD/Merck); human EGFR antibody, HuMax-EGFR (GenMab); fully human antibodies known as E1.1, E2.4, E2.5, E6.2, E6.4, E2.11, E6. 3 and E7.6. 3 and described in US 6,235,883; MDX-447 (Medarex Inc); and mAb 806 or humanized mAb 806 (Johns *et al., J. Biol. Chem.* 279(29):30375-30384 (2004)). The anti-EGFR antibody may be conjugated with a cytotoxic agent, thus generating an immunoconjugate (see, *e.g.*, EP659,439A2, Merck Patent GmbH). EGFR antagonists include

small molecules such as compounds described in US Patent Nos: 5,616,582, 5,457,105, 5,475,001, 5,654,307, 5,679,683, 6,084,095, 6,265,410, 6,455,534, 6,521,620, 6,596,726, 6,713,484, 5,770,599, 6,140,332, 5,866,572, 6,399,602, 6,344,459, 6,602,863, 6,391,874, 6,344,455, 5,760,041, 6,002,008, and 5,747,498, as well as the following PCT publications: WO98/14451, WO98/50038, WO99/09016, and WO99/24037. Particular small molecule EGFR antagonists include OSI-774 (CP-358774, erlotinib, TARCEVA® Genentech/OSI Pharmaceuticals); PD 183805 (CI 1033, 2-propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(4-morpholinyl)propoxy]-6-quinazolinyl]-, dihydrochloride, Pfizer Inc.); ZD1839, gefitinib (IRESSA®) 4-(3'-Chloro-4'-fluoroanilino)-7-methoxy-6-(3-morpholinopropoxy)quinazoline, AstraZeneca); ZM 105180 ((6-amino-4-(3-methylphenyl-amino)-quinazoline, Zeneca); BIBX-1382 (N8-(3-chloro-4-fluoro-phenyl)-N2-(1-methyl-piperidin-4-yl)-pyrimido[5,4-d]pyrimidine-2,8-diamine, Boehringer Ingelheim); PKI-166 ((R)-4-[4-[(1-phenylethyl)amino]-1H-pyrrolo[2,3-d]pyrimidin-6-yl]-phenol); (R)-6-(4-hydroxyphenyl)-4-[(1-phenylethyl)amino]-7H-pyrrolo[2,3-d]pyrimidine); CL-387785 (N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-2-butynamide); EKB-569 (N-[4-[(3-chloro-4-fluorophenyl)amino]-3-cyano-7-ethoxy-6-quinolinyl]-4-(dimethylamino)-2-butenamide) (Wyeth); AG1478 (Pfizer); AG1571 (SU 5271; Pfizer); dual EGFR/HER2 tyrosine kinase inhibitors such as lapatinib (TYKERB®, GSK572016 or N-[3-chloro-4-[(3 fluorophenyl)methoxy]phenyl]-6[5[[[2methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-4-quinazolinamine).

Chemotherapeutic agents also include "tyrosine kinase inhibitors" including the EGFR-targeted drugs noted in the preceding paragraph; small molecule HER2 tyrosine kinase inhibitor such as TAK165 available from Takeda; CP-724,714, an oral selective inhibitor of the ErbB2 receptor tyrosine kinase (Pfizer and OSI); dual-HER inhibitors such as EKB-569 (available from Wyeth) which preferentially binds EGFR but inhibits both HER2 and EGFR-overexpressing cells; lapatinib (GSK572016; available from Glaxo-SmithKline), an oral HER2 and EGFR tyrosine kinase inhibitor; PKI-166 (available from Novartis); pan-HER inhibitors such as canertinib (CI-1033; Pharmacia); Raf-1 inhibitors such as antisense agent ISIS-5132 available from ISIS Pharmaceuticals which inhibit Raf-1 signaling; non-HER targeted TK inhibitors such as imatinib mesylate (GLEEVEC®, available from Glaxo SmithKline); multi-targeted tyrosine kinase inhibitors such as sunitinib (SUTENT®, available from Pfizer); VEGF receptor tyrosine kinase inhibitors such as vatalanib (PTK787/ZK222584, available from Novartis/Schering AG); MAPK extracellular regulated kinase I inhibitor CI-1040 (available from Pharmacia); quinazolines, such as PD 153035,4-(3-chloroanilino) quinazoline; pyridopyrimidines; pyrimidopyrimidines; pyrrolopyrimidines, such as CGP 59326, CGP 60261 and CGP 62706;

pyrazolopyrimidines, 4-(phenylamino)-7H-pyrrolo[2,3-d] pyrimidines; curcumin (diferuloyl methane, 4,5-bis (4-fluoroanilino)phthalimide); tyrphostines containing nitrothiophene moieties; PD-0183805 (Warner-Lamber); antisense molecules *(e.g.* those that bind to HER-encoding nucleic acid); quinoxalines (US Patent No. 5,804,396); tryphostins (US Patent No. 5,804,396); ZD6474 (Astra Zeneca); PTK-787 (Novartis/Schering AG); pan-HER inhibitors such as CI-1033 (Pfizer); Affinitac (ISIS 3521; Isis/Lilly); imatinib mesylate (GLEEVEC®); PKI 166 (Novartis); GW2016 (Glaxo SmithKline); CI-1033 (Pfizer); EKB-569 (Wyeth); Semaxinib (Pfizer); ZD6474 (AstraZeneca); PTK-787 (Novartis/Schering AG); INC-1C11 (Imclone), rapamycin (sirolimus, RAPAMUNE®); or as described in any of the following patent publications: US Patent No. 5,804,396; WO 1999/09016 (American Cyanamid); WO 1998/43960 (American Cyanamid); WO 1997/38983 (Warner Lambert); WO 1999/06378 (Warner Lambert); WO 1999/06396 (Warner Lambert); WO 1996/30347 (Pfizer, Inc); WO 1996/33978 (Zeneca); WO 1996/3397 (Zeneca) and WO 1996/33980 (Zeneca).

Chemotherapeutic agents also include dexamethasone, interferons, colchicine, metoprine, cyclosporine, amphotericin, metronidazole, alemtuzumab, alitretinoin, allopurinol, amifostine, arsenic trioxide, asparaginase, BCG live, bevacuzimab, bexarotene, cladribine, clofarabine, darbepoetin alfa, denileukin, dexrazoxane, epoetin alfa, elotinib, filgrastim, histrelin acetate, ibritumomab, interferon alfa-2a, interferon alfa-2b, lenalidomide, levamisole, mesna, methoxsalen, nandrolone, nelarabine, nofetumomab, oprelvekin, palifermin, pamidronate, pegademase, pegaspargase, pegfilgrastim, pemetrexed disodium, plicamycin, porfimer sodium, quinacrine, rasburicase, sargramostim, temozolomide, VM-26, 6-TG, toremifene, tretinoin, ATRA, valrubicin, zoledronate, and zoledronic acid, and pharmaceutically acceptable salts thereof.

Chemotherapeutic agents also include hydrocortisone, hydrocortisone acetate, cortisone acetate, tixocortol pivalate, triamcinolone acetonide, triamcinolone alcohol, mometasone, amcinonide, budesonide, desonide, fluocinonide, fluocinolone acetonide, betamethasone, betamethasone sodium phosphate, dexamethasone, dexamethasone sodium phosphate, fluocortolone, hydrocortisone-17-butyrate, hydrocortisone-17-valerate, aclometasone dipropionate, betamethasone valerate, betamethasone dipropionate, prednicarbate, clobetasone-17-butyrate, clobetasol-17-propionate, fluocortolone caproate, fluocortolone pivalate and fluprednidene acetate; immune selective anti-inflammatory peptides (ImSAIDs) such as phenylalanine-glutamine-glycine (FEG) and its D-isomeric form (feG) (IMULAN BioTherapeutics, LLC); anti-rheumatic drugs such as azathioprine, ciclosporin (cyclosporine A), D-penicillamine, gold salts, hydroxychloroquine, leflunomideminocycline, sulfasalazine, tumor necrosis factor alpha (TNFα) blockers such as etanercept (Enbrel), infliximab (Remicade),

adalimumab (Humira), certolizumab pegol (Cimzia), golimumab (Simponi), Interleukin 1 (IL-1) blockers such as anakinra (Kineret), T cell costimulation blockers such as abatacept (Orencia), Interleukin 6 (IL-6) blockers such as tocilizumab (ACTEMERA®); Interleukin 13 (IL-13) blockers such as lebrikizumab; Interferon alpha (IFN) blockers such as Rontalizumab; Beta 7 integrin blockers such as rhuMAb Beta7; IgE pathway blockers such as Anti-M1 prime; Secreted homotrimeric LTa3 and membrane bound heterotrimer LTa1/β2 blockers such as Anti-lymphotoxin alpha (LTa); radioactive isotopes (e.g., At^{211}, I^{131}, I^{125}, Y^{90}, Re^{186}, Re^{188}, Sm^{153}, Bi^{212}, P^{32}, Pb^{212} and radioactive isotopes of Lu); miscellaneous investigational agents such as thioplatin, PS-341, phenylbutyrate, ET-18- OCH_3, or farnesyl transferase inhibitors (L-739749, L-744832); polyphenols such as quercetin, resveratrol, piceatannol, epigallocatechine gallate, theaflavins, flavanols, procyanidins, betulinic acid and derivatives thereof; autophagy inhibitors such as chloroquine; delta-9-tetrahydrocannabinol (dronabinol, MARINOL®); beta-lapachone; lapachol; colchicines; betulinic acid; acetylcamptothecin, scopolectin, and 9-aminocamptothecin); podophyllotoxin; tegafur (UFTORAL®); bexarotene (TARGRETIN®); bisphosphonates such as clodronate (for example, BONEFOS® or OSTAC®), etidronate (DIDROCAL®), NE-58095, zoledronic acid/zoledronate (ZOMETA®), alendronate (FOSAMAX®), pamidronate (AREDIA®), tiludronate (SKELID®), or risedronate (ACTONEL®); and epidermal growth factor receptor (EGF-R); vaccines such as THERATOPE® vaccine; perifosine, COX-2 inhibitor (*e.g.* celecoxib or etoricoxib), proteosome inhibitor (*e.g.* PS341); CCI-779; tipifarnib (R11577); orafenib, ABT510; Bcl-2 inhibitor such as oblimersen sodium (GENASENSE®); pixantrone; farnesyltransferase inhibitors such as lonafarnib (SCH 6636, SARASAR™); and pharmaceutically acceptable salts, acids or derivatives of any of the above; as well as combinations of two or more of the above such as CHOP, an abbreviation for a combined therapy of cyclophosphamide, doxorubicin, vincristine, and prednisolone; and FOLFOX, an abbreviation for a treatment regimen with oxaliplatin (ELOXATIN™) combined with 5-FU and leucovorin.

Chemotherapeutic agents also include non-steroidal anti-inflammatory drugswith analgesic, antipyretic and anti-inflammatory effects. NSAIDs include non-selective inhibitors of the enzyme cyclooxygenase. Specific examples of NSAIDs include aspirin, propionic acid derivatives such as ibuprofen, fenoprofen, ketoprofen, flurbiprofen, oxaprozin and naproxen, acetic acid derivatives such as indomethacin, sulindac, etodolac, diclofenac, enolic acid derivatives such as piroxicam, meloxicam, tenoxicam, droxicam, lornoxicam and isoxicam, fenamic acid derivatives such as mefenamic acid, meclofenamic acid, flufenamic acid, tolfenamic acid, and COX-2 inhibitors such as celecoxib, etoricoxib, lumiracoxib, parecoxib, rofecoxib, rofecoxib, and valdecoxib. NSAIDs can be indicated for the symptomatic relief of

conditions such as rheumatoid arthritis, osteoarthritis, inflammatory arthropathies, ankylosing spondylitis, psoriatic arthritis, Reiter's syndrome, acute gout, dysmenorrhoea, metastatic bone pain, headache and migraine, postoperative pain, mild-to-moderate pain due to inflammation and tissue injury, pyrexia, ileus, and renal colic.

Chemotherapeutic agents also include treatments for Alzheimer's Disease such as donepezil hydrochloride and rivastigmine; treatments for Parkinson's Disease such as L-DOPA/carbidopa, entacapone, ropinrole, pramipexole, bromocriptine, pergolide, trihexephendyl, and amantadine; agents for treating multiple sclerosis (MS) such as beta interferon (e.g., Avonex® and Rebif®), glatiramer acetate, and mitoxantrone; treatments for asthma such as albuterol and montelukast sodium; agents for treating schizophrenia such as zyprexa, risperdal, seroquel, and haloperidol; anti-inflammatory agents such as corticosteroids, TNF blockers, IL-1 RA, azathioprine, cyclophosphamide, and sulfasalazine; immunomodulatory and immunosuppressive agents such as cyclosporin, tacrolimus, rapamycin, mycophenolate mofetil, interferons, corticosteroids, cyclophophamide, azathioprine, and sulfasalazine; neurotrophic factors such as acetylcholinesterase inhibitors, MAO inhibitors, interferons, anti-convulsants, ion channel blockers, riluzole, and anti-Parkinsonian agents; agents for treating cardiovascular disease such as beta-blockers, ACE inhibitors, diuretics, nitrates, calcium channel blockers, and statins; agents for treating liver disease such as corticosteroids, cholestyramine, interferons, and anti-viral agents; agents for treating blood disorders such as corticosteroids, anti-leukemic agents, and growth factors; and agents for treating immunodeficiency disorders such as gamma globulin.

Additionally, chemotherapeutic agents include pharmaceutically acceptable salts, acids or derivatives of any of chemotherapeutic agents, described herein, as well as combinations of two or more of them.

For treating an inflammatory disease or an autoimmune disease, a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with methotrexate, tofacitinib, 6-mercaptopurine, azathioprine sulphasalazine, mesalazine, olsalazine chloroquinine/hydroxychloroquinine, penicillamine, aurothiomalate (intramuscular and oral), azathioprine, cochicine, corticosteroids (oral, inhaled, and local injection), a beta-2 adrenoreceptor agonist (salbutamol, terbutaline, salmeteral), a xanthine (theophylline, aminophylline), cromoglycate, nedocromil, ketotifen, ipratropium and oxitropium, cyclosporin, FK506, rapamycin, mycophenolate mofetil, leflunomide, an NSAID (e.g. ibuprofen), a corticosteroid (e.g. prednisolone), a phosphodiesterase inhibitor, an adensosine agonist, an antithrombotic agent, a complement inhibitor, an adrenergic agent, an agent that interferes with signalling by proinflammatory cytokines such as TNFor IL-1

(e.g., a NIK, IKK, p38 or MAP kinase inhibitor), an IL-l converting enzyme inhibitor, a T-cell signalling inhibitor (e.g. a kinase inhibitor), a metalloproteinase inhibitor, sulfasalazine, a 6-mercaptopurine, an angiotensin converting enzyme inhibitor, a soluble cytokine receptor (e.g. soluble p55 or p75 TNF receptors and the derivatives p75TNFRigG (etanercept) and p55TNFRigG (Lenercept), siL-lRI, siL-lRII, siL-6R), an antiinflammatory cytokine (e.g. IL-4, IL-l 0, IL-11, IL-13 and TGF), celecoxib, folic acid, hydroxychloroquine sulfate, rofecoxib, etanercept, infliximab, adalimumab, certolizumab, tocilizumab, abatacept, naproxen, valdecoxib, sulfasalazine, methylprednisolone, meloxicam, methylprednisolone acetate, gold sodium thiomalate, aspirin, triamcinolone acetonide, propoxyphene napsylate/apap, folate, nabumetone, diclofenac, piroxicam, etodolac, diclofenac sodium, oxaprozin, oxycodone HCl, hydrocodone bitartrate/apap, diclofenac sodium/misoprostol, fentanyl, anakinra, tramadol HCl, salsalate, sulindac, cyanocobalamin/fa/pyridoxine, acetaminophen, alendronate sodium, prednisolone, cortisone, betamethasone, morphine sulfate, lidocaine hydrochloride, indomethacin, glucosamine sulf/chondroitin, amitriptyline HCl, sulfadiazine, oxycodone HCVacetaminophen, olopatadine HCl misoprostol, naproxen sodium, omeprazole, cyclophosphamide, rituximab, IL-l TRAP, MRA, CTLA4-IG, IL-18 BP, anti-IL-12, Anti- ILlS, BIRB-796, SCI0-469, VX-702, AMG-548, VX-740, Roflumilast, IC-485, CDC-801, SlPl agonists (such as FTY720), a PKC family inhibitor (e.g. Ruboxistaurin or AEB-071) or Mesopram. In certain embodiments, a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with methotrexate or leflunomide. In moderate or severe rheumatoid arthritis cases, a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with cyclosporine and anti-TNF antibodies as noted above. A compound of formula (I) or a pharmaceutically acceptable salt thereof may also be co-administered with: budenoside; epidermal growth factor; a corticosteroid; cyclosporin, sulfasalazine; an aminosalicylate; 6-mercaptopurine; azathioprine; metronidazole; a lipoxygenase inhibitor; mesalamine; olsalazine; balsalazide;an antioxidant; a thromboxane inhibitor; an IL-l receptor antagonist; an anti-IL-l monoclonal antibody; an anti-IL-6 monoclonal antibody; a growth factor; an elastase inhibitor; a pyridinyl-imidazole compound; an antibody to or antagonist of other human cytokines or growth factors (e.g. TNF, LT, IL-l, IL-2, IL-6, IL-7, IL-8, IL-12, IL-15, IL-16, IL-23, EMAP-II, GM-CSF, FGF, and PDGF); a cell surface molecule (e.g. CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, or CD90 or their ligands); methotrexate; cyclosporine; FK506; rapamycin; mycophenolate mofetil; leflunomide; an NSAID (e.g. ibuprofen); a corticosteroid(e.g. prednisolone); a phosphodiesterase inhibitor; an adenosine agonist; an antithrombotic agent; a complement inhibitor; an adrenergic agent; an agent that interferes with signalling by

proinflammatory cytokines such as TNF 5 or IL-l (e.g. a NIK, IKK, or MAP kinase inhibitor); an IL-l converting enzyme inhibitor; a TNF converting enzyme inhibitor; a T-cell signalling inhibitor such as kinase inhibitors; a metalloproteinase inhibitor; sulfasalazine; azathioprine; a 6-mercaptopurine; an angiotensin converting enzyme inhibitor; a soluble cytokine receptor (e.g. soluble p55 or p75 TNF receptors, siL-lRI, siL-lRII, siL-6R), and an antiinflammatory cytokine (e.g. IL-4, IL-l 0, IL-11, IL-13 or TGF).

For treating Crohn's disease, a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with a TNF antagonist (e.g. an anti-TNF antibody), D2E7 (adalimumab), CA2 (infliximab), CDP 571, a TNFR-Ig construct, (p75TNFRigG (etanercept)), a p55TNFRigG (LENERCEPT™) inhibitor, or a PDE4 inhibitor.

For treating inflammatory bowel disease, a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with a corticosteroid (e.g. budenoside or dexamethasone); sulfasalazine, 5-aminosalicylic acid; olsalazine; an agent that interferes with synthesis or action of proinflammatory cytokines such as IL-l (e.g. an IL-l converting enzyme inhibitor or IL-lra); a T cell signaling inhibitor (e.g. a tyrosine kinase inhibitor); 6-mercaptopurine; IL-11; mesalamine; prednisone; azathioprine; mercaptopurine; infliximab; methylprednisolone sodium succinate; diphenoxylate/atrop sulfate; loperamide hydrochloride; methotrexate; omeprazole; folate; ciprofloxacin/dextrose-water; hydrocodone bitartrate/apap; tetracycline hydrochloride; fluocinonide; metronidazole; thimerosal/boric acid; cholestyramine/sucrose; ciprofloxacin hydrochloride; hyoscyamine sulfate; meperidine hydrochloride; midazolam hydrochloride; oxycodone HCl/acetaminophen; promethazine hydrochloride; sodium phosphate; sulfamethoxazole/trimethoprim; celecoxib; polycarbophil; propoxyphene napsylate; hydrocortisone; multivitamins; balsalazide disodium; codeine phosphate/apap; colesevelam HCl; cyanocobalamin; folic acid; levofloxacin; methylprednisolone; natalizumab or interferon-gamma.

For treating multiple sclerosis, a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with a corticosteroid; prednisolone; methylprednisolone; azathioprine; cyclophosphamide; cyclosporine; methotrexate; 4-aminopyridine; tizanidine; interferon- la (AVONEX®; Biogen); interferon-lb (BETASERON®; Chiron/Berlex); interferon -n3) (Interferon Sciences/Fujimoto), interferon- (Alfa Wassermann/J&J), interferon lA-IF (Serono/Inhale Therapeutics), Peginterferon 2b (Enzon/Schering-Plough), Copolymer 1 (Cop-1; COPAXONE®; Teva Pharmaceutical Industries, Inc.); hyperbaric oxygen; intravenous immunoglobulin; cladribine; an antibody to or antagonist of other human cytokines or growth factors and their receptors (e.g. TNF, LT,

IL-1, IL-2, IL-6, IL-7, IL-8, IL-12, IL-23, IL-15, IL-16, EMAP-II, GM-CSF, FGF, or PDGF).

For treating AIDS a compound of formula (I) or a pharmaceutically acceptable salt therof may be co-administered with antibodies to cell surface molecules such as CD2, CD3, CD4, CD8, CD19, CD20, CD25, CD28, CD30, CD40, CD45, CD69, CD80, CD86, CD90 or their ligands. A compound of Formula (I) or a pharmaceutically acceptable salt therof may also be co-administered with methotrexate, cyclosporine, FK506, rapamycin, mycophenolate mofetil, leflunomide, an S1P1 agonist, an NSAID (e.g. ibuprofen), a corticosteroid (e.g. prednisolone), a phosphodiesterase inhibitor, an adensosine agonist, an antithrombotic agent, acomplement inhibitor, an adrenergic agent, an agent that interferes with signalling by proinflammatory cytokines such as TNF or IL-1 (e.g., a NIK, IKK, p38 or MAP kinase inhibitor), an IL-1 converting enzyme inhibitor, a TACE inhibitor, a T-cell signaling inhibitor (e.g. a kinase inhibitor), a metalloproteinase inhibitor, sulfasalazine, azathioprine, a 6-mercaptopurine, an angiotensin converting enzyme inhibitor, a soluble cytokine receptor (e.g. soluble p55 or p75 TNF receptors, siL-1RI, siL-1RII, or siL-6R), or an antiinflammatory cytokine (e.g. IL-4, IL-1 0, IL-13 or TGF).

A compound of formula (I) or a pharmaceutically acceptable salt thereof may also be co-administered with agents, such as alemtuzumab, dronabinol, daclizumab, mitoxantrone, xaliproden hydrochloride, fampridine, glatiramer acetate, natalizumab, sinnabidol, immunokine NNS03, ABR-215062, AnergiX.MS, chemokine receptor antagonists, BBR-2778, calagualine, CPI-1189, LEM (liposome encapsulated mitoxantrone), THC.CBD (cannabinoid agonist), MBP-8298, mesopram (PDE4 inhibitor), MNA-715, an anti-IL-6 receptor antibody, neurovax, pirfenidone allotrap 1258 (RDP-1258), sTNF-RI, talampanel, teriflunomide, TGF-beta2, tiplimotide, a VLA-4 antagonist (e.g. TR-14035, VLA4 Ultrahaler, or Antegran-ELAN/Biogen), an interferon gamma antagonist, or an IL-4 agonist.

For treating ankylosing spondylitis a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with ibuprofen, diclofenac, misoprostol, naproxen, meloxicam, indomethacin, diclofenac, celecoxib, rofecoxib, sulfasalazine, methotrexate, azathioprine, minocyclin, prednisone, an anti-TNF antibody, D2E7 (HUMIRA®), CA2 (infliximab), CDP 571, a TNFR-Ig construct, (p75TNFRigG (ENBREL®), or p55TNFRigG (LENERCEPT®).

For treating asthma a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with albuterol, salmeterol/fluticasone, montelukast sodium, fluticasone propionate, budesonide, prednisone, salmeterol xinafoate, levalbuterol HCl, albuterol sulfate/ipratropium, prednisolone sodium phosphate, triamcinolone acetonide,

beclomethasone dipropionate, ipratropium bromide, azithromycin, pirbuterol acetate, prednisolone, theophylline anhydrous, methylprednisolone sodium succinate, clarithromycin, zafirlukast, formoterol fumarate, influenza virus vaccine, amoxicillin trihydrate, flunisolide, cromolyn sodium, fexofenadine hydrochloride, flunisolide/menthol, amoxicillin/clavulanate, levofloxacin, guaifenesin, dexamethasone sodium phosphate, moxifloxacin HCl, doxycycline hyclate, guaifenesin/d-methorphan, p-ephedrine/cod/-chlorphenir, gatifloxacin, cetirizine hydrochloride, mometasone furoate, salmeterol xinafoate, benzonatate, cephalexin, pe/hydrocodone/chlorphenir, cetirizine HCl/pseudoephed, phenylephrine/cod/promethazine, codeine/promethazine, cefprozil, dexamethasone, guaifenesin/pseudoephedrine, chlorpheniramine/hydrocodone, nedocromil sodium, terbutaline sulfate, epinephrine, methylprednisolone, an anti-IL-13 antibody, or metaproterenol sulfate.

For treating COPD a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with albuterol sulfate/ipratropium, ipratropium bromide, salmeterol/fluticasone, albuterol, salmeterol xinafoate, fluticasone propionate, prednisone, theophylline anhydrous, methylprednisolone sodium succinate, montelukast sodium, budesonide, formoterol fumarate, triamcinolone acetonide, levofloxacin, guaifenesin, azithromycin, beclomethasone dipropionate, levalbuterol HCl, flunisolide, ceftriaxone sodium, amoxicillin trihydrate, gatifloxacin, zafirlukast, amoxicillin/clavulanate, flunisolide/menthol, chlorpheniramine/hydrocodone, metaproterenol sulfate, methylprednisolone, mometasone furoate, p-ephedrine/cod/chlorphenir, pirbuterol acetate, p-ephedrine/loratadine, terbutaline sulfate, tiotropium bromide, (R,R)-formoterol, TgAAT, cilomilast, or roflumilast.

For treating psoriasis, a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with calcipotriene, clobetasol propionate, triamcinolone acetonide, halobetasol propionate, tazarotene, methotrexate, fluocinonide, betamethasone diprop augmented, fluocinolone acetonide, acitretin, tar shampoo, betamethasone valerate, mometasone furoate, ketoconazole, pramoxine/fluocinolone, hydrocortisone valerate, flurandrenolide, urea, betamethasone, clobetasol propionate/emoll, fluticasone propionate, azithromycin, hydrocortisone, moisturizing formula, folic acid, desonide, pimecrolimus, coal tar, diflorasone diacetate, etanercept folate, lactic acid, methoxsalen, he/bismuth subgal/znox/resor, methylprednisolone acetate, prednisone, sunscreen, halcinonide, salicylic acid, anthralin, clocortolone pivalate, coal extract, coal tar/salicylic acid, coal tar/salicylic acid/sulfur, desoximetasone, diazepam, emollient, fluocinonide/emollient, mineral oil/castor oil/na lact, mineral oil/peanut oil, petroleum/isopropyl myristate, psoralen, salicylic acid, soap/tribromsalan, thimerosal/boric acid, celecoxib, infliximab, cyclosporine, alefacept,

efalizumab, tacrolimus, pimecrolimus, PUVA, UVB, sulfasalazine, ABT-874 or ustekinamab.

For treating psoriatic arthritis, a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with methotrexate, etanercept, rofecoxib, celecoxib, folic acid, sulfasalazine, naproxen, leflunomide, methylprednisolone acetate, indomethacin, hydroxychloroquine sulfate, prednisone, sulindac, betamethasone diprop augmented, infliximab, methotrexate, folate, triamcinolone acetonide, diclofenac, dimethylsulfoxide, piroxicam, diclofenac sodium, ketoprofen, meloxicam, methylprednisolone, nabumetone, tolmetin sodium, calcipotriene, cyclosporine, diclofenac sodium/misoprostol, fluocinonide, glucosamine sulfate, gold sodium thiomalate, hydrocodone bitartrate/apap, ibuprofen, risedronate sodium, sulfadiazine, thioguanine, valdecoxib, alefacept, D2E7 (adalimumab), or efalizumab.

For treating lupus, a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with an NSAID (e.g. diclofenac, naproxen, ibuprofen, piroxicam, or indomethacin); a COX2 inhibitor (e.g. celecoxib, rofecoxib, or valdecoxib); an anti-malarial (e.g. hydroxychloroquine); a steroid (e.g. prednisone, prednisolone, budenoside, or dexamethasone); a cytotoxic (e.g. azathioprine, cyclophosphamide, mycophenolate mofetil, or methotrexate); an inhibitor ofPDE4, or a purine synthesis inhibitor (e.g. Cellcept®). For example, a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with sulfasalazine, 5-aminosalicylic acid, olsalazine, Imuran®, an agent that interferes with the synthesis, production, or action of a proinflammatory cytokine (e.g. IL-1), or a caspase inhibitor (e.g. a IL-1 converting enzyme inhibitor or IL-1ra).

A compound of formula (I) or a pharmaceutically acceptable salt thereof may also be co-administered with a T cell signaling inhibitor (e.g. a tyrosine kinase inhibitor), or a molecule that targets T cell activation (e.g. CTLA-4-IgG, an anti-B7 family antibody, or an anti-PD-1 family antibody).

A compound of formula (I) or a pharmaceutically acceptable salt thereof can also be co-administered with an IL-11 antibody, an anti-cytokine antibody (e.g. fonotolizumab (anti-IFNg antibody)), or an anti-receptor receptor antibodies (e.g. an anti-IL-6 receptor antibody or an antibody to a B-cell surface molecule).

A compound of formula (I) or a pharmaceutically acceptable salt thereof can also be co-administered with LJP 394 (abetimus), an agent that depletes or inactivates B-cells (e.g. Rituximab (anti-CD20 antibody) or lymphostat-B (anti-BlyS antibody)), a TNF antagonist

(e.g. an anti-TNF antibody), D2E7 (adalimumab), CA2 (infliximab), CDP 571, a TNFR-Ig construct, (p75TNFRigG (etanercept), or p55TNFRigG (LENERCEPT™).

A compound of formula (I) or a pharmaceutically acceptable salt thereof can also be co-administered with one or more agents used in the prevention or treatment of AIDS: an HIV reverse transcriptase inhibitor, an HIV protease inhibitor, an immunomodulator, or another retroviral drug. Examples of reverse transcriptase inhibitors include, but are not limited to, abacavir, adefovir, didanosine, dipivoxil delavirdine, efavirenz, emtricitabine, lamivudine, nevirapine, rilpivirine, stavudine, tenofovir, zalcitabine, and zidovudine. Examples of protease inhibitors include, but are not limited to, amprenavir, atazanavir, darunavir, indinavir, fosamprenavir, lopinavir, nelfinavir, ritonavir, saquinavir, and tipranavir. Examples of other retroviral drugs include, but are not limited to, elvitegravir, enfuvirtide, maraviroc and raltegravir.

For treating type II diabetes, hepatic steatosis, insulin resistance, metabolic syndrome or a related disorder, a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with insulin or insulins that have been modified to improve the duration of action in the body; agents that stimulate insulin secretion such as acetohexamide, chlorpropamide, glyburide, glimepiride, glipizide, glicazide, glycopyramide, gliquidone, rapaglinide, nataglinide, tolazamide or tolbutamide; agents that are glucagon-like peptide agonists such as exanatide, liraglutide or taspoglutide; agents that inhibit dipeptidyl-peptidase IV such as vildagliptin, sitagliptin, saxagliptin, linagliptin, allogliptin or septagliptin; agents that bind to the peroxisome proliferator-activated receptor gamma such as rosiglitazone or pioglitazone; agents that decrease insulin resistance such as metformin; or agents that reduce glucose absorbance in the small intestine such as acarbose, miglitol or voglibose.

For treating acute kidney disorders or a chronic kidney disease, a compound of formula (I) or a pharmaceutically acceptable salt thereof may be co-administered with dopamine, a diuretic (e.g. furosemide), bumetanide, thiazide, mannitol, calcium gluconate, sodium bicarbonate, albuterol, paricalcitol, doxercalciferol, cinacalcet, or bardoxalone methyl.

The amount of both the compound of formula (I) or salt thereof and additional agent (in those compositions which comprise an additional therapeutic agent as described above) that may be combined with the carrier materials to produce a single dosage form will vary depending upon the host treated and the particular mode of administration. In certain embodiments, compositions of this invention are formulated such that a dosage of between 0.01 - 100 mg/kg body weight/day of an inventive can be administered.

The additional therapeutic agent and the compound of formula (I) may act synergistically. Therefore, the amount of additional therapeutic agent in such compositions may be less than that required in a monotherapy utilizing only that therapeutic agent, or there may be fewer side effects for the patient given that a lower dose is used. In certain embodiments, in such compositions a dosage of between 0.01 – 1,000 μg/kg body weight/day of the additional therapeutic agent can be administered.

Provided herein are methods of extending the duration of response to a cytotoxic agent in an individual with cancer comprising administering to the individual (a) an effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof and (b) an effective amount of the cytotoxic agent.

In certain embodiments of any of the methods, the cytotoxic agent is a targeted therapy. In certain embodiments, the targeted therapy is one or more of an EGFR antagonist, RAF inhibitor, and/or PI3K inhibitor.

In certain embodiments of any of the methods, the targeted therapy is an EGFR antagonist. In certain embodiments of any of the methods, the EGFR antagonist is N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine and/or a pharmaceutical acceptable salt thereof. In certain embodiments, the EGFR antagonist is N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine. In certain embodiments, the EGFR antagonist is N-(4-(3-fluorobenzyloxy)-3-chlorophenyl)-6-(5-((2-(methylsulfonyl)ethylamino)methyl)furan-2-yl)quinazolin-4-amine,di4-methylbenzenesulfonate or a pharmaceutically acceptable salt thereof (*e.g.*, lapatinib).

In certain embodiments of any of the methods, targeted therapy is a RAF inhibitor. In certain embodiments, the RAF inhibitor is a BRAF inhibitor. In certain embodiments, the RAF inhibitor is a CRAF inhibitor. In certain embodiments, the BRAF inhibitor is vemurafenib. In certain embodiments, the RAF inhibitor is 3-(2-cyanopropan-2-yl)-N-(4-methyl-3-(3-methyl-4-oxo-3,4-dihydroquinazolin-6-ylamino)phenyl)benzamide or a pharmaceutically acceptable salt thereof (*e.g.*, AZ628 (CAS# 878739-06-1)).

In certain embodiments of any of the methods, the targeted therapy is a PI3K inhibitor.

In certain embodiments of any of the methods, the cytotoxic agent is chemotherapy. In certain embodiments of any of the methods, the chemotherapy is a taxane. In certain embodiments, the taxane is paclitaxel. In certain embodiments, the taxane is docetaxel.

In certain embodiments of any of the methods, the cytotoxic agent is a platinum agent. In certain embodiments, the platinum agent is carboplatin. In certain embodiments, the platinum agent is cisplatin. In certain embodiments of any of the methods, the cytotoxic agent is a taxane

and a platinum agent. In certain embodiments, the taxane is paclitaxel. In certain embodiments, the taxane is docetaxel. In certain embodiments, the platinum agent is carboplatin. In certain embodiments, the platinum agent is cisplatin.

In certain embodiments of any of the methods, the cytotoxic agent is a vinca alkyloid. In certain embodiments, the vinca alkyloid is vinorelbine. In certain embodiments of any of the methods, the chemotherapy is a nucleoside analog. In certain embodiments, the nucleoside analog is gemcitabine.

In certain embodiments of any of the methods, the cytotoxic agent is radiotherapy.

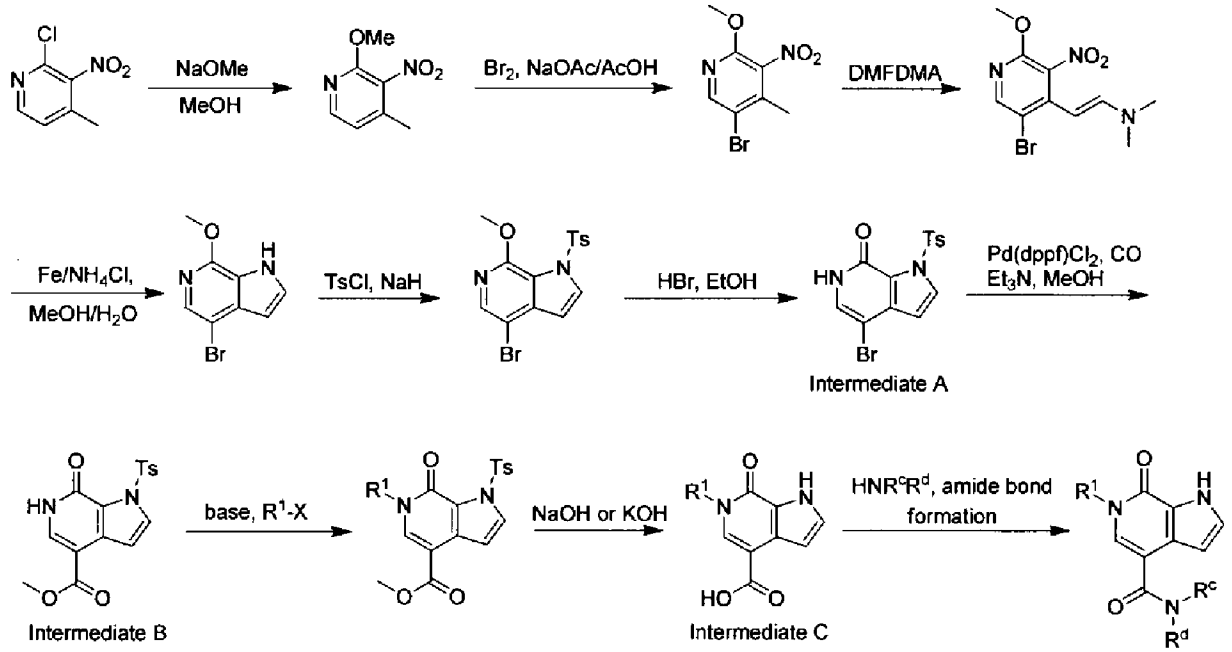
In certain embodiments of any of the methods, the compound of formula (I) or a pharmaceutically acceptable salt thereof is concomitantly administered with the cytotoxic agent (*e.g.*, targeted therapy, chemotherapy, and/or radiotherapy). In certain embodiments, the compound of formula (I) or a pharmaceutically acceptable salt thereof is administered prior to and/or concurrently with the cytotoxic agent (*e.g.*, targeted therapy, chemotherapy, and/or radiotherapy).

EXEMPLIFICATION

As depicted in the Examples below, in certain exemplary embodiments, compounds are prepared according to the following general procedures. It will be appreciated that, although the general methods depict the synthesis of certain compounds of the present invention, the following general methods, and other methods known to one of ordinary skill in the art, can be applied to all compounds and subclasses and species of each of these compounds, as described herein.

Scheme A

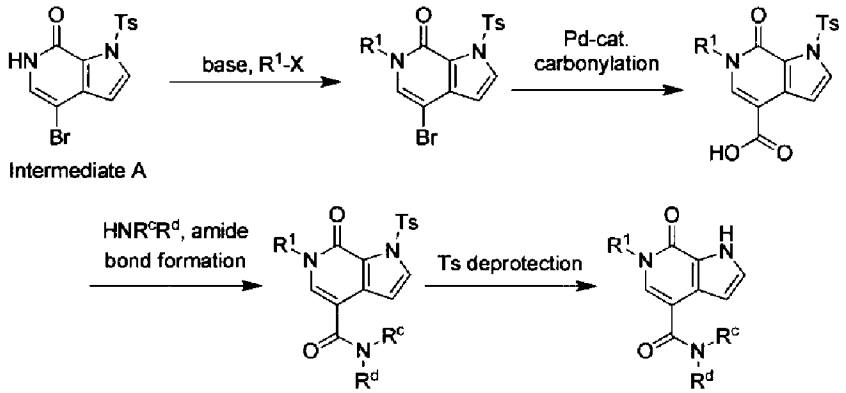
(Examples 1 – 82, 139 – 180, 210, 244 – 251)



Representative Compounds of formula (I) were prepared according to the scheme shown above. Intermediate A (prepared as described below) was converted into the corresponding methyl ester under Pd-catalyzed carbonylation conditions, and the resultant intermediates were alkylated with various R^1-halides. Hydrolysis of those esters simultaneously removed the tosyl protecting group and revealed the carboxylic acid, which was coupled with various amines to yield compounds of formula (I).

General Scheme B

(Examples 83 – 138)

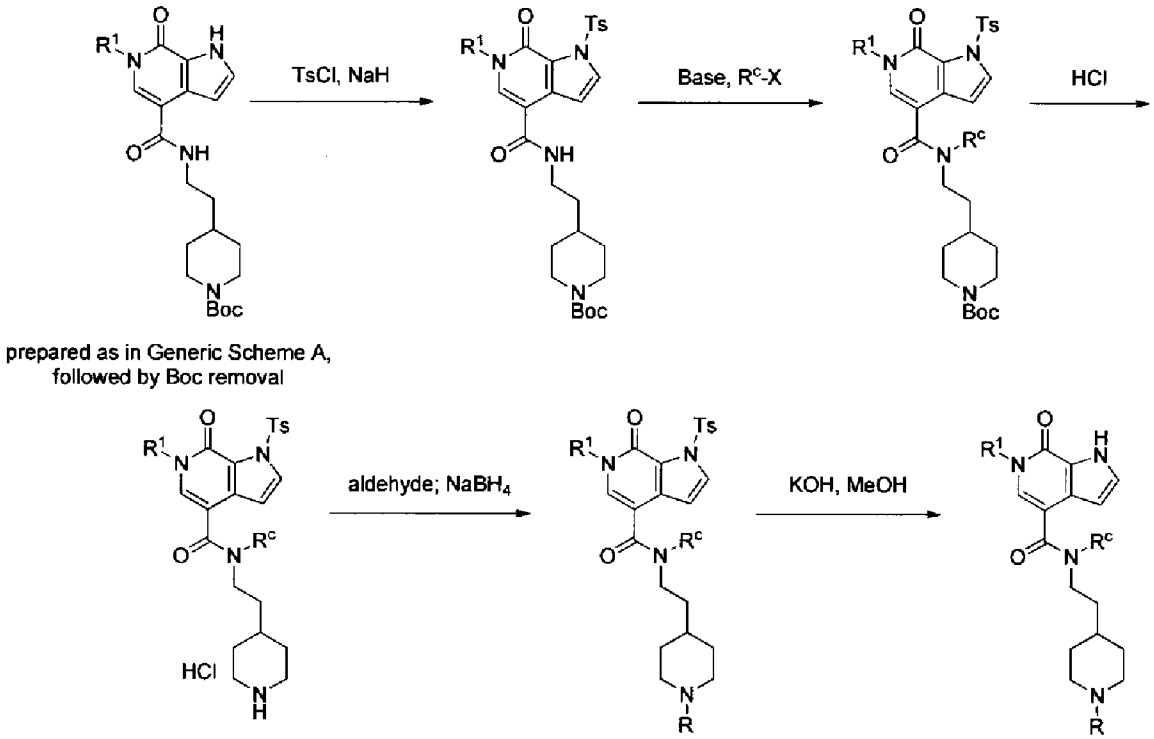


Representative compounds of formula (I) were prepared according to the scheme shown above. Intermediate A (prepared as described below) was alkylated with various R^1-halides before being converted into the corresponding carboxylic acids under Pd-catalyzed carbonylation

conditions. Subsequent amide bond formation, followed by hydrolytic removal of the tosyl group, yielded compounds of formula (I).

General Scheme C

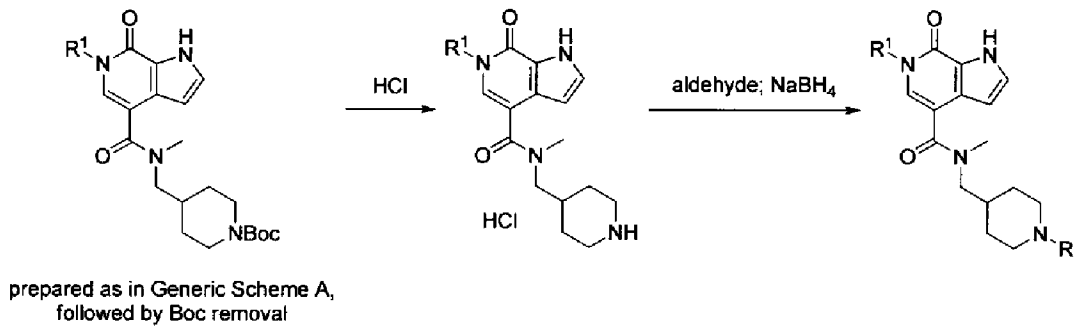
(Examples 181 – 186)



Representative compounds of formula (I) were prepared according to the scheme shown above. Variously N-substituted derivatives of tert-butyl 4-(2-(7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamido)ethyl)piperidine-1-carboxylate (prepared as in Generic Scheme A) were protected with tosyl chloride under basic conditions. The resultant compounds were alkylated with R^c-halides on the amide nitrogen before acidic removal of the Boc protecting group. Reductive amination with various aldehydes introduced substituents on the piperidine, and subsequent hydrolytic removal of the tosyl group yielded compounds of formula (I).

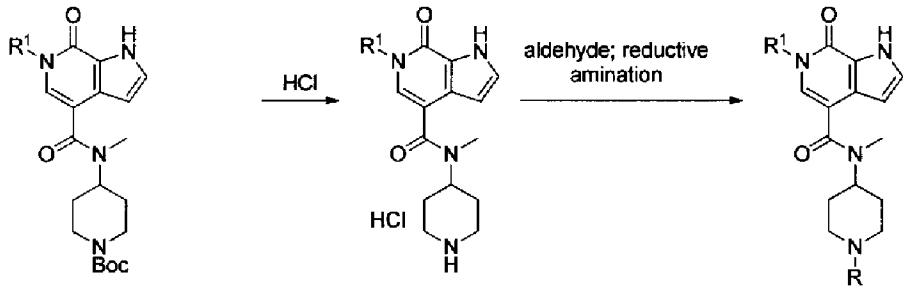
General Scheme D

(Examples 187 – 206)



Representative compounds of formula (I) were prepared according to the scheme shown above. Variously pyrrolopyridone N-substituted derivatives of tert-butyl 4-((N-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamido)methyl)piperidine-1-carboxylate (prepared as in Generic Scheme A) were deprotected under acidic conditions. Reductive amination of the resultant amines with various aldehydes yielded compounds of formula (I).

General Scheme E (Examples 207 – 209)

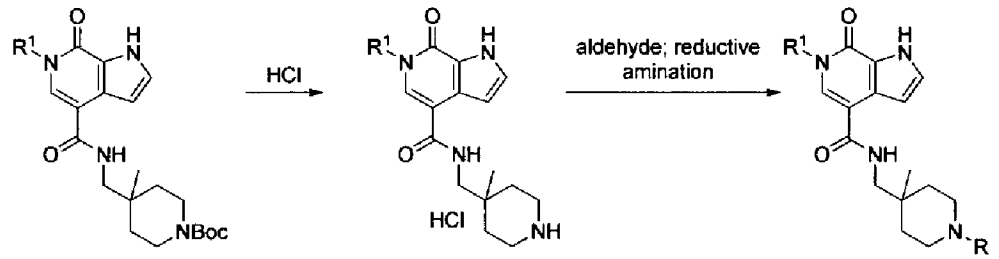


prepared as in Generic Scheme A, followed by Boc removal

Representative compounds of formula (I) were prepared according to the scheme shown above. Variously pyrrolopyridone N-substituted derivatives of tert-butyl 4-(N-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamido)piperidine-1-carboxylate (prepared as in Generic Scheme A) were deprotected under acidic conditions. Reductive amination of the resultant amines with various aldehydes yielded compounds of formula (I).

General Scheme F

(Examples 211 – 212)

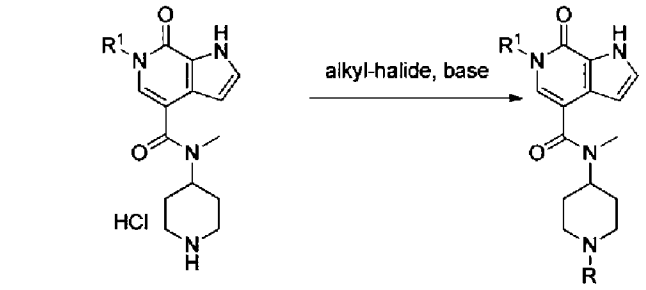


prepared as in Generic Scheme A, followed by Boc removal

Representative compounds of formula (I) were prepared according to the scheme shown above. Variously pyrrolopyridone N-substituted derivatives of tert-butyl 4-methyl-4-((7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamido)methyl)piperidine-1-carboxylate (prepared as in Generic Scheme A) were deprotected under acidic conditions. Reductive amination of the resultant amines with various aldehydes yielded compounds of formula (I).

General Scheme G

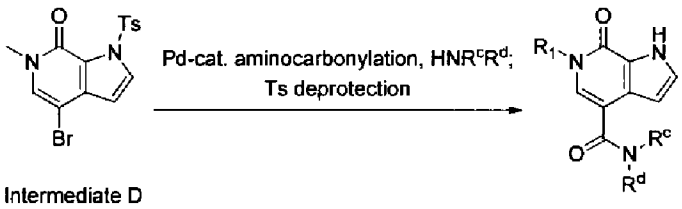
(Examples 213 – 243, 252 – 255)



Representative compounds of formula (I) were prepared according to the scheme shown above. Variously pyrrolopyridone N-substituted derivatives of N-methyl-7-oxo-N-(piperidin-4-yl)-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide hydrochloride (prepared as in Generic Scheme A) were alkylated on the piperidine nitrogen to yield compounds of formula (I).

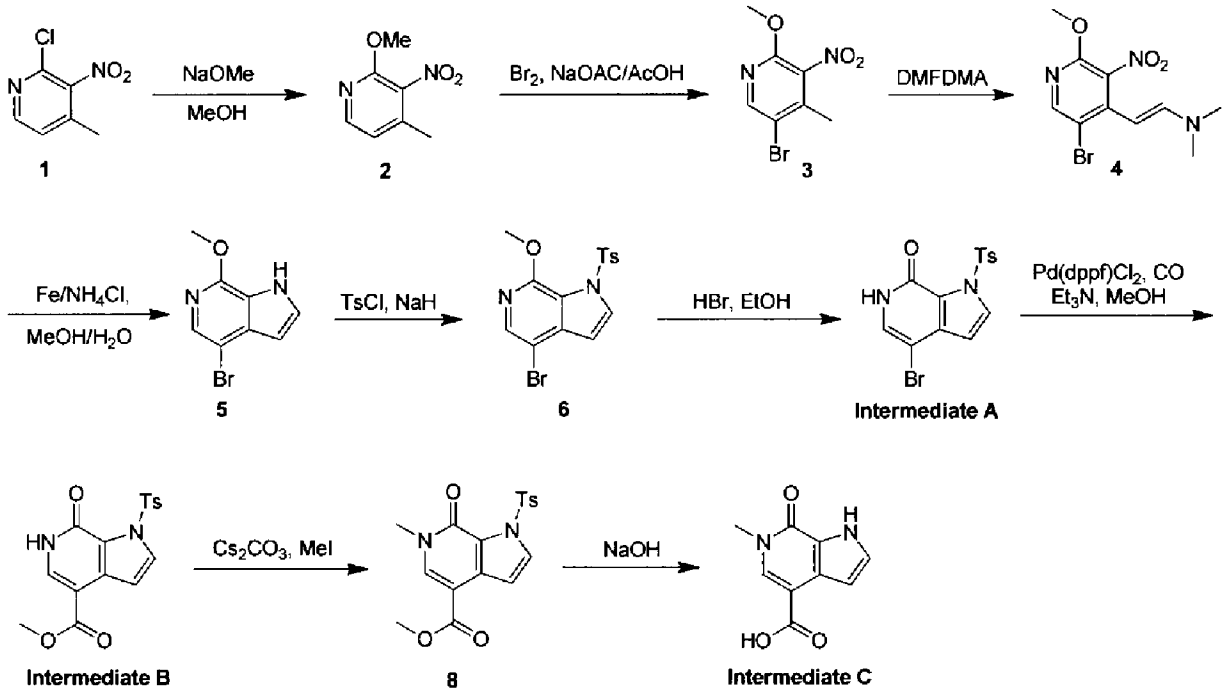
General Scheme H

(Examples 256 – 265)



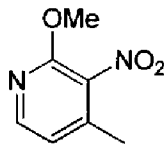
Representative compounds of formula (I) were prepared according to the scheme shown above. Intermediate D (prepared as described below) was converted into compounds of formula (I) by Pd-catalyzed amino carbonylation in the presence of variously substituted amines.

General procedure for the preparation of Intermediates A, B, and C



Step 1:

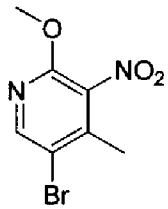
2-methoxy-4-methyl-3-nitropyridine



A solution of 2-chloro-4-methyl-3-nitropyridine (250 g, 1.45 mol) in methanol (1.0 L) was added dropwise (2 h) to a stirred and cooled (0 °C) solution of sodium methoxide (250 g, 4.63 mol) in methanol (850 mL). After addition, the mixture was heated to reflux for 23 h, at which time TLC indicated the reaction had gone to completion. The mixture was concentrated under reduced pressure to a volume of approximately 900 mL, and quenched by addition of water (1.5 L). The resulting solid was collected by filtration, washed with water and dried under reduced pressure to give the title compound (250 g, 100% yield) as a brown solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.22 (d, *J* = 5.2 Hz, 1 H), 7.10 (d, *J* = 5.6 Hz, 1 H), 3.92 (s, 3 H), 2.26 (s, 3 H).

Step 2:

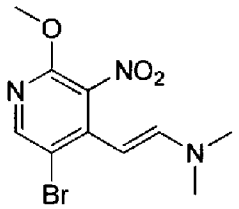
5-bromo-2-methoxy-4-methyl-3-nitropyridine



Sodium acetate (365 g, 5.37 mol) was added to a stirred solution of 2-methoxy-4-methyl-3-nitropyridine (250 g, 1.49 mol) in acetic acid (1.5 L) at ambient temperature and then Br_2 (639 g, 4.00 mol) was added dropwise (30 min). After addition, the mixture was heated at 80 °C for 12 h, at which time TLC indicated the reaction had gone to completion. The mixture was cooled (0 °C) and quenched by sequential addition of 10% aqueous (1.5 L) and saturated aqueous Na_2SO_3 (1.5 L). The resulting solid was collected by filtration washed with water, and dried under reduced pressure to give the title compound (302 g, 82.2% yield) as a light yellow solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.25 (s, 1 H), 3.94 (s, 3 H), 2.29 (s, 3 H).

Step 3:

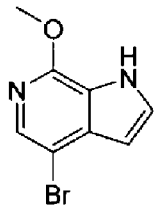
(E)-2-(5-bromo-2-methoxy-3-nitro-4-pyridyl)-N,N-dimethyl-ethenamine



DMF-DMA (600 mL) was slowly added to a stirred and heated (80 °C) solution of 5-bromo-2-methoxy-4-methyl-3-nitropyridine (134 g, 0.54 mol) in DMF (1.1 L). After addition, the mixture was heated at 95 °C for 5 h, at which time TLC indicated the reaction had gone to completion. The mixture was cooled to room temperature and poured into ice-cold water (3 L). The resulting red solid was collected by filtration, washed with water, and dried under reduced pressure to give the title compound (167 g, 100% yield) as red solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.24 (s, 1 H), 7.05 (d, J = 13.6 Hz, 1 H), 7.05 (d, J = 13.6 Hz, 1 H), 4.80 (d, J = 13.2 Hz, 1 H), 3.88 (s, 3 H), 2.90 (s, 6 H).

Step 4:

4-bromo-7-methoxy-1H-pyrrolo[2,3-c]pyridine

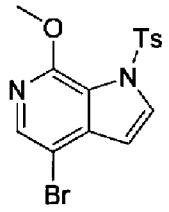


A mixture of 2-(5-bromo-2-methoxy-3-nitropyridin-4-yl)-N,N-dimethylethenamine (50.0 g, 165 mmol), Fe (50.0 g, 893 mmol) and NH_4Cl (50.0 g, 943 mmol) in methanol/H_2O (1900/250 mL) was heated at reflux for 7 h, at which time LCMS indicated that the reaction had gone to completion. The mixture was filtered while hot and the cake was washed with methanol (3 x 200

mL). The combined filtrate was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography (petroleum ether : Ethyl acetate=5:1) to give the crude product. This crude material was triturated with acetonitrile to give the title compound (37.4 g, 99.5% yield) as a light brown solid. LCMS M/Z (M+H) 226.7, 228.7.

Step 5:

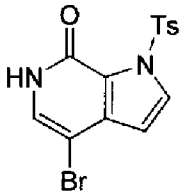
4-bromo-7-methoxy-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine



A solution of 4-bromo-7-methoxy-1H-pyrrolo[2,3-c]pyridine (34.3 g, 0.15 mol) in THF (700 mL) was added dropwise to a stirred and cooled (0 °C) solution of sodium hydride (60%, 19.2 g, 0.48 mol) in THF (700 mL). After addition, the mixture was stirred at room temperature for 1 h, and then cooled again to 0 °C. Tosyl chloride (38.0 g, 0.20 mol) in THF (700 mL) was added dropwise and the resulting mixture was stirred at ambient temperature for 2 h. The reaction was quenched by addition of saturated aqueous ammonium chloride (1.0 L), and then extracted with ethyl acetate (3 x 600 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was triturated with acetonitrile to give the title compound (51.2 g, 88.9% yield) as a brown solid. This crude material was used in the next step without further purification.

Step 6:

4-bromo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridin-7-one

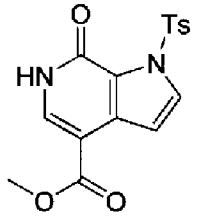


HBr (40% aqueous, 1.1 L) was added to a solution of 4-bromo-7-methoxy-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine (102.5 g, 0.27 mol) in ethanol (200 mL). After addition, the mixture was heated at 90 °C for 2h, at which time TLC indicated that the reaction had gone to completion. The mixture was cooled to 0 °C and the resulting white solid was collected by filtration. This solid was washed with water and dried under vacuum to give the title compound (**Intermediate A**) (87.5 g, 88.6% yield) as a light brown solid. ^{1}H NMR (400 MHz, DMSO-*d6*):

δ 11.48 (s, 1 H), 8.01 (d, *J* = 3.6 Hz, 1 H), 8.90 (d, *J* = 8.0 Hz, 2 H), 7.38 (d, *J* = 8.0 Hz, 2 H), 7.32 (s, 1 H), 6.57 (d, *J* = 3.2 Hz, 1 H), 2.34 (s, 3 H).

Step 7:

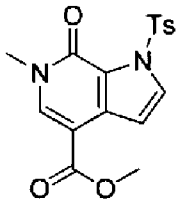
methyl 7-oxo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridine-4-carboxylate



[1,1'-bis(diphenylphosphino)ferrocene]palladium(ii) dichloride (5.0 g, 8.5 mmol) was added to a mixture of 4-bromo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridin-7-one (10.0 g, 27.3 mmol), Et_3N (20.0 mL, 143.5 mmol) in methanol (1 L). After addition, the mixture was stirred under CO atmosphere (50 psi) at 80 °C for 24 h, at which time TLC (petroleum ether :ethyl acetate=1:1) showed the completion of the reaction. The resulting mixture was concentrated under reduced pressure and the residue was purified by flash column (petroleum ether : ethyl acetate=5:1 to 3:1) to give the title compound **(Intermediate B)** (7.5 g, 79.5% yield) as a brown solid. ^1H NMR (400 MHz, DMSO-*d6*): δ 11.79 (s, 1 H), 8.03 (d, *J* = 3.6 Hz, 1 H), 7.88 (d, *J* = 8.4 Hz, 2 H), 7.80 (s, 1 H),7.37 (d, *J* = 8.0 Hz, 2 H), 7.05 (d, *J* = 3.2 Hz, 1 H), 3.77 (s, 3 H), 2.33 (s, 3 H).

Step 8:

methyl 6-methyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxylate

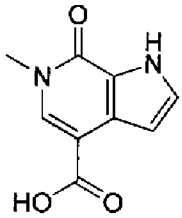


Methyl iodide (18.1 g, 127.24 mmol) was added dropwise to a stirred solution of methyl 7-oxo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridine-4-carboxylate (11.6 g, 33.49 mmol) and Cs_2CO_3 (13.1 g, 40.18 mmol) in dioxane (230 mL). After addition, the resulting mixture was stirred at room temperature for 4 hr, at which time TLC indicated the reaction was completed. The solid was removed by filtration and the filtrate was concentrated. The residue was dissolved in ethyl acetate (250 mL) and washed with water (50 mL x 2). The organic layer was dried over sodium sulfate and concentrated under reduced pressure to give the title compound (11.0 g, 91.1% yield)

as a white solid. This crude was used into next step without further purification. LCMS M/Z (M+H) 360.9.

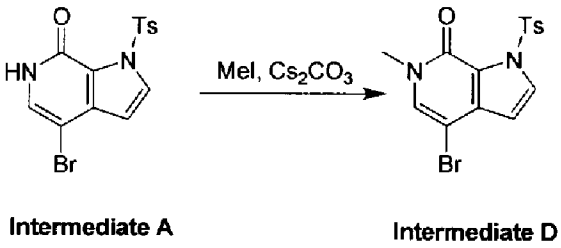
Step 9:

6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid

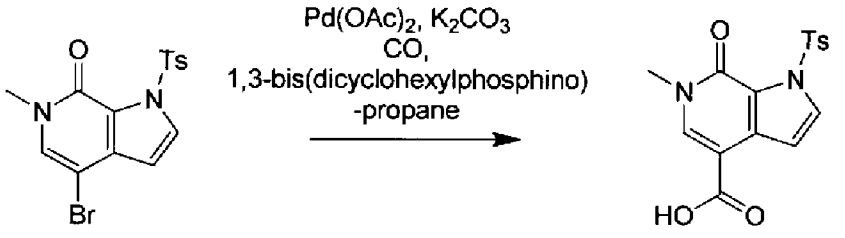


Sodium hydroxide (6.0 g, 150.0 mmol) was added in portions to a stirred solution of methyl 6-methyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxylate (12.0 g, 33.3 mmol) in methanol/water (260/30 mL). After addition, the mixture was stirred at 80 °C for 2 h, at which time LCMS indicated the reaction had gone to completion. After cooling, the mixture was concentrated under reduced pressure. The residue was dissolved in water (30 mL) and the aqueous solution was acidified to pH 3-4 using 5 N hydrochloric acid. The resulting precipitate was collected by filtration, washed with water, and dried under reduced pressure to give the title compound (**Intermediate C**) (4.3 g, 67.2% yield) as a brown solid. This crude material was used in the next step without further treatment. LCMS M/Z (M+H) 192.8.

General procedure for the prepraration of Intermediates D, E

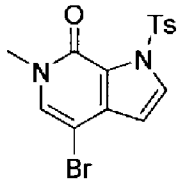


Intermediate A **Intermediate D**



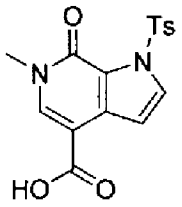
Intermediate D **Intermediate E**

4-bromo-6-methyl-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-7-one



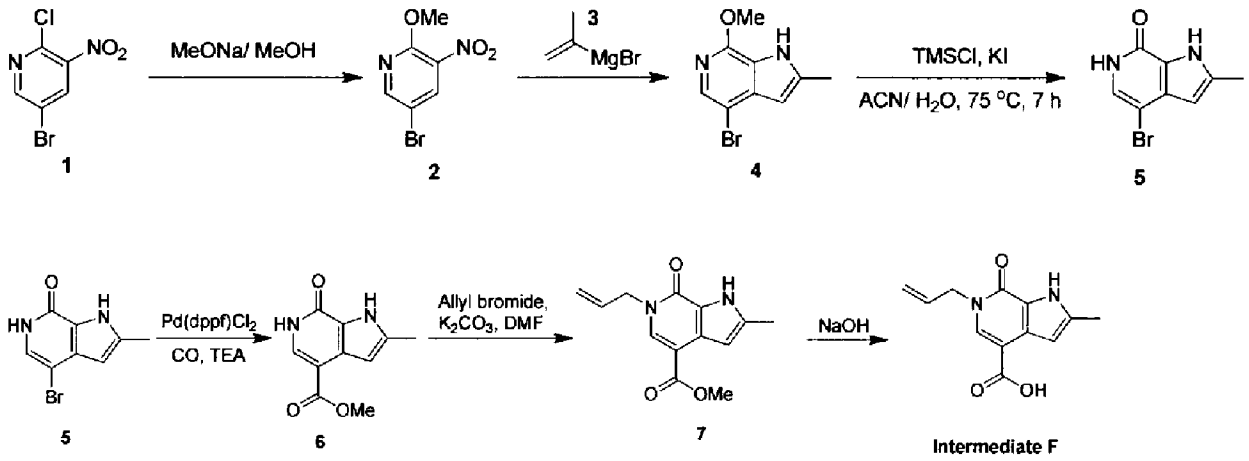
Methyl iodide (24.5 g, 172.8 mmol) was added dropwise to a stirred suspension of 4-bromo-1-tosyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (Intermediate A) (16.7 g, 45.5 mmol) and cesium carbonate (17.8 g, 54.6 mmol) in dioxane (250 mL). After addition, the reaction mixture was stirred at room temperature for 18 h, at which time LCMS indicated the reaction had gone to completion. The solvent was evaporated under reduced pressure, and the residue was diluted with water (200 mL). The mixture was extracted with EtOAc (3 x 200 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/ethyl acetate = 3:1) to give the title compound **(Intermediate D)** (14.0 g, 81.4% yield) as a brown solid. ^{1}H NMR (400MHz, DMSO-*d6*): δ 8.03 (d, *J* = 3.6 Hz, 1 H), 7.92 (d, *J* = 8.4 Hz, 2 H), 7.78 (s, 1 H), 7.39 (d, *J* = 8.4 Hz, 2 H), 6.57 (d, *J* = 3.6 Hz, 1 H), 3.35 (s, 3 H), 2.35 (s, 3 H).

6-methyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxylic acid



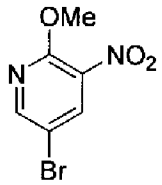
A disposable tube was charged with 4-bromo-6-methyl-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-7-one **(Intermediate D)** , 2 g, 5.25 mmol), 1,3-bis(dicyclohexylphosphino)propane (0.642 g, 1.049 mmol), palladium acetate (0.118 g, 0.525 mmol), and potassium carbonate (1.450 g, 10.49 mmol) before being evacuated and purged with carbon monoxide three times. Water (0.189 ml, 10.49 mmol) and dimethylsulfoxide (5 mL) were added, and the mixture was stirred at 100 °C for 6 h. The reaction mixture was cooled and diluted with ethyl acetate (100 mL). The crude product was extracted with 1 N aqueous sodium hydroxide. This aqueous extract was then acidified using 1 N hydrochloric acid resulting in formation of a precipitate. This material was collected and lyophilized to yield title compound **(Intermediate E)** (1.08 g, 59%) as a grey amorphous solid that was used crude in subsequent reactions. LCMS M/Z (M+H) 347.

General procedure for Intermediate F



Step 1:

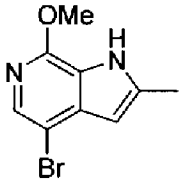
5-bromo-2-methoxy-3-nitropyridine



Sodium methoxide (17.2 g, 318.4 mmol) was added to a stirred solution of 5-bromo-2-chloro-3-nitropyridine (15.0 g, 64.2 mmol) in methanol (125 mL). After addition, the reaction mixture was heated at reflux for 2 h. The mixture was concentrated under reduced pressure, and the residue was diluted with water (200 mL). The resulting precipitate was collected by filtration, washed with water, and dried under reduced pressure to give the title compound (12.0 g, 81.5% yield) as a brown solid. ^{1}H NMR (400MHz, $CDCl_3$): δ 8.43 (d, J = 2.4 Hz, 1 H), 8.38 (d, J = 2.0 Hz, 1 H), 4.09 (s, 3 H).

Step 2:

4-bromo-7-methoxy-2-methyl-1H-pyrrolo[2,3-c]pyridine

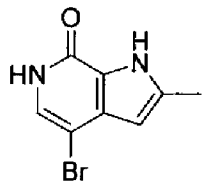


Isopropenyl magnesium bromide (0.5 M in THF, 105.0 mL, 55.0 mmol) was added dropwise to a stirred and cooled (-78°C) solution of 5-bromo-2-methoxy-3-nitropyridine (4.0 g, 17.1 mmol) in THF (40 mL). After addition, the resulting mixture was allowed to warm to room temperature gradually and stirred for an additional 3 h. The reaction mixture was quenched by addition of 1 M aqueous ammonium chloride (150 mL), and then extracted with ethyl acetate (3 x 100 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced

pressure. The residue was purified by silica gel chromatography (petroleum ether : ethyl acetate = 10:1) to give the title compound (1.65 g, 39.9% yield) as brown oil. LCMS M/Z (M+H) 240/ 242.

Step 3:

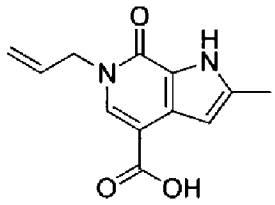
4-bromo-2-methyl-1,6-dihydropyrrolo[2,3-c]pyridin-7-one



Hydrogen bromide (40% aqueous, 20 mL) was added to a solution of 4-bromo-7-methoxy-2-methyl-1H-pyrrolo[2,3-c]pyridine (1.65 g, 6.8 mmol) in ethanol (10 mL). After addition, the reaction mixture was heated at 90°C for 15 h, at which time TLC indicated the reaction had gone to completion. The mixture was cooled to 0 °C and the resulting solid was collected by filtration. This solid was washed with water and dried to give title compound (0.9 g, 57.9% yield) as a brown solid. ^{1}H NMR (400MHz, DMSO-*d6*): δ 12.06 (s, 1 H), 11.00 (s, 1 H), 7.03 (s, 1 H), 5.97 (s, 1 H), 2.29 (s, 3 H). LCMS M/Z (M+H) 226/ 228

Step 4:

6-allyl-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (Intermediate F)



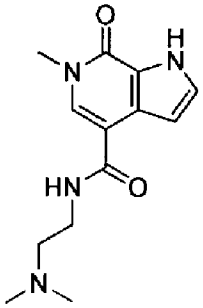
To a solution of methyl 2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4- carboxylate (10.0 g, 48.5 mmol) in DMF (100 mL) was added K_2CO_3 (20.1 g, 145.0 mmol) and allyl bromide (5.9 g, 48.5 mmol). After addition, the mixture was stirred at ambient temperature for 12 h, at which time LCMS showed the completion of the reaction. The reaction mixture was diluted with ice-water (200 mL). The resulting precipitate was collected by filtration, washed with water and dried.

A suspension of the above crude product in methanol (150 mL) and was added KOH (10.9 g, 194 mmol) in water (50 mL). The mixture was heated at 50 °C for 4 h, at which time LCMS showed the completion of the reaction. Methanol was evaporated under reduced pressure, and the aqueous solution was acidified by adding 2 N HCl to pH 2. The resulting precipitate was

collected by filtration and dried to give the title compound (**Intermediate F**) (10.2 g, 91% yield) as a grey solid.

Example 1

N-(2-dimethylaminoethyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



To an 8 mL vial was added N,N-dimethylethane-1,2-diamine (26 mg, 0.30 mmol) followed by 6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (**Intermediate C**, 0.80 mL, 0.20 mmol, 0.25 mol/L in DMF) , HATU (0.48 mL, 0.24 mmol, 0.50 mol/L in DMF) , and TEA (0.56 mL, 0.40 mmol). The reaction was capped and shaken at room temperature overnight. The reaction was then concentrated under reduced pressure and the residue was then partitioned between dichloromethane and water. The organic phase was separated and concentrated under reduced pressure. The residue was purified by reverse phase chromatography (0-25%ACN/0.1%NH4OH in H2O) yielding N-(2-dimethylaminoethyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide. (21 mg, 40%). ^{1}H NMR (400 MHz, DMSO-*d6*) δ 12.07 (s, 1H), 7.86 – 7.68 (m, 2H), 7.33 (d, *J* = 2.2 Hz, 1H), 6.70 (d, *J* = 2.7 Hz, 1H), 3.55 (s, 3H), 3.37 – 3.31 (m, 2H), 2.40 (t, *J* = 6.8 Hz, 2H), 2.19 (s, 6H). LCMS M/Z (M+H) 367.2.

The following compounds were prepared in a similar manner to Example 1:

Examples 2-82

Example	Compound Name	NMR	m/z
2	N-[2-(dimethylamino)-1-methyl-ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO) δ 12.07 (s, 1H), 7.86 – 7.68 (m, 2H), 7.33 (d, J = 2.2 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 3.55 (s, 3H), 3.37 – 3.31 (m, 2H), 2.40 (t, J = 6.8 Hz, 2H), 2.19 (s, 6H).	277

3	6-methyl-N-[(1-methyl-4-piperidyl)methyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO) δ 12.07 (s, 1H), 7.86 – 7.68 (m, 2H), 7.33 (d, J = 2.2 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 3.55 (s, 3H), 3.37 – 3.31 (m, 2H), 2.40 (t, J = 6.8 Hz, 2H), 2.19 (s, 6H).	303
4	6-methyl-N-(1-methyl-4-piperidyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO) δ 12.07 (s, 1H), 7.86 – 7.68 (m, 2H), 7.33 (d, J = 2.2 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 3.55 (s, 3H), 3.37 – 3.31 (m, 2H), 2.40 (t, J = 6.8 Hz, 2H), 2.19 (s, 6H).	289
5	6-methyl-7-oxo-N-[2-(1-piperidyl)ethyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO) δ 12.09 (s, 1H), 7.80 (s, 1H), 7.76 – 7.71 (m, 1H), 7.38 – 7.29 (m, 1H), 6.71 (s, 1H), 3.55 (s, 3H), 3.42 – 3.33 (m, 2H), 2.48 – 2.35 (m, 6H), 1.55 – 1.45 (m, 4H), 1.45 – 1.34 (m, 2H).	303
6	6-methyl-N-(1-methylpyrrolidin-3-yl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO) δ 12.07 (s, 1H), 7.86 – 7.68 (m, 2H), 7.33 (d, J = 2.2 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 3.55 (s, 3H), 3.37 – 3.31 (m, 2H), 2.40 (t, J = 6.8 Hz, 2H), 2.19 (s, 6H).	275
7	6-methyl-N-[2-(1-methylpyrrolidin-2-yl)ethyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO) δ 12.07 (s, 1H), 7.86 – 7.68 (m, 2H), 7.33 (d, J = 2.2 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 3.55 (s, 3H), 3.37 – 3.31 (m, 2H), 2.40 (t, J = 6.8 Hz, 2H), 2.19 (s, 6H).	303
8	6-methyl-N-(2-morpholinoethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO) δ 12.07 (s, 1H), 7.86 – 7.68 (m, 2H), 7.33 (d, J = 2.2 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 3.55 (s, 3H), 3.37 – 3.31 (m, 2H), 2.40 (t, J = 6.8 Hz, 2H), 2.19 (s, 6H).	305

9	6-but-2-enyl-N-[3-(4-methylpiperazin-1-yl)propyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (s, 1H), 7.93 (t, J = 5.5 Hz, 1H), 7.70 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 6.69 (d, J = 2.7 Hz, 1H), 5.67 – 5.59 (m, 2H), 4.58 – 4.51 (m, 2H), 3.27 (d, J = 7.4 Hz, 4H), 2.74 – 2.69 (m, 2H), 2.30 (h, J = 7.8, 4.6 Hz, 6H), 2.13 (d, J = 4.3 Hz, 4H), 1.73 – 1.60 (m, 5H).	372
10	tert-butyl 3-[[(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]methyl]azetidine-1-carboxylate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.08 (s, 1H), 8.10 (t, J = 5.8 Hz, 1H), 7.71 (s, 1H), 7.34 (t, J = 2.6 Hz, 1H), 6.68 (dd, J = 2.8, 1.5 Hz, 1H), 5.70 – 5.53 (m, 2H), 4.55 (dd, J = 3.5, 1.9 Hz, 2H), 3.96 – 3.79 (m, 2H), 3.72 – 3.54 (m, 2H), 3.43 (t, J = 6.3 Hz, 2H), 2.81 – 2.65 (m, 1H), 1.73 – 1.59 (m, 3H), 1.36 (s, 9H).	401
11	6-but-2-enyl-N-[(1-methyl-4-piperidyl)methyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.32 (d, J = 2.8 Hz, 1H), 7.25 (s, 1H), 6.19 (d, J = 2.8 Hz, 1H), 5.75 – 5.48 (m, 2H), 4.62 – 4.46 (m, 2H), 2.82 (s, 5H), 2.12 (s, 3H), 1.89 – 1.69 (m, 4H), 1.68 – 1.59 (m, 3H), 1.60 – 1.53 (m, 2H).	343
12	6-but-2-enyl-N-[2-(4-methylpiperazin-1-yl)ethyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75 (t, J = 5.5 Hz, 1H), 7.71 (s, 1H), 7.36 (d, J = 2.8 Hz, 1H), 6.71 (d, J = 2.8 Hz, 1H), 5.71 – 5.58 (m, 2H), 4.56 (dd, J = 3.7, 1.7 Hz, 2H), 3.41 – 3.33 (m, 6H), 2.50 – 2.41 (m, 2H), 2.40 – 2.26 (m, 4H), 2.14 (s, 3H), 1.70 – 1.60 (m, 3H).	358
13	benzyl N-[2-[[6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl]amino]ethyl]carbamate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 7.98 (t, J = 5.7 Hz, 1H), 7.73 (s, 1H), 7.38 – 7.25 (m, 7H), 6.75 – 6.69 (m, 1H), 5.67 – 5.59 (m, 2H), 5.02 (s, 2H), 4.57 – 4.50 (m, 2H), 3.32 – 3.27 (m, 2H), 3.23 – 3.14 (m, 2H), 1.68 – 1.62 (m, 3H).	409

14	N-(2-acetamidoethyl)-6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (s, 1H), 8.05 – 7.91 (m, 2H), 7.73 (s, 1H), 7.39 – 7.31 (m, 1H), 6.81 – 6.65 (m, 1H), 5.81 – 5.50 (m, 2H), 4.64 – 4.46 (m, 3H), 3.36 – 3.27 (m, 2H), 3.25 – 3.13 (m, 2H), 1.81 (s, 3H), 1.72 – 1.55 (m, 4H).	317
15	6-but-2-enyl-N-tert-butyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 7.68 (s, 1H), 7.43 – 7.15 (m, 2H), 6.63 (d, J = 2.7 Hz, 1H), 5.70 – 5.44 (m, 2H), 4.54 (dd, J = 3.9, 2.0 Hz, 2H), 1.73 – 1.59 (m, 3H), 1.38 (s, 10H).	288
16	N-[2-(4-benzylpiperazin-1-yl)ethyl]-6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.10 (s, 1H), 7.73 (d, J = 18.6 Hz, 2H), 7.38 – 7.19 (m, 7H), 6.70 (d, J = 2.8 Hz, 1H), 5.69 – 5.59 (m, 2H), 4.58 – 4.52 (m, 2H), 3.45 (s, 2H), 3.40 – 3.31 (m, 2H), 2.58 – 2.28 (m, 10H), 1.69 – 1.62 (m, 3H).	434
17	benzyl N-[3-[(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]propyl]carbamate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (s, 1H), 7.91 (t, J = 5.7 Hz, 1H), 7.72 (s, 1H), 7.41 – 7.22 (m, 7H), 6.71 (d, J = 2.8 Hz, 1H), 5.71 – 5.59 (m, 2H), 5.02 (s, 2H), 4.55 (d, J = 4.9 Hz, 2H), 3.31 – 3.21 (m, 2H), 3.12 – 3.02 (m, 2H), 1.72 – 1.61 (m, 5H).	423
18	6-but-2-enyl-N-(1-methylcyclohexyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 7.66 (s, 1H), 7.34 (d, J = 2.7 Hz, 1H), 6.99 (s, 1H), 6.60 (d, J = 2.7 Hz, 1H), 5.78 – 5.52 (m, 2H), 4.62 – 4.49 (m, 2H), 2.28 – 2.11 (m, 2H), 1.72 – 1.62 (m, 3H), 1.56 – 1.44 (m, 4H), 1.44 – 1.17 (m, 7H).	328

19	benzyl 3-[2-[(6-but-2-enyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]ethyl]pyrrolidine-1-carboxylate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 7.96 (s, 1H), 7.71 (d, J = 3.0 Hz, 1H), 7.50 – 7.18 (m, 7H), 6.71 (d, J = 2.7 Hz, 1H), 5.74 – 5.53 (m, 2H), 5.06 (s, 2H), 4.54 (s, 2H), 3.69 – 3.51 (m, 1H), 3.52 – 3.36 (m, 1H), 3.32 – 3.14 (m, 2H), 3.00 – 2.84 (m, 1H), 2.27 – 2.13 (m, 1H), 2.13 – 1.97 (m, 1H), 1.70 – 1.40 (m, 7H).	463
20	6-methyl-7-oxo-N-[2-[1-(2,2,2-trifluoroethyl)-4-piperidyl]ethyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.07 (s, 1H), 7.90 (t, J = 5.6 Hz, 1H), 7.79 (s, 1H), 7.31 (t, J = 2.5 Hz, 1H), 6.69 (dd, J = 2.9, 1.5 Hz, 1H), 3.55 (s, 3H), 3.32 – 3.22 (m, 2H), 3.11 (q, J = 10.3 Hz, 2H), 2.89 (dt, J = 12.0, 3.4 Hz, 2H), 2.28 (dd, J = 12.8, 10.1 Hz, 2H), 1.66 (dd, J = 11.8, 3.6 Hz, 2H), 1.45 (q, J = 7.1 Hz, 2H), 1.35 – 1.24 (m, 1H), 1.17 (qd, J = 11.9, 3.8 Hz, 2H).	385
21	N-[4-(dimethylamino)cyclohexyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.02 (s, 1H), 7.86 – 7.76 (m, 1H), 7.75 – 7.63 (m, 1H), 7.30 (d, J = 2.7 Hz, 1H), 6.68 (d, J = 2.7 Hz, 1H), 3.95 – 3.62 (m, 1H), 3.54 (s, 3H), 2.17 (s, 6H), 2.14 – 1.97 (m, 1H), 1.95 – 1.87 (m, 1H), 1.86 – 1.67 (m, 3H), 1.59 – 1.42 (m, 2H), 1.36 – 1.21 (m, 2H).	317
22	N-(1-benzylpyrrolidin-3-yl)-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.36 – 7.27 (m, 6H), 7.27 – 7.19 (m, 1H), 6.19 – 6.13 (m, 1H), 4.69 (s, 1H), 3.60 (d, J = 13.1 Hz, 1H), 3.54 – 3.44 (m, 4H), 2.94 (s, 3H), 2.82 – 2.71 (m, 1H), 2.71 – 2.63 (m, 1H), 2.42 (t, J = 9.2 Hz, 1H), 2.22 (q, J = 8.2 Hz, 1H), 2.07 – 1.99 (m, 1H), 1.90 – 1.76 (m, 1H).	365

23	N-[(1-isopropylpyrrolidin-3-yl)methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.10 (s, 1H), 7.39 (s, 1H), 7.32 (d, J = 2.8 Hz, 1H), 6.18 (d, J = 2.8 Hz, 1H), 3.53 (s, 3H), 3.44 – 3.36 (m, 2H), 2.94 (s, 3H), 2.47 – 2.34 (m, 3H), 2.29 – 2.16 (m, 2H), 1.87 – 1.75 (m, 1H), 1.36 – 1.25 (m, 1H), 1.02 – 0.90 (m, 7H).	331
24	6-methyl-N-[(1-methyl-3-piperidyl)methyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 7.93 (t, J = 5.8 Hz, 1H), 7.82 (s, 1H), 7.34 – 7.28 (m, 1H), 6.73 – 6.67 (m, 1H), 3.55 (s, 3H), 3.21 – 3.04 (m, 2H), 2.76 – 2.67 (m, 1H), 2.65 – 2.57 (m, 1H), 2.13 (s, 3H), 1.88 – 1.74 (m, 2H), 1.71 – 1.57 (m, 3H), 1.50 – 1.37 (m, 1H), 0.98 – 0.85 (m, 1H).	303
25	6-methyl-N-[2-(1-methyl-4-piperidyl)ethyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 7.88 (t, J = 5.6 Hz, 1H), 7.78 (s, 1H), 7.31 (t, J = 2.7 Hz, 1H), 6.69 (t, J = 2.3 Hz, 1H), 3.55 (s, 3H), 3.32 – 3.22 (m, 2H), 2.76 – 2.67 (m, 2H), 2.12 (s, 3H), 1.85 – 1.74 (m, 2H), 1.70 – 1.61 (m, 2H), 1.50 – 1.40 (m, 2H), 1.33 – 1.08 (m, 3H).	317
26	6-methyl-N-[2-(4-methyl-1-piperidyl)ethyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H), 7.80 (s, 1H), 7.75 (t, J = 5.6 Hz, 1H), 7.34 (t, J = 2.6 Hz, 1H), 6.73 – 6.67 (m, 1H), 3.55 (s, 3H), 3.40 – 3.30 (m, 2H), 2.90 – 2.81 (m, 2H), 2.44 (t, J = 6.9 Hz, 2H), 2.00 – 1.88 (m, 2H), 1.62 – 1.53 (m, 2H), 1.39 – 1.27 (m, 1H), 1.20 – 1.06 (m, 2H), 0.89 (d, J = 6.4 Hz, 3H).	317
27	N-[(1-ethylpyrrolidin-3-yl)methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.39 (s, 1H), 7.32 (d, J = 2.8 Hz, 1H), 6.18 (d, J = 2.7 Hz, 1H), 3.53 (s, 3H), 3.43 – 3.36 (m, 2H), 2.94 (s, 3H), 2.41 – 2.29 (m, 1H), 2.19 (s, 1H), 1.83 (s, 1H), 1.31 (s, 1H), 1.03 – 0.90 (m, 4H).	317

28	6-methyl-4-(7-methyl-2,7-diazaspiro[3.4]octane-2-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 7.58 (s, 1H), 7.31 (d, J = 2.7 Hz, 1H), 6.55 (d, J = 2.7 Hz, 1H), 4.06 (s, 4H), 3.55 (s, 3H), 2.63 (s, 2H), 2.44 (t, J = 7.1 Hz, 2H), 2.22 (s, 3H), 2.02 (t, J = 7.1 Hz, 2H).	301
29	6-methyl-N-[3-(2-methyl-1-piperidyl)propyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 7.94 (t, J = 5.6 Hz, 1H), 7.78 (s, 1H), 7.32 (d, 1H), 6.69 (d, J = 2.7 Hz, 1H), 3.55 (s, 3H), 3.30 – 3.19 (m, 2H), 2.83 – 2.62 (m, 2H), 2.31 – 2.19 (m, 2H), 2.10 – 1.99 (m, 1H), 1.70 – 1.46 (m, 5H), 1.46 – 1.31 (m, 1H), 1.30 – 1.10 (m, 2H), 0.98 (d, J = 6.2 Hz, 3H).	331
30	N-[2-(4-hydroxy-1-piperidyl)ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H), 7.79 (s, 1H), 7.75 (t, J = 5.5 Hz, 1H), 7.34 (d, J = 2.8 Hz, 1H), 6.70 (d, J = 2.8 Hz, 1H), 4.51 (d, J = 4.1 Hz, 1H), 3.55 (s, 3H), 3.49 – 3.38 (m, 1H), 3.38 – 3.30 (m, 2H), 2.80 – 2.70 (m, 2H), 2.44 (t, J = 6.9 Hz, 2H), 2.13 – 2.02 (m, 2H), 1.76 – 1.65 (m, 2H), 1.46 – 1.32 (m, 2H).	319
31	6-methyl-N-(3-morpholinopropyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 7.94 (t, J = 5.5 Hz, 1H), 7.79 (s, 1H), 7.32 (d, J = 2.7 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 3.59 – 3.52 (m, 7H), 3.31 – 3.23 (m, 2H), 2.39 – 2.29 (m, 6H), 1.68 (p, J = 7.1 Hz, 2H).	319
32	6-methyl-N-[2-(4-methylpiperazin-1-yl)ethyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H), 7.79 (s, 1H), 7.76 (t, J = 5.5 Hz, 1H), 7.34 (d, J = 2.7 Hz, 1H), 6.71 (d, J = 2.8 Hz, 1H), 3.55 (s, 3H), 3.41 – 3.32 (m, 2H), 2.49 – 2.42 (m, 3H), 2.32 (s, 6H), 2.15 (s, 3H).	318

33	N-[2-(3,5-dimethyl-1-piperidyl)ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H), 7.79 (s, 1H), 7.75 (t, J = 5.5 Hz, 1H), 7.34 (d, J = 2.8 Hz, 1H), 6.69 (d, J = 2.7 Hz, 1H), 3.55 (s, 3H), 3.36 (q, J = 6.5 Hz, 2H), 2.88 – 2.80 (m, 2H), 2.44 (t, J = 6.9 Hz, 2H), 1.71 – 1.52 (m, 3H), 1.46 (t, J = 10.8 Hz, 2H), 0.82 (d, J = 6.4 Hz, 6H), 0.49 (q, J = 11.7 Hz, 1H).	331
34	6-methyl-N-[3-(4-methylpiperazin-1-yl)propyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 7.94 (t, J = 5.5 Hz, 1H), 7.79 (s, 1H), 7.32 (d, J = 2.8 Hz, 1H), 6.69 (d, J = 2.7 Hz, 1H), 3.55 (s, 3H), 3.31 – 3.22 (m, 2H), 2.38 – 2.26 (m, 10H), 2.12 (s, 3H), 1.66 (p, J = 7.0 Hz, 2H).	332
35	N-(1,1-dimethyl-2-morpholino-ethyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H), 7.74 (s, 1H), 7.37 – 7.31 (m, 1H), 7.22 (s, 1H), 6.65 (d, J = 2.7 Hz, 1H), 3.59 – 3.51 (m, 7H), 2.62 (s, 2H), 2.55 – 2.49 (m, 2H), 1.36 (s, 6H).	333
36	6-methyl-N-(2-methyl-2-morpholino-propyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.20 (s, 1H), 7.81 (s, 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.34 (t, J = 5.5 Hz, 1H), 6.72 (d, J = 2.8 Hz, 1H), 3.58 (d, J = 5.9 Hz, 7H), 3.31 (s, 1H), 2.53 (t, J = 4.5 Hz, 4H), 1.02 (s, 6H).	333
37	N-[2-(1,1-dioxo-1,4-thiazinan-4-yl)ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.08 (s, 1H), 7.85 (t, J = 5.7 Hz, 1H), 7.79 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 3.55 (s, 3H), 3.37 (q, J = 6.3 Hz, 2H), 3.12 – 3.04 (m, 4H), 3.01 – 2.94 (m, 4H), 2.67 (t, J = 6.6 Hz, 2H).	353

38	6-methyl-4-(4-methylpiperazine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.13 (s, 1H), 7.42 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 6.26 (d, J = 2.8 Hz, 1H), 3.53 (s, 3H), 3.51 – 3.44 (m, 4H), 2.30 (t, J = 5.0 Hz, 4H), 2.19 (s, 3H).	275
39	N,6-dimethyl-N-(1-methyl-4-piperidyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.36 (s, 1H), 7.31 (d, J = 2.6 Hz, 1H), 6.18 (d, J = 2.7 Hz, 1H), 3.95 (s, 1H), 3.52 (s, 3H), 2.84 – 2.76 (m, 5H), 2.12 (s, 3H), 1.85 – 1.73 (m, 4H), 1.61 – 1.54 (m, 2H).	303
40	4-[4-(dimethylamino)piperidine-1-carbonyl]-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.41 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 6.24 (d, J = 2.8 Hz, 1H), 4.04 (s, 2H), 3.53 (s, 3H), 2.97 – 2.86 (m, 2H), 2.36 – 2.24 (m, 1H), 2.16 (s, 6H), 1.75 (d, J = 12.2 Hz, 2H), 1.38 – 1.23 (m, 2H).	303
41	N-(1-isopropyl-4-piperidyl)-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.36 (s, 1H), 7.32 (t, J = 2.7 Hz, 1H), 6.21 – 6.15 (m, 1H), 3.93 (s, 1H), 3.52 (s, 3H), 2.85 – 2.77 (m, 5H), 2.66 (p, J = 6.6 Hz, 1H), 2.10 – 2.02 (m, 2H), 1.81 – 1.66 (m, 2H), 1.65 – 1.57 (m, 2H), 0.92 (d, J = 6.5 Hz, 6H).	331
42	6-methyl-7-oxo-N-[1-(2-pyridyl)-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 8.14 – 8.07 (m, 1H), 7.84 – 7.77 (m, 2H), 7.57 – 7.47 (m, 1H), 7.30 (t, J = 2.7 Hz, 1H), 6.87 (d, J = 8.6 Hz, 1H), 6.70 (t, J = 2.4 Hz, 1H), 6.64 – 6.56 (m, 1H), 4.33 – 4.24 (m, 2H), 4.13 – 3.98 (m, 1H), 3.54 (s, 3H), 3.02 – 2.89 (m, 2H), 1.91 – 1.82 (m, 2H), 1.59 – 1.44 (m, 2H).	352

43	N-(1-cyclopentyl-4-piperidyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 7.80 (s, 1H), 7.30 (t, J = 2.8 Hz, 1H), 6.68 (t, J = 2.4 Hz, 1H), 3.72 (s, 1H), 3.55 (s, 3H), 3.28 (s, 2H), 2.98 – 2.93 (m, 2H), 1.84 – 1.79 (m, 4H), 1.63 – 1.58 (m, 2H), 1.56 – 1.46 (m, 3H), 1.38 – 1.33 (m, 2H).	343
44	6-methyl-7-oxo-N-(1-pyrimidin-2-yl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 8.36 (d, J = 4.7 Hz, 2H), 7.84 – 7.77 (m, 2H), 7.30 (t, J = 2.7 Hz, 1H), 6.70 (t, J = 2.4 Hz, 1H), 6.60 (t, J = 4.7 Hz, 1H), 4.67 – 4.57 (m, 2H), 4.16 – 4.01 (m, 1H), 3.54 (s, 3H), 3.12 – 3.00 (m, 2H), 1.93 – 1.84 (m, 2H), 1.54 – 1.39 (m, 2H).	353
45	6-methyl-N-[2-(3-methyl-1-piperidyl)ethyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H), 7.79 (s, 1H), 7.74 (t, J = 5.5 Hz, 1H), 7.34 (d, J = 2.8 Hz, 1H), 6.70 (d, J = 2.8 Hz, 1H), 3.55 (s, 3H), 3.41 – 3.31 (m, 2H), 2.85 – 2.76 (m, 2H), 2.43 (t, J = 6.9 Hz, 2H), 1.94 – 1.83 (m, 1H), 1.69 – 1.38 (m, 6H), 0.84 (d, J = 6.1 Hz, 3H).	317
46	6-methyl-4-[4-(3-pyridylmethyl)piperidine-1-carbonyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 8.50 – 8.34 (m, 2H), 7.64 – 7.55 (m, 1H), 7.39 (s, 1H), 7.37 – 7.25 (m, 2H), 6.24 (d, J = 2.8 Hz, 1H), 4.32 – 3.84 (m, 2H), 3.53 (s, 3H), 2.85 (t, J = 12.2 Hz, 2H), 2.55 (d, J = 7.1 Hz, 2H), 1.87 – 1.70 (m, 1H), 1.57 (d, J = 12.8 Hz, 2H), 1.23 – 1.03 (m, 2H).	351.18
47	4-(4-tert-butylpiperidine-1-carbonyl)-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 7.39 (s, 1H), 7.32 (d, J = 2.7 Hz, 1H), 6.21 (d, J = 2.7 Hz, 1H), 4.11 (d, J = 16.3 Hz, 2H), 3.52 (s, 3H), 2.90 – 2.82 (m, 2H), 1.81 – 1.58 (m, 2H), 1.33 – 1.17 (m, 1H), 1.17 – 1.01 (m, 2H), 0.84 (s, 9H), 0.81 (d, J = 2.8 Hz, 1H).	316.2

48	4-[4-(4-chlorophenyl)piperidine-1-carbonyl]-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 7.46 (s, 1H), 7.39 – 7.27 (m, 5H), 6.35 – 6.28 (m, 1H), 4.19 (s, 2H), 3.54 (s, 3H), 3.00 (t, J = 12.7 Hz, 2H), 2.88 – 2.75 (m, 1H), 1.78 (d, J = 12.7 Hz, 2H), 1.64 – 1.48 (m, 2H).	370.13
49	4-[4-(3-fluorophenyl)piperidine-1-carbonyl]-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 7.46 (s, 1H), 7.40 – 7.29 (m, 2H), 7.17 – 7.10 (m, 2H), 7.07 – 6.98 (m, 1H), 6.34 (d, J = 2.8 Hz, 1H), 4.20 (s, 2H), 3.54 (s, 3H), 3.08 – 2.93 (m, 2H), 2.89 (t, J = 5.6 Hz, 1H), 1.80 (d, J = 13.2 Hz, 2H), 1.68 – 1.51 (m, 2H).	354.16
50	4-[4-(benzimidazol-1-yl)piperidine-1-carbonyl]-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.18 (s, 1H), 8.39 (s, 1H), 7.74 – 7.61 (m, 2H), 7.50 (s, 1H), 7.36 (d, J = 2.8 Hz, 1H), 7.32 – 7.16 (m, 2H), 6.39 (d, J = 2.8 Hz, 1H), 4.77 – 4.63 (m, 1H), 4.29 (d, J = 15.4 Hz, 2H), 3.56 (s, 3H), 3.17 (t, J = 12.7 Hz, 2H), 2.20 – 1.89 (m, 4H).	376.18
51	6-methyl-4-(4-pyrazin-2-ylpiperidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 8.64 (d, J = 1.5 Hz, 1H), 8.61 – 8.56 (m, 1H), 8.50 (d, J = 2.5 Hz, 1H), 7.46 (s, 1H), 7.35 (t, J = 2.6 Hz, 1H), 6.33 – 6.28 (m, 1H), 4.20 (s, 2H), 3.54 (s, 3H), 3.15 – 2.99 (m, 3H), 1.89 (d, J = 12.8 Hz, 2H), 1.79 – 1.60 (m, 2H).	338.16
52	4-[4-[cyclohexyl(methyl)amino]piperidine-1-carbonyl]-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.42 (s, 1H), 7.38 – 7.29 (m, 1H), 6.24 (d, J = 2.8 Hz, 1H), 4.27 – 3.88 (m, 2H), 3.53 (d, J = 2.2 Hz, 3H), 2.95 – 2.84 (m, 2H), 2.75 – 2.65 (m, 1H), 2.14 (d, J = 5.0 Hz, 3H), 1.69 (d, J = 18.6 Hz, 6H), 1.55 (d, J = 12.3 Hz, 2H), 1.44 – 1.31 (m, 1H), 1.30 – 1.12 (m, 4H), 1.05 (s, 2H).	371.24

53	4-(4-fluoropiperidine-1-carbonyl)-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.21 (d, J = 46.1 Hz, 1H), 7.56 – 7.18 (m, 2H), 6.28 (d, J = 2.8 Hz, 1H), 5.07 – 4.68 (m, 1H), 3.59 (d, J = 9.9 Hz, 2H), 3.53 (s, 3H), 3.51 – 3.43 (m, 2H), 1.98 – 1.78 (m, 2H), 1.78 – 1.60 (m, 2H).	278.13
54	N-[2-[1-(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)-4-piperidyl]ethyl]methanesulfonamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 7.39 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 6.25 (d, J = 2.7 Hz, 1H), 4.06 (s, 2H), 3.53 (s, 3H), 3.15 – 3.05 (m, 1H), 3.03 – 2.92 (m, 4H), 1.80 – 1.58 (m, 5H), 1.48 – 1.37 (m, 3H), 1.13 – 1.02 (m, 2H).	381.16
55	6-methyl-4-[4-(2-pyridyl)piperidine-1-carbonyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 8.55 – 8.46 (m, 1H), 7.77 – 7.68 (m, 1H), 7.46 (d, J = 1.2 Hz, 1H), 7.37 – 7.26 (m, 2H), 7.26 – 7.19 (m, 1H), 6.32 – 6.28 (m, 1H), 4.18 (s, 2H), 3.54 (d, J = 1.2 Hz, 3H), 3.11 – 2.92 (m, 3H), 1.92 – 1.79 (m, 2H), 1.77 – 1.61 (m, 2H).	337.17
56	6-methyl-4-(4-pyrimidin-4-ylpiperidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.16 (s, 1H), 9.21 – 9.00 (m, 1H), 8.86 – 8.61 (m, 1H), 7.51 – 7.44 (m, 2H), 7.35 (d, J = 2.7 Hz, 1H), 6.29 (d, J = 2.7 Hz, 1H), 4.19 (s, 2H), 3.54 (s, 2H), 3.11 – 2.92 (m, 3H), 2.92 – 2.82 (m, 1H), 1.96 – 1.83 (m, 2H), 1.77 – 1.59 (m, 2H).	338.16
57	6-methyl-4-[4-(trifluoromethyl)piperidine-1-carbonyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.16 (s, 1H), 7.47 (s, 1H), 7.34 (d, J = 2.8 Hz, 1H), 6.25 (d, J = 2.8 Hz, 1H), 4.15 (s, 2H), 3.53 (s, 3H), 2.95 (t, J = 13.2 Hz, 2H), 2.70 – 2.57 (m, 1H), 1.84 (d, J = 12.5 Hz, 2H), 1.48 – 1.29 (m, 2H).	328.13

58	6-methyl-4-[4-(2-pyridylmethyl)piperidine-1-carbonyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 8.52 – 8.43 (m, 1H), 7.73 – 7.62 (m, 1H), 7.39 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 7.27 – 7.13 (m, 2H), 6.24 (d, J = 2.7 Hz, 1H), 4.02 (s, 2H), 3.52 (s, 3H), 2.88 (d, J = 12.3 Hz, 2H), 2.68 (d, J = 7.1 Hz, 2H), 2.43 – 2.30 (m, 0H), 2.15 – 1.88 (m, 1H), 1.57 (d, J = 12.8 Hz, 2H), 1.27 – 1.09 (m, 2H).	351.2
59	6-methyl-4-[4-(1-piperidyl)piperidine-1-carbonyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.13 (s, 1H), 7.41 (s, 1H), 7.35 – 7.31 (m, 1H), 6.24 (d, J = 2.7 Hz, 1H), 4.06 (s, 2H), 3.53 (s, 3H), 2.85 (d, J = 11.6 Hz, 2H), 2.46 – 2.36 (m, 5H), 1.72 (d, J = 12.3 Hz, 2H), 1.47 (t, J = 5.5 Hz, 4H), 1.41 – 1.32 (m, 4H).	343.2
60	4-[3-(dimethylamino)pyrrolidine-1-carbonyl]-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.10 (s, 1H), 7.52 (s, 1H), 7.31 (d, J = 2.8 Hz, 1H), 6.33 (d, J = 2.7 Hz, 1H), 3.53 (s, 3H), 3.33 (s, 1H), 2.87 (s, 3H), 2.77 – 2.55 (m, 1H), 2.17 – 1.95 (m, 7H), 1.89 – 1.65 (m, 1H).	289.2
61	6-methyl-4-[4-(4-methylpiperazin-1-yl)piperidine-1-carbonyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.13 (s, 1H), 7.41 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 6.24 (d, J = 2.8 Hz, 1H), 4.05 (s, 2H), 3.53 (s, 4H), 2.97 – 2.80 (m, 4H), 2.35 – 2.18 (m, 4H), 2.13 (d, J = 4.6 Hz, 5H), 1.81 – 1.70 (m, 2H), 1.42 – 1.23 (m, 2H).	358.2
62	6-methyl-4-[4-(4-methyl-1-piperidyl)piperidine-1-carbonyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 7.40 (s, 1H), 7.32 (d, J = 2.8 Hz, 1H), 6.23 (d, J = 2.8 Hz, 1H), 3.52 (s, 3H), 3.00 – 2.72 (m, 6H), 2.49 – 2.39 (m, 2H), 2.17 – 2.01 (m, 2H), 1.86 – 1.64 (m, 2H), 1.64 – 1.50 (m, 2H), 1.47 – 1.17 (m, 2H), 1.17 – 0.96 (m, 2H), 0.96 – 0.79 (m, 3H).	357.2

63	6-methyl-4-(4-morpholinopiperidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.42 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 2.47 – 2.46 (m, 0H), 6.25 (d, J = 2.7 Hz, 1H), 4.08 (d, J = 16.5 Hz, 2H), 3.54 (d, J = 11.3 Hz, 8H), 3.01 – 2.81 (m, 3H), 2.45 (d, J = 4.7 Hz, 3H), 1.79 (d, J = 12.5 Hz, 2H), 1.32 (q, J = 14.3, 12.7 Hz, 2H).	345.2
64	1-(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)piperidine-4-carbonitrile	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.16 (s, 1H), 7.45 (s, 1H), 7.34 (d, J = 2.7 Hz, 1H), 6.29 (d, J = 2.7 Hz, 1H), 3.70 (s, 2H), 3.53 (s, 3H), 3.32 (s, 2H), 3.13 (m, J = 8.7, 4.5 Hz, 1H), 1.97 – 1.83 (m, 2H), 1.71 (m, J = 13.7, 9.2, 4.5 Hz, 2H).	285.2
65	6-methyl-4-(4-methylpiperidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 7.38 (s, 1H), 7.32 (d, J = 2.7 Hz, 1H), 6.23 (d, J = 2.7 Hz, 1H), 3.52 (s, 3H), 2.95 – 2.82 (m, 4H), 1.72 – 1.54 (m, 4H), 1.12 – 0.98 (m, 2H), 0.91 (d, J = 6.0 Hz, 3H).	274.2
66	4-(4-methoxypiperidine-1-carbonyl)-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.42 (s, 1H), 7.36 – 7.30 (m, 1H), 6.25 (d, J = 2.7 Hz, 1H), 3.71 (d, J = 10.6 Hz, 2H), 3.53 (s, 3H), 3.47 – 3.36 (m, 1H), 3.25 (s, 3H), 3.25 – 3.17 (m, 2H), 1.88 – 1.78 (m, 2H), 1.48 – 1.34 (m, 2H).	290.2
67	6-methyl-4-[4-(3-methyl-1-piperidyl)piperidine-1-carbonyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 7.40 (s, 1H), 7.32 (d, J = 2.7 Hz, 1H), 6.23 (d, J = 2.7 Hz, 1H), 4.06 (s, 2H), 3.52 (s, 3H), 2.86 (d, J = 4.2 Hz, 2H), 2.80 – 2.69 (m, 3H), 2.12 – 1.95 (m, 2H), 1.84 – 1.67 (m, 4H), 1.44 – 1.29 (m, 4H), 0.89 – 0.76 (m, 5H).	357.2

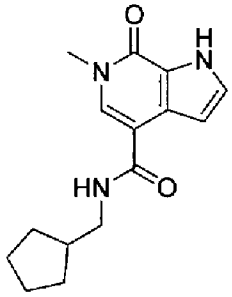
68	4-[4-(1-hydroxy-1-methyl-ethyl)piperidine-1-carbonyl]-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.40 (s, 1H), 7.33 (d, J = 2.7 Hz, 1H), 6.23 (d, J = 2.8 Hz, 1H), 4.14 (s, 2H), 3.53 (s, 3H), 2.95 – 2.85 (m, 1H), 2.84 – 2.71 (m, 2H), 1.81 – 1.61 (m, 2H), 1.50 – 1.34 (m, 1H), 1.22 – 1.08 (m, 2H), 1.03 (s, 6H).	318.2
69	4-[4-[(4-fluorophenyl)methyl]piperidine-1-carbonyl]-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.39 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 7.20 (m, J = 9.1, 5.7, 2.8 Hz, 2H), 7.14 – 7.04 (m, 2H), 6.24 (d, J = 2.7 Hz, 1H), 4.02 (s, 2H), 3.52 (s, 3H), 2.84 (t, J = 12.7 Hz, 2H), 2.53 (s, 2H), 1.74 (m, J = 11.3, 4.9 Hz, 1H), 1.57 (d, J = 13.0 Hz, 2H), 1.13 (m, J = 13.6, 6.7 Hz, 2H).	368.2
70	6-methyl-4-(piperidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.39 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 6.24 (d, J = 2.7 Hz, 1H), 3.53 (s, 3H), 3.44 (t, J = 5.3 Hz, 2H), 2.88 (d, J = 10.4 Hz, 2H), 1.76 – 1.55 (m, 2H), 1.55 – 1.37 (m, 4H).	260.2
71	6-methyl-4-(4-phenylpiperidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 7.46 (s, 1H), 7.35 (d, J = 2.8 Hz, 1H), 7.33 – 7.24 (m, 4H), 7.24 – 7.16 (m, 1H), 6.32 (d, J = 2.7 Hz, 1H), 4.20 (s, 2H), 3.54 (s, 3H), 3.01 (t, J = 12.6 Hz, 2H), 2.87 – 2.73 (m, 1H), 1.79 (d, J = 12.8 Hz, 2H), 1.68 – 1.47 (m, 2H).	336.2
72	4-[4-(methoxymethyl)piperidine-1-carbonyl]-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 7.39 (s, 1H), 7.33 (d, J = 2.7 Hz, 1H), 6.24 (d, J = 2.7 Hz, 1H), 4.05 (s, 2H), 3.53 (s, 3H), 3.24 (d, J = 7.3 Hz, 4H), 3.19 (d, J = 6.3 Hz, 2H), 2.88 – 2.77 (m, 2H), 1.66 (d, J = 12.8 Hz, 2H), 1.21 – 1.00 (m, 2H).	304.2

73	6-methyl-4-(2-oxa-7-azaspiro[3.5]nonane-7-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 7.40 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 6.25 (d, J = 2.8 Hz, 1H), 4.33 (s, 4H), 3.52 (s, 3H), 3.40 (t, J = 5.7 Hz, 4H), 1.83 – 1.72 (m, 4H).	302.1
74	N,N-dimethyl-1-(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)piperidine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 7.43 (s, 1H), 7.34 (t, J = 2.2 Hz, 1H), 6.23 (d, J = 2.7 Hz, 1H), 4.07 (s, 2H), 3.53 (s, 3H), 3.08 – 2.71 (m, 7H), 2.64 (d, J = 8.0 Hz, 2H), 1.64 (t, J = 8.0 Hz, 2H), 1.57 – 1.35 (m, 2H), 1.10 (s, 0H).	331.2
75	4-[4-(hydroxymethyl)piperidine-1-carbonyl]-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.40 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 6.24 (d, J = 2.7 Hz, 1H), 4.49 (d, J = 5.7 Hz, 1H), 4.06 (s, 2H), 3.53 (s, 3H), 3.28 – 3.17 (m, 2H), 2.92 – 2.81 (m, 2H), 1.76 – 1.53 (m, 3H), 1.17 – 0.96 (m, 2H).	290.2
76	6-methyl-4-[4-[2-(4-pyridyl)ethyl]piperidine-1-carbonyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 8.49 – 8.39 (m, 2H), 7.40 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 7.24 (d, J = 5.6 Hz, 1H), 6.25 (d, J = 2.9 Hz, 1H), 4.05 (s, 2H), 3.53 (s, 3H), 2.96 – 2.74 (m, 2H), 2.68 – 2.54 (m, 2H), 7.22 – 7.17 (m, 0H), 1.73 (d, J = 12.5 Hz, 2H), 1.65 – 1.39 (m, 4H), 1.20 – 0.99 (m, 2H).	365.2
77	6-methyl-4-(4-pyrrolidin-1-ylpiperidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.41 (s, 1H), 7.33 (d, J = 2.8 Hz, 1H), 6.24 (d, J = 2.8 Hz, 1H), 3.93 (s, 2H), 3.53 (s, 3H), 3.08 – 2.96 (m, 2H), 2.48 – 2.44 (m, 4H), 2.26 – 2.15 (m, 1H), 1.86 – 1.78 (m, 2H), 1.72 – 1.62 (m, 4H), 1.43 – 1.28 (m, 2H).	329.2

78	4-[4-(dimethylamino)-3-methyl-piperidine-1-carbonyl]-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d6) δ 7.38 (s, 1H), 7.32 (d, J = 2.7 Hz, 1H), 6.21 (d, J = 2.7 Hz, 1H), 3.53 (s, 3H), 2.86 (d, J = 17.9 Hz, 2H), 2.15 (m, 2H), 2.12 (s, 6H), 1.95 (dt, J = 11.5, 4.0 Hz, 1H), 1.69 (d, J = 12.7 Hz, 1H), 1.33 (dt, J = 12.5, 6.3 Hz, 1H), 0.80 (dd, J = 22.1, 6.9 Hz, 4H).	317.2
79	4-[4-(diethylamino)piperidine-1-carbonyl]-6-methyl-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d6) δ 12.19 (s, 1H), 7.44 (s, 1H), 7.35 (t, J = 2.8 Hz, 1H), 6.29 (t, J = 2.4 Hz, 1H), 4.16 (m, 2H), 3.54 (s, 3H), 3.11 – 2.80 (m, 6H), 1.93 (s, 2H), 1.55 (s, 2H), 1.18 (t, J = 7.1 Hz, 6H).	331.2
80	6-methyl-N-(m-tolyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) d 12.07 - 12.21 (m, 1H), 9.84 (s, 1H), 8.03 (s, 1H), 7.57 (s, 1H), 7.48 - 7.53 (m, 1H), 7.35 (t, J = 2.70 Hz, 1H), 7.22 (s, 1H), 6.86 - 6.92 (m, 1H), 6.72 (t, J = 2.39 Hz, 1H), 3.60 (s, 3H), 2.31 (s, 3H).	282
81	N-cyclopropyl-6-methyl-N-(1-methyl-4-piperidyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 7.93 (d, J = 4.2 Hz, 1H), 7.76 (s, 1H), 7.33 – 7.27 (m, 1H), 6.72 – 6.66 (m, 1H), 3.53 (s, 3H), 3.06 (d, J = 8.7 Hz, 2H), 2.95 (d, J = 3.8 Hz, 1H), 2.42 – 2.32 (m, 3H), 1.57 (s, 2H), 0.98 (d, J = 6.2 Hz, 6H).	328
82	N-cyclopropyl-6-methyl-7-oxo-N-(1-propyl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 7.45 (s, 1H), 7.28 (d, J = 2.8 Hz, 1H), 6.25 (d, J = 2.7 Hz, 1H), 3.89 (tt, J = 12.1, 3.9 Hz, 1H), 3.53 (s, 3H), 3.30 (d, J = 16.5 Hz, 2H), 2.96 – 2.89 (m, 2H), 2.72 – 2.61 (m, 1H), 2.26 – 2.17 (m, 2H), 2.10 – 1.95 (m, 2H), 1.94 – 1.83 (m, 2H), 1.82 – 1.74 (m, 2H), 1.50 – 1.36 (m, 2H), 0.85 (t, J = 7.4 Hz, 3H), 0.61 – 0.51 (m, 2H), 0.47 – 0.38 (m, 2H).	356

Example 83

N-(cyclopentylmethyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



To a 1 dram vial was added cyclopentylmethanamine hydrochloride (34 mg, 0.25 mmol) followed by 6-methyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxylic acid **(Intermediate E)** (Step 1, 0.5 mL, 0.25 mmol, 0.5 M in DMF), HATU (0.76 mL, 0.38 mmol, 0.5 M in DMF) and triethylamine (3 equiv., 0.75mmol). The reaction was shaken at room temperature overnight. The DMF was removed under reduced pressure, and then methanol (1.5 mL) and potassium hydroxide (1 mL, 1.0 mmol, 1M in water) were added. The reaction was heated at 60°C overnight. After cooling the reaction was partitioned between dichloromethane and water. The organic solution was separated and concentrated under reduced pressure. The residue was purified by reverse phase chromatography (5-85%ACN/0.1%NH4OH in H2O) yielding N-(cyclopentylmethyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide. (7.5 mg, 11%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 7.93 (t, J = 5.8 Hz, 1H), 7.79 (s, 1H), 7.31 (t, J = 2.4 Hz, 1H), 6.72 – 6.66 (m, 1H), 3.55 (s, 3H), 3.23 – 3.07 (m, 2H), 2.14 (p, J = 7.4 Hz, 1H), 1.76 – 1.65 (m, 2H), 1.65 – 1.44 (m, 4H), 1.33 – 1.19 (m, 2H). LCMS M/Z (M+H) 274.

The following compounds were prepared in a similar manner to Example 83:

Examples 84-138

Example	Compound Name	NMR	m/z
84	N-(2-methoxyethyl)-6-methyl-N-(1-methyl-4-piperidyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.37 – 7.24 (m, 2H), 6.17 (dd, J = 2.7, 1.9 Hz, 1H), 3.71 (d, J = 12.1 Hz, 1H), 3.52 (s, 3H), 3.49 – 3.36 (m, 2H), 3.23 (s, 2H), 2.95 – 2.77 (m, 2H), 2.18 (s, 2H), 1.98 – 1.80 (m, 4H), 1.71 – 1.56 (m, 2H).	346

85	6-methyl-4-(2-phenylpyrrolidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d6) δ 12.07 (br. s., 1H), 7.48 - 7.85 (m, 1H), 7.09 - 7.44 (m, 6H), 6.34 (br. s., 1H), 5.27 - 6.10 (m, 3H), 5.14 (br. s., 1H), 3.82 (br. s., 1H), 3.38 - 3.73 (m, 2H), 2.37 (dd, J = 6.23, 12.46 Hz, 1H), 1.66 - 1.97 (m, 2H).	322
86	N-(cyclohexylmethyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) d 11.96 (bs, 1H), 7.81 (t, J = 5.49 Hz, 1H), 7.71 (s, 1H), 7.19 - 7.23 (m, 1H), 6.59 (d, J = 2.44 Hz, 1H), 3.50-4.00 (bs, 3H), 2.98 (t, J = 6.35 Hz, 2H), 1.34 - 1.72 (m, 6H), 0.98 - 1.15 (m, 3H), 0.70 - 0.90 (m, 2H).	288
87	N-benzyl-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) d 12.05 (br. s., 1H), 7.39 (s, 1H), 7.05 - 7.33 (m, 6H), 6.14 (bs, 1H), 4.54 (s, 2H), 3.27 - 3.50 (m, 3H), 2.65 - 2.86 (m, 3H).	296
88	6-methyl-4-(1,2,3,5-tetrahydro-1,4-benzodiazepine-4-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d6) δ 12.14 (br. s., 1H), 7.28 - 7.34 (m, 1H), 7.14 - 7.27 (m, 1H), 7.06 (t, J = 7.48 Hz, 1H), 6.85 (d, J = 7.89 Hz, 1H), 6.74 (br. s., 1H), 6.20 - 6.24 (m, 1H), 4.56 (br. s., 2H), 3.70 (br. s., 1H), 3.45 (s, 3H), 3.15 (br. s., 2H).	323
89	6-methyl-4-(3-phenylpyrrolidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400MHz ,DMSO-d6) d = 12.09 (br. s., 1 H), 7.55 (s, 1 H), 7.39 - 7.26 (m, 5 H), 7.26 - 7.18 (m, 1 H), 6.38 (t, J = 2.4 Hz, 1 H), 3.88 (br. s, 1 H), 3.73 - 3.31 (m, 7 H), 2.26 (br. s., 1 H), 2.07 (s, 1 H).	322
90	N-[(1S)-2-amino-2-oxo-1-phenyl-ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.00 - 12.38 (m, 1H), 8.16 - 8.25 (m, 1H), 8.04 (s, 1H), 7.72 - 7.81 (m, 1H), 7.47 - 7.56 (m, 2H), 7.36 (s, 5H), 6.67 - 6.72 (m, 1H), 5.56 - 5.63 (m, 1H), 3.56 (s, 3H).	325

91	N-benzhydryl-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 11.95 - 12.18 (m, 1H), 8.69 - 8.87 (m, 1H), 8.05 (s, 1H), 7.32 - 7.41 (m, 7H), 7.30 (s, 3H), 6.64 - 6.73 (m, 1H), 6.33 - 6.41 (m, 1H), 3.56 (s, 3H).	358
92	6-methyl-N-[(4-methylsulfonylphenyl)methyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400MHz, DMSO-d6) d = 12.12 (br. s., 1 H), 8.65 (t, J = 5.9 Hz, 1 H), 7.94 (s, 1 H), 7.92 - 7.85 (m, 2 H), 7.60 (d, J = 8.5 Hz, 2 H), 7.33 (t, J = 2.8 Hz, 1 H), 6.80 - 6.69 (m, 1 H), 4.56 (d, J = 5.8 Hz, 2 H), 3.56 (s, 3 H), 3.19 (s, 3 H).	360
93	methyl (2S)-2-cyclohexyl-2-[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]acetate	^{1}H NMR (400 MHz, DMSO-d6) δ 12.09 (br. s., 1H), 8.08 (d, J = 7.69 Hz, 1H), 7.97 (s, 1H), 7.32 (t, J = 2.80 Hz, 1H), 6.68 (t, J = 2.39 Hz, 1H), 4.33 (t, J = 7.69 Hz, 1H), 3.65 (s, 3H), 3.57 (s, 3H), 1.56 - 1.88 (m, 4H), 1.00 - 1.30 (m, 6H).	346
94	N-[(1R)-1-cyclohexylethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	. ^{1}H NMR (400 MHz, DMSO-d6) δ 12.05 (br. s., 1H), 7.81 (s, 1H), 7.63 (d, J = 8.52 Hz, 1H), 7.30 (t, J = 2.70 Hz, 1H), 6.68 (t, J = 2.39 Hz, 1H), 3.77 - 3.91 (m, 1H), 3.53 - 3.58 (m, 3H), 1.66 - 1.81 (m, 4H), 1.61 (d, J = 9.14 Hz, 1H), 1.39 (dd, J = 3.43, 7.17 Hz, 1H), 1.12 - 1.26 (m, 2H), 1.09 (d, J = 6.65 Hz, 3H), 0.89 - 1.04 (m, 2H).	302
95	N-[(1S)-2-methoxy-1-phenyl-ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.09 (br. s., 1H), 8.33 (d, J = 8.10 Hz, 1H), 7.94 (s, 1H), 7.39 - 7.46 (m, 2H), 7.29 - 7.38 (m, 3H), 7.21 - 7.28 (m, 1H), 6.68 (t, J = 2.39 Hz, 1H), 5.21 - 5.30 (m, 1H), 3.64 - 3.71 (m, 1H), 3.58 (s, 3H), 3.53 - 3.57 (m, 2H), 3.30 (s, 3H).	326

96	(2S)-2-[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]-2-phenyl-acetic acid	^{1}H NMR (400 MHz, DMSO-d6) δ 12.94 (br. s., 1H), 12.10 (br. s., 1H), 8.48 (d, J = 7.27 Hz, 1H), 8.04 (s, 1H), 7.50 (d, J = 7.27 Hz, 2H), 7.31 - 7.43 (m, 3H), 6.73 (s, 1H), 5.56 (d, J = 7.06 Hz, 1H), 3.34 (br. s., 3H).	326
97	N-[(1R)-2-amino-2-oxo-1-phenyl-ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.15 (br. s., 1H), 8.21 (d, J = 7.48 Hz, 1H), 8.04 (s, 1H), 7.76 (s, 1H), 7.51 (d, J = 7.27 Hz, 2H), 7.34 - 7.39 (m, 3H), 7.26 - 7.32 (m, 2H), 6.70 (t, J = 2.39 Hz, 1H), 5.60 (d, J = 7.69 Hz, 1H), 3.56 (s, 3H).	325
98	N-[(1S)-1-carbamoyl-2-methyl-propyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.14 (br. s., 1H), 7.96 (s, 1H), 7.57 (d, J = 8.72 Hz, 1H), 7.52 (s, 1H), 7.35 (t, J = 2.80 Hz, 1H), 7.13 (s, 1H), 6.68 (t, J = 2.29 Hz, 1H), 4.35 (dd, J = 6.65, 8.72 Hz, 1H), 3.55 - 3.60 (m, 3H), 2.03 - 2.14 (m, 1H), 0.93 (t, J = 6.54 Hz, 6H).	291
99	1-(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)pyrrolidine-2-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.06 (br. s., 1H), 7.57 (br. s., 1H), 7.24 - 7.40 (m, 2H), 6.94 (br. s., 1H), 6.39 (br. s., 1H), 4.41 (br. s., 1H), 3.60 (br. s., 2H), 2.11 - 2.25 (m, 1H), 1.68 - 1.94 (m, 3H).	289
100	6-methyl-7-oxo-N-(tetrahydropyran-3-ylmethyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.06 (br. s., 1H), 7.96 (t, J = 5.82 Hz, 1H), 7.81 (s, 1H), 7.31 (t, J = 2.80 Hz, 1H), 6.58 - 6.74 (m, 1H), 3.76 - 3.84 (m, 1H), 3.71 (td, J = 3.61, 11.06 Hz, 1H), 3.54 (s, 3H), 3.31 (dt, J = 2.80, 10.75 Hz, 1H), 3.00 - 3.19 (m, 3H), 1.71 - 1.87 (m, 2H), 1.53 - 1.64 (m, 1H), 1.45 (m, 1H), 1.13 - 1.32 (m, 1H).	290

101	6-methyl-7-oxo-N-(tetrahydropyran-4-ylmethyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) d 12.06 (bs, 1H), 7.98 (t, J = 5.77 Hz, 1H), 7.82 (s, 1H), 7.30 (t, J = 2.61 Hz, 1H), 6.68 (t, J = 2.47 Hz, 1H), 3.60 - 3.97 (m, 5H), 3.26 (dt, J = 1.79, 11.60 Hz, 2H), 3.13 (t, J = 6.32 Hz, 2H), 1.76 (dt, J = 4.12, 7.55 Hz, 1H), 1.60 (d, J = 12.91 Hz, 2H), 1.05 - 1.32 (m, 3H).	290
102	6-methyl-7-oxo-N-(tetrahydrofuran-3-ylmethyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) d 12.07 (br. s., 1H), 8.06 (t, J = 5.91 Hz, 1H), 7.80 (s, 1H), 7.31 (t, J = 2.75 Hz, 1H), 6.68 (t, J = 2.47 Hz, 1H), 3.57 - 3.80 (m, 2H), 3.54 (s, 2H), 3.47 (dd, J = 5.22, 8.51 Hz, 1H), 3.10 - 3.27 (m, 1H), 1.94 (dd, J = 5.63, 12.22 Hz, 1H), 1.45 - 1.70 (m, 1H).	276
103	N-(cycloheptylmethyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) d 12.06 (bs, 1H), 7.93 (t, J = 5.77 Hz, 1H), 7.81 (s, 1H), 7.31 (t, J = 2.75 Hz, 1H), 6.68 (t, J = 2.33 Hz, 1H), 3.07 (t, J = 6.04 Hz, 2H), 1.26 - 1.75 (m, 11H), 1.04 - 1.25 (m, 2H).	302
104	6-methyl-7-oxo-N-tetrahydrofuran-3-yl-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) d 12.05 (bs, 1H), 8.09 (d, J = 6.32 Hz, 1H), 7.86 (s, 1H), 7.30 (t, J = 2.61 Hz, 1H), 6.69 (s, 1H), 4.43 (d, J = 5.77 Hz, 1H), 3.78 - 3.92 (m, 2H), 3.65 - 3.78 (m, 2H), 2.14 (dd, J = 7.14, 12.63 Hz, 1H), 1.71 - 1.97 (m, 1H).	262
105	N-[(1,1-dioxothiolan-3-yl)methyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.10 (br. s., 1H), 8.16 (t, J = 5.71 Hz, 1H), 7.84 (s, 1H), 7.33 (t, J = 2.80 Hz, 1H), 6.70 (t, J = 2.18 Hz, 1H), 3.54 - 3.58 (m, 3H), 3.30 - 3.44 (m, 2H), 3.16 - 3.30 (m, 2H), 3.02 - 3.13 (m, 1H), 2.87 (dd, J = 9.56, 13.09 Hz, 1H), 2.60 - 2.73 (m, 1H), 2.24 (d, J = 4.78 Hz, 1H), 1.79 - 1.92 (m, 1H).	324

106	6-methyl-N-(1-norbornan-2-ylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.05 (br. s., 1H), 7.75 - 7.82 (m, 1H), 7.57 - 7.74 (m, 1H), 7.23 - 7.36 (m, H), 6.59 - 6.75 (m, 1H), 3.60 - 3.92 (m, 2H), 3.52 - 3.58 (m, 3H), 2.10 - 2.30 (m, 2H), 1.91 (br. s., 1H), 1.72 t, J = 11.84 Hz, 1H), 0.99 - 1.61 (m, 11H), 0.65 - 0.85 (m, 1H).	314
107	N-[(1R,2S)-2-hydroxy-1,2-diphenyl-ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 11.99 - 12.13 (m, 1H), 8.09 - 8.21 (m, 1H), 7.63 (s, 1H), 7.33 - 7.42 (m, 4H), 7.15 - 7.32 (m, 7H), 6.44 (s, 1H), 5.49 - 5.57 (m, 1H), 5.11 - 5.21 (m, 1H), 4.87 - 4.97 (m, 1H), 3.53 (s, 3H).	388
108	N-(chroman-3-ylmethyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 8.13 (t, J = 5.8 Hz, 1H), 7.86 (s, 1H), 7.32 (t, J = 2.7 Hz, 1H), 7.11 – 7.03 (m, 2H), 6.86 – 6.79 (m, 1H), 6.78 – 6.69 (m, 2H), 4.28 – 4.20 (m, 1H), 3.92 – 3.84 (m, 1H), 3.56 (s, 2H), 3.30 (s, 3H), 2.91 – 2.81 (m, 1H), 2.71 – 2.53 (m, 1H), 2.28 (s, 1H).	338
109	tert-butyl 3-[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]pyrrolidine-1-carboxylate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 8.08 (d, J = 6.6 Hz, 1H), 7.85 (s, 1H), 7.31 (t, J = 2.5 Hz, 1H), 6.74 – 6.62 (m, 1H), 4.39 (s, 1H), 3.55 (s, 4H), 3.51 – 3.35 (m, 1H), 3.28 – 3.26 (m, 1H), 3.18 (s, 1H), 2.10 (s, 1H), 1.98 – 1.73 (m, 1H), 1.41 (s, 9H).	361
110	N-(2,3-dihydrobenzofuran-2-ylmethyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 8.17 (t, J = 5.8 Hz, 1H), 7.77 (s, 1H), 7.31 (t, J = 2.6 Hz, 1H), 7.23 – 7.16 (m, 1H), 7.14 – 7.04 (m, 1H), 6.86 – 6.72 (m, 2H), 6.72 – 6.63 (m, 1H), 5.01 – 4.91 (m, 1H), 3.53 (s, 5H), 3.29 – 3.26 (m, 1H), 3.08 – 2.95 (m, 1H).	324

111	N-(2,3-dihydro-1,4-benzodioxin-3-ylmethyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.08 (s, 1H), 8.23 (t, J = 5.8 Hz, 1H), 7.89 (s, 1H), 7.34 – 7.26 (m, 1H), 6.92 – 6.80 (m, 4H), 6.73 (d, J = 2.7 Hz, 1H), 4.41 – 4.29 (m, 2H), 4.05 – 3.97 (m, 1H), 3.65 – 3.45 (m, 5H).	340
112	N-(1-cyclopropylethyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 7.80 (d, J = 9.9 Hz, 2H), 7.30 (d, J = 2.7 Hz, 1H), 6.69 (d, J = 2.7 Hz, 1H), 3.56 (s, 3H), 3.53 – 3.43 (m, 1H), 1.21 (d, J = 6.7 Hz, 3H), 1.05 – 0.85 (m, 1H), 0.51 – 0.26 (m, 3H), 0.26 – 0.14 (m, 1H).	260
113	6-methyl-N-[3-(morpholinomethyl)phenyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.90 (s, 1H), 8.31 (s, 2H), 8.06 (s, 1H), 7.73 – 7.62 (m, 2H), 7.34 (d, J = 2.7 Hz, 1H), 7.31 – 7.24 (m, 1H), 7.04 – 6.98 (m, 1H), 6.73 (d, J = 2.7 Hz, 1H), 3.60 (s, 3H), 3.58 (s, 3H), 3.45 (s, 2H), 2.43 – 2.30 (m, 4H).	367
114	6-methyl-N-(1-naphthylmethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (s, 1H), 8.50 (s, 1H), 8.26 – 8.14 (m, 1H), 8.02 – 7.82 (m, 3H), 7.61 – 7.45 (m, 4H), 7.32 (t, J = 2.7 Hz, 1H), 6.77 – 6.72 (m, 1H), 4.94 (d, J = 5.6 Hz, 2H), 3.53 (s, 3H).	332
115	6-methyl-7-oxo-N-[1-(4-pyridyl)ethyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 8.54 – 8.48 (m, 2H), 8.43 (d, J = 7.5 Hz, 1H), 7.97 (s, 1H), 7.41 – 7.37 (m, 2H), 7.30 (d, J = 2.7 Hz, 1H), 6.67 (d, J = 2.7 Hz, 1H), 5.10 (t, J = 7.2 Hz, 1H), 3.58 (s, 3H), 1.47 (d, J = 7.1 Hz, 3H).	297
116	N-[1-(2-fluorophenyl)ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 8.38 (d, J = 7.6 Hz, 1H), 7.97 (s, 1H), 7.56 – 7.45 (m, 1H), 7.33 – 7.24 (m, 2H), 7.22 – 7.10 (m, 2H), 6.68 – 6.64 (m, 1H), 5.37 (p, J = 7.1 Hz, 1H), 3.58 (s, 3H), 1.46 (d, J = 7.0 Hz, 3H).	314

117	N-(2-ethoxypropyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (s, 1H), 7.84 (d, J = 9.9 Hz, 2H), 7.33 (d, J = 2.7 Hz, 1H), 6.69 (d, J = 2.7 Hz, 1H), 3.63 – 3.40 (m, 6H), 3.28 – 3.21 (m, 2H), 1.11 (t, J = 6.8 Hz, 6H).	278
118	N-[1-(2-chlorophenyl)ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 8.46 (d, J = 7.4 Hz, 1H), 8.00 (s, 1H), 7.61 – 7.52 (m, 1H), 7.47 – 7.38 (m, 1H), 7.37 – 7.21 (m, 3H), 6.68 – 6.64 (m, 1H), 5.42 (t, J = 7.1 Hz, 1H), 3.59 (s, 3H), 1.44 (d, J = 7.0 Hz, 3H).	331
119	N-[1-(2-methoxyphenyl)ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 8.21 (d, J = 8.0 Hz, 1H), 7.96 (s, 1H), 7.40 – 7.33 (m, 1H), 7.30 (t, J = 2.4 Hz, 1H), 7.27 – 7.17 (m, 1H), 7.03 – 6.95 (m, 1H), 6.95 – 6.87 (m, 1H), 6.66 – 6.63 (m, 1H), 5.47 – 5.35 (m, 1H), 3.85 (s, 3H), 3.58 (s, 3H), 1.38 (d, J = 7.0 Hz, 3H).	326
120	N-[1-(2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 8.20 (d, J = 7.9 Hz, 1H), 7.90 (s, 1H), 7.29 (t, J = 2.2 Hz, 1H), 6.89 (d, J = 2.1 Hz, 1H), 6.86 – 6.82 (m, 1H), 6.78 (d, J = 8.3 Hz, 1H), 6.69 – 6.66 (m, 1H), 5.03 (t, J = 7.3 Hz, 1H), 4.23 – 4.17 (m, 4H), 3.56 (s, 3H), 1.41 (d, J = 7.0 Hz, 3H).	354
121	N-isochroman-4-yl-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 8.28 (d, J = 8.4 Hz, 1H), 7.95 (s, 1H), 7.37 – 7.30 (m, 2H), 7.29 – 7.21 (m, 2H), 7.15 – 7.09 (m, 1H), 6.77 (d, J = 2.7 Hz, 1H), 5.29 – 5.13 (m, 1H), 4.83 – 4.67 (m, 2H), 4.04 – 3.91 (m, 1H), 3.86 – 3.75 (m, 1H), 3.52 (s, 3H).	324

122	6-methyl-N-[1-methyl-2-(3-methylisoxazol-5-yl)ethyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.77 (s, 1H), 7.31 (d, J = 2.8 Hz, 1H), 6.66 (d, J = 2.7 Hz, 1H), 6.14 (s, 1H), 4.37 – 4.23 (m, 1H), 3.55 (s, 3H), 3.07 – 2.85 (m, 2H), 2.17 (s, 3H), 1.19 (d, J = 6.6 Hz, 3H).	315
123	6-methyl-N-(2-methyl-1-phenyl-propyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 8.21 (d, J = 8.8 Hz, 1H), 7.87 (s, 1H), 7.45 – 7.12 (m, 6H), 6.62 (m, J = 2.9, 1.3 Hz, 1H), 4.70 (t, J = 8.9 Hz, 1H), 3.57 (s, 3H), 2.10 (m, J = 9.1, 6.6 Hz, 1H), 1.02 (d, J = 6.6 Hz, 3H), 0.74 (d, J = 6.7 Hz, 3H).	324
124	N-[4-(4-fluorophenyl)tetrahydrofuran-3-yl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.98 (s, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.41 (s, 1H), 7.32 – 7.26 (m, 2H), 7.22 (t, J = 2.4 Hz, 1H), 7.07 (t, J = 8.9 Hz, 2H), 6.33 – 6.30 (m, 1H), 4.92 – 4.81 (m, 1H), 4.18 – 4.10 (m, 2H), 4.07 – 3.99 (m, 1H), 3.82 – 3.74 (m, 1H), 3.73 – 3.64 (m, 1H), 3.47 (s, 3H).	356
125	6-methyl-7-oxo-N-tetralin-1-yl-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 8.24 (d, J = 8.6 Hz, 1H), 7.91 (s, 1H), 7.32 (t, J = 2.6 Hz, 1H), 7.27 – 7.21 (m, 1H), 7.19 – 7.08 (m, 3H), 6.79 – 6.75 (m, 1H), 5.31 – 5.15 (m, 1H), 3.52 (s, 3H), 3.28 – 3.26 (m, 1H), 2.86 – 2.69 (m, 2H), 2.05 – 1.91 (m, 2H), 1.87 – 1.71 (m, 1H).	322
126	N-[1-(4-chlorophenyl)ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 8.34 (d, J = 7.7 Hz, 1H), 7.93 (s, 1H), 7.48 – 7.33 (m, 3H), 7.29 (t, J = 2.7 Hz, 1H), 6.67 (d, J = 2.0 Hz, 1H), 5.12 (t, J = 7.2 Hz, 1H), 3.57 (s, 3H), 1.46 (d, J = 7.1 Hz, 3H).	331

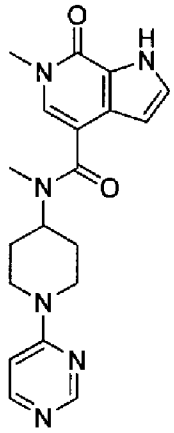
127	6-methyl-N-[2-(o-tolyl)ethyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.32 – 12.04 (m, 1H), 7.48 (s, 1H), 7.32 (d, J = 2.8 Hz, 1H), 7.26 – 7.05 (m, 4H), 6.24 (d, J = 2.8 Hz, 1H), 4.70 (s, 2H), 3.74 (t, J = 5.9 Hz, 2H), 3.54 (s, 3H), 3.27 (d, J = 0.9 Hz, 1H), 2.94 – 2.73 (m, 3H).	310
128	N,6-dimethyl-7-oxo-N-(1-phenylethyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.13 (s, 1H), 7.64 – 7.07 (m, 8H), 5.62 (d, J = 16.2 Hz, 1H), 3.53 (s, 3H), 3.27 (s, 1H), 2.63 (s, 3H), 1.57 (d, J = 7.0 Hz, 3H).	310
129	N-[1-(4-fluorophenyl)ethyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 8.31 (d, J = 7.8 Hz, 1H), 7.92 (s, 1H), 7.46 – 7.39 (m, 2H), 7.29 (t, J = 2.5 Hz, 1H), 7.18 – 7.10 (m, 2H), 6.69 – 6.65 (m, 1H), 5.14 (t, J = 7.3 Hz, 1H), 3.57 (s, 3H), 1.46 (d, J = 7.1 Hz, 3H).	314
130	tert-butyl 3-[[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]methyl]azetidine-1-carboxylate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (s, 1H), 8.10 (t, J = 5.8 Hz, 1H), 7.32 (t, J = 2.5 Hz, 1H), 6.73 – 6.63 (m, 1H), 3.87 (d, J = 8.8 Hz, 2H), 3.55 (s, 5H), 3.47 – 3.39 (m, 2H), 3.27 (t, J = 0.8 Hz, 1H), 2.82 – 2.63 (m, 1H), 1.36 (s, 9H).	361
131	6-methyl-N-(1-methyl-1-phenyl-ethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.02 (s, 1H), 7.95 (d, J = 15.2 Hz, 2H), 7.45 – 7.35 (m, 2H), 7.33 – 7.24 (m, 3H), 7.21 – 7.12 (m, 1H), 6.63 – 6.55 (m, 1H), 3.58 (s, 3H), 1.67 (s, 6H).	310
132	tert-butyl 2-[[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]methyl]piperidine-1-carboxylate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 7.90 (s, 1H), 7.78 (s, 1H), 7.31 (t, J = 2.5 Hz, 1H), 6.76 – 6.66 (m, 1H), 4.35 (d, J = 7.0 Hz, 1H), 3.86 (d, J = 13.3 Hz, 1H), 3.54 (s, 3H), 3.36 (m, J = 13.1, 6.3 Hz, 1H), 3.27 (s, 1H), 2.93 (s, 1H), 1.71 – 1.34 (m, 5H), 1.28 (s, 10H).	390

133	tert-butyl 4-[[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]methyl]piperidine-1-carboxylate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 7.97 (t, J = 5.8 Hz, 1H), 7.81 (s, 1H), 7.31 (t, J = 2.7 Hz, 1H), 6.78 – 6.62 (m, 1H), 4.08 – 3.81 (m, 2H), 3.55 (s, 3H), 3.14 (t, J = 6.1 Hz, 2H), 2.85 – 2.60 (m, 2H), 1.84 – 1.57 (m, 3H), 1.39 (s, 9H), 1.18 – 0.89 (m, 2H).	390
134	tert-butyl 2-[[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]methyl]morpholine-4-carboxylate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.08 (s, 1H), 8.03 (t, J = 5.8 Hz, 1H), 7.85 (s, 1H), 7.32 (d, J = 2.8 Hz, 1H), 6.71 (d, J = 2.7 Hz, 1H), 3.92 – 3.77 (m, 2H), 3.70 (d, J = 13.4 Hz, 1H), 3.52 – 3.43 (m, 1H), 3.43 – 3.35 (m, 1H), 3.33 (d, J = 6.0 Hz, 5H), 2.89 (s, 1H), 2.71 – 2.55 (m, 1H), 1.39 (s, 9H).	391
135	tert-butyl 3-[[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]methyl]piperidine-1-carboxylate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 7.98 (t, J = 5.8 Hz, 1H), 7.81 (s, 1H), 7.32 (t, J = 2.7 Hz, 1H), 6.71 (d, J = 2.7 Hz, 1H), 3.89 (s, 1H), 3.76 (d, J = 13.2 Hz, 1H), 3.55 (s, 3H), 3.27 (s, 2H), 3.17 – 3.08 (m, 2H), 2.84 – 2.72 (m, 1H), 1.77 (d, J = 12.5 Hz, 1H), 1.71 – 1.56 (m, 2H), 1.36 (s, 10H), 1.22 – 1.12 (m, 1H).	390
136	tert-butyl 2-[[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]methyl]pyrrolidine-1-carboxylate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 7.98 (s, 1H), 7.82 (s, 1H), 7.31 (t, J = 2.4 Hz, 1H), 6.71 (s, 1H), 3.90 (s, 1H), 3.55 (s, 3H), 1.41 (s, 9H).	275
137	tert-butyl 3-[[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]methyl]pyrrolidine-1-carboxylate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 8.06 (t, J = 5.8 Hz, 1H), 7.82 (s, 1H), 7.32 (t, J = 2.4 Hz, 1H), 6.72 – 6.66 (m, 1H), 3.55 (s, 3H), 3.28 – 3.16 (m, 4H), 3.05 – 2.92 (m, 1H), 2.42 (s, 1H), 1.91 (d, J = 5.5 Hz, 1H), 1.58 (d, J = 28.8 Hz, 1H), 1.39 (s, 10H).	375

138	tert-butyl 3-[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]piperidine-1-carboxylate	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 7.82 (s, 1H), 7.75 (d, J = 7.5 Hz, 1H), 7.31 (t, J = 2.3 Hz, 1H), 6.70 – 6.65 (m, 1H), 4.05 – 3.59 (m, 3H), 3.55 (s, 3H), 3.27 (t, J = 0.7 Hz, 2H), 2.85 (t, J = 11.6 Hz, 1H), 1.90 (d, J = 8.4 Hz, 1H), 1.71 (s, 1H), 1.39 (s, 10H).	375

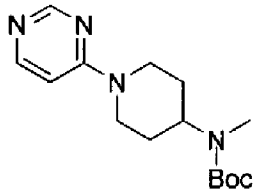
Example 139

N,6-dimethyl-7-oxo-N-(1-pyrimidin-4-yl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

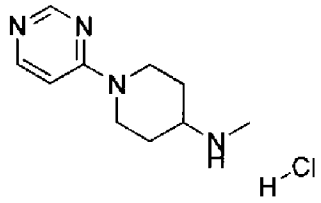
tert-butyl methyl(1-(pyrimidin-4-yl)piperidin-4-yl)carbamate



A mixture of tert-butyl methyl(piperidin-4-yl)carbamate (500 mg, 2.3 mmol), cesium carbonate (836 mg, 2.6 mmol) and 4-chloropyrimidine (294 mg, 2.6 mmol) in DMF (10 mL) was heated at 80 °C for 3 h, at which time LCMS indicated full conversion of starting material. The reaction mixture was poured into ice water (10 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced pressure to give the title compound (450 mg, 66.0% yield) as a yellow solid. This crude material was used in the next step without further purification.

Step 2:

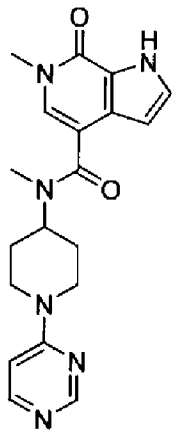
N-methyl-1-(pyrimidin-4-yl)piperidin-4-amine hydrochloride



To a cooled (0 °C) solution of tert-butyl methyl(1-(pyrimidin-4-yl)piperidin-4-yl)carbamate (300 mg, 1.0 mmol) in ethyl acetate (50 mL) was added hydrogen chloride (2N in ethyl acetate, 10 mL). After addition, the reaction mixture was stirred at 25 °C for 3 h. The solvent was evaporated under reduced pressure to give the crude title compound (165 mg, 72% yield) as a yellow solid.

Step 3:

N,6-dimethyl-7-oxo-N-(1-pyrimidin-4-yl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



A mixture of 6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (**Intermediate C**) (100 mg, 0.5 mmol), diisopropylethylamine (134 mg, 1.0 mmol), HATU (150 mg, 0.6 mmol) and 1-(pyrimidin-4-yl)piperidin-4-amine hydrochloride (110 mg, 0.5 mmol) in DMF (5 mL) was stirred at 25 °C for 3 h, at which time LCMS indicated the reaction had gone to completion. The reaction mixture was added to ice water (5 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by preparative HPLC, acetonitrile : water (10 nM ammonia) : 32%-62%, to give the title compound (11 mg, 5.8% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.12 (s, 1 H), 8.43 (d, *J* = 9.6 Hz, 1 H), 8.12 (m, 1 H), 7.38 (s, 1 H), 7.30 (s, 1 H), 6.83 (d, *J* = 6.4 Hz, 1 H), 6.19 (d, *J* = 2.4 Hz, 1 H), 4.51-4.43 (m, 2 H), 4.43-4.25 (m, 1 H), 3.50 (s, 3 H), 2.91-2.81 (m, 2 H), 2.75 (s, 3 H), 1.76-1.63 (m, 4 H). LCMS M/Z (M+H) 367.2.

The following compounds were prepared in a similar fashion to Example 139.

Examples 140-158

Example	Compound Name	NMR	m/z
140	N,6-dimethyl-N-[1-(5-methylpyrimidin-2-yl)-4-piperidyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.15 (br. s., 1 H), 8.21 (s, 2 H), 7.41 (s, 1 H), 7.33 (s, 1 H), 6.22 (s, 1 H), 4.72 (d, *J* = 12.4 Hz, 2 H), 4.39-4.31 (m, 1 H), 3.53 (s, 3 H), 2.79-2.74 (m, 5 H), 2.07 (s, 3 H), 1.69-1.66 (m, 4 H)	381
141	N-[1-(5-cyanopyrimidin-2-yl)-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.15 (br. s., 1 H), 8.75-8.72 (m, 2 H), 7.41 (s, 1 H), 7.33 (s, 1 H), 6.22 (d, *J* = 3.2 Hz, 1 H), 4.85-4.81 (m, 2 H), 4.48-4.42 (m, 1 H), 3.53 (s, 3 H), 3.05-2.96 (m, 2 H), 2.79 (s, 3 H), 1.78-1.72 (m, 4 H)	392
142	N,6-dimethyl-7-oxo-N-[1-[4-(trifluoromethyl)pyrimidin-2-yl]-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.15 (br. s., 1 H), 8.67 (d, *J* = 4.4 Hz, 1 H), 7.42 (s, 1 H), 7.33 (s, 1 H), 7.00 (d, *J* = 5.2 Hz, 1 H), 6.22 (s, 1 H), 4.79-4.75 (m, 2 H), 4.47-4.39 (m, 1 H), 3.53 (s, 3 H), 2.99-2.92 (m., 2 H), 2.80 (s, 3 H), 1.77-1.70 (m, 4 H)	435
143	N,6-dimethyl-7-oxo-N-(1-pyrazin-2-yl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.13 (br. s., 1 H), 8.34 (s, 1 H), 8.06 (s, 1 H), 7.80 (d, *J* = 2.4 Hz, 1 H), 7.41 (s, 1 H), 7.38-7.31 (m, 1 H), 6.22 (s, 1 H), 4.47-4.34 (m, 3 H), 3.53 (s, 3 H), 2.86-2.79 (m, 5 H), 1.78-1.71 (m, 4 H)	367

144	N,6-dimethyl-N-[1-(4-methylpyrimidin-2-yl)-4-piperidyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 8.14 (d, *J* = 5.2 Hz, 1 H), 7.40-7.39 (m, 2 H), 6.47 (d, *J* = 5.2 H z, 1 H), 6.36 (d, *J* = 2.8 Hz, 1 H), 4.88 (s, 3 H), 3.67 (s, 3 H), 2.93-2.75 (m, 5 H), 2.32 (s, 3 H), 1.87-1.81 (m, 4 H).	381
145	N,6-dimethyl-7-oxo-N-(1-pyridazin-3-yl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO- *d6*): δ 12.15 (br. s., 1 H), 8.52 (d, *J* = 3.6 Hz, 1 H), 7.42-7.26 (m, 4 H), 6.23 (d, *J* = 2.4 Hz, 1 H), 4.50 (d, *J* = 12.4 Hz, 2 H), 4.38-4.32 (m, 1 H), 3.54 (s, 3 H), 2.91-2.85 (m, 2 H), 2.80 (s, 3 H), 1.83-1.75 (m, 4 H).	367
146	N-[1-(4-cyanopyrimidin-2-yl)-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.10 (br. s., 1 H), 8.62 (d, *J* = 4.5 Hz, 1 H), 7.40 (s, 1 H), 7.33 (s, 1 H), 7.11 (d, *J* = 4.5 Hz, 1 H), 6.22 (s, 1 H), 4.74-4.72 (m, 2 H), 4.38-4.30 (m, 1 H), 3.53 (s, 3 H), 2.96-2.86 (m, 2 H), 2.79-2.76 (m, 3 H), 1.76-1.70 (m, 4 H)	392
147	N-[1-(5-fluoropyrimidin-2-yl)-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.15 (s, 1 H), 8.44 (s, 2 H), 7.41 (s, 1 H), 7.33 (s, 1 H), 6.22 (s, 1 H), 4.70-4.65 (m, 2 H), 3.53 (s, 3 H), 3.31-3.28 (m, 1 H), 2.90-2.86 (m, 2 H), 2.79 (s, 3 H), 2.67 (s, 1 H), 1.72-1.70 (m, 4 H).	385
148	6-methyl-7-oxo-N-(1-pyrimidin-4-yl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.05 (s, 1 H), 8.48 (s, 1 H), 8.16 (d, *J* = 6.4 Hz, 1 H), 7.85-7.79 (m, 2 H), 7.30 (d, *J* = 2.4 Hz, 1 H), 6.87 (d, *J* = 6.4 Hz, 1 H), 6.68 (d, *J* = 2.8 Hz, 1 H), 4.38-4.34 (m, 2 H), 4.10-4.08 (m, 1 H), 3.53 (s, 3 H), 3.25-3.04 (m, 2 H), 1.90-1.87 (m, 2 H), 1.46-1.43 (m, 2 H).	353

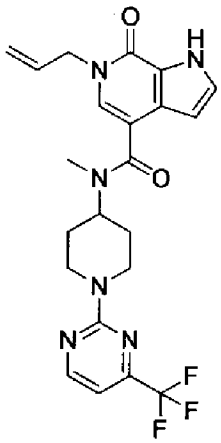
149	6-methyl-N-[1-(5-methylpyrimidin-2-yl)-4-piperidyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.03 (s, 1 H), 8.20 (s, 1 H), 7.80-7.78 (m, 2 H), 7.28 (d, *J* = 2.4 Hz, 1 H), 6.67 (d, *J* = 2.8 Hz, 1 H), 4.56-4.53 (m, 2 H), 4.10-3.90 (m, 1 H), 3.51 (s, 3 H), 3.03-2.96 (m, 2 H), 2.06 (s, 3 H), 1.85-1.83 (m, 2 H), 1.44-1.39 (m, 2 H).	367
150	6-methyl-N-[1-(4-methylpyrimidin-2-yl)-4-piperidyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.03 (s, 1 H), 8.19 (d, *J* = 5.2 Hz, 1 H), 7.81-7.78 (m, 2 H), 7.28 (s, 1 H), 6.67 (s, 1 H), 6.47 (d, *J* = 5.2 Hz, 1 H), 4.63-4.59 (m, 2 H), 4.05-4.02 (m, 1 H), 3.51 (s, 3 H), 2.99 (t, *J* = 11.6 Hz, 2 H), 2.25 (s, 3 H), 1.86-1.84 (m, 2 H), 1.47-1.42 (m, 2 H).	367
151	6-methyl-7-oxo-N-(1-pyrazin-2-yl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.07 (s, 1 H), 8.37 (d, *J* = 1.2 Hz, 1 H), 8.09 (d, *J* = 0.8 Hz, 1 H), 7.89-7.79 (m, 3 H), 7.31 (s, 1 H), 6.71 (s, 1 H), 4.36-4.32 (m, 2 H), 4.10-4.08 (m, 1 H), 3.54 (s, 3 H), 3.06 (t, *J* = 11.6 Hz, 2 H), 1.91-1.89 (m, 2 H), 1.56-1.47 (m, 2 H).	353
152	N-[1-(5-cyanopyrimidin-2-yl)-4-piperidyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.06 (s, 1 H), 8.74 (s, 2 H), 7.87 (d, *J* = 7.2 Hz, 1 H), 7.79 (s, 1 H), 7.29-7.28 (m, 1 H), 6.66 (s, 1 H), 4.65-4.61 (m, 2 H), 4.11-4.09 (m, 1 H), 3.52 (s, 3 H), 3.24-3.18 (m, 2 H), 1.94-1.91 (m, 2 H), 1.47-1.42 (m, 2 H).	378

153	6-methyl-7-oxo-N-[1-[4-(trifluoromethyl)pyrimidin-2-yl]-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.04 (s, 1 H), 8.66-8.63 (m, 1 H), 7.84-7.78 (m, 2 H), 7.28 (d, *J* = 2.8 Hz, 1 H), 6.98-6.94 (m, 1 H), 6.66 (d, *J* = 2.8 Hz, 1 H), 4.58-4.55 (m, 2 H), 4.08-4.06 (m, 1 H), 3.50 (s, 3 H), 3.15-3.12 (m, 2 H), 1.91-1.86 (m, 2 H), 1.49-1.41 (m, 2 H).	421
154	N-[1-(5-fluoropyrimidin-2-yl)-4-piperidyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.05 (s, 1 H), 8.43 (s, 2 H), 7.84-7.79 (m, 2 H), 7.29-7.28 (m, 1 H), 6.67 (s, 1 H), 4.52-4.48 (m, 2 H), 4.06-4.03 (m, 1 H), 3.51 (s, 3 H), 3.05 (t, *J* = 11.6 Hz, 2 H), 1.87-1.84 (m, 2 H), 1.48-1.40 (m, 2 H).	371
155	6-methyl-7-oxo-N-(1-pyridazin-3-yl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.07 (s, 1 H), 8.53 (d, *J* = 3.6 Hz, 1 H), 7.87-7.82 (m, 2 H), 7.39-7.29 (m, 3 H), 6.71 (s, 1 H), 4.40-4.36 (m, 2 H), 4.11-4.10 (m, 1 H), 3.54 (s, 3 H), 3.08 (t, *J* = 11.6 Hz, 2 H), 1.92-1.89 (m, 2 H), 1.58-1.50 (m, 2 H).	353
156	N-[1-(4-cyanopyrimidin-2-yl)-4-piperidyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.08 (s, 1 H), 8.66 (d, *J* = 4.5 Hz, 1 H), 7.88-7.82 (m, 2 H), 7.32 (s, 1 H), 7.15 (d, *J* = 4.5 Hz, 1 H), 6.70 (s, 1 H), 4.57-4.54 (m, 2 H), 4.12-4.10 (m, 1 H), 3.55 (s, 3 H), 3.16 (t, *J* = 11.6 Hz, 2 H), 1.95-1.92 (m, 2 H), 1.53-1.45 (m, 2H).	378

157	N,6-dimethyl-7-oxo-N-[(1-pyrimidin-2-yl-4-piperidyl)methyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 – 12.09 (m, 2H), 8.31 (d, J = 4.7 Hz, 2H), 7.41 (s, 1H), 7.35 – 7.29 (m, 1H), 6.56 (t, J = 4.7 Hz, 1H), 6.23 – 6.16 (m, 1H), 4.62 (d, J = 12.8 Hz, 2H), 3.53 (s, 3H), 3.38 – 3.33 (m, 2H), 2.98 (s, 3H), 2.92 – 2.81 (m, 2H), 2.05 – 2.00 (m, 1H), 1.68 – 1.63 (m, 2H), 1.04 – 0.99 (m, 2H).	381
158	N,6-dimethyl-7-oxo-N-[(1-pyrimidin-4-yl-4-piperidyl)methyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.08 (s, 1H), 8.44 (s, 1H), 8.12 (d, J = 6.2 Hz, 1H), 7.39 (s, 1H), 7.32 (d, J = 2.8 Hz, 1H), 6.78 (d, J = 6.3 Hz, 1H), 6.26 – 6.11 (m, 1H), 4.36 (d, J = 13.0 Hz, 2H), 3.52 (s, 3H), 3.41 – 3.32 (m, 2H), 2.97 (s, 3H), 2.95 – 2.83 (m, 2H), 2.22 – 1.95 (m, 1H), 1.79 – 1.51 (m, 2H), 1.21 – 0.96 (m, 2H).	381

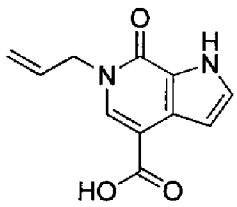
Example 159

6-allyl-N-methyl-7-oxo-N-[1-[4-(trifluoromethyl)pyrimidin-2-yl]-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

6-allyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid

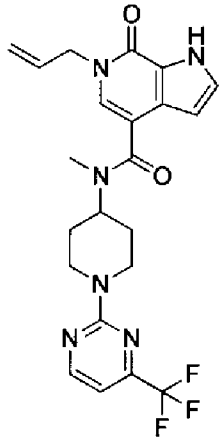


Sodium hydride, 60% in mineral oil (870 mg, 21.65 mmol) was added in 3 portions to a cooled (0° C) solution of methyl 7-oxo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridine-4-carboxylate (Intermediate B, 5.0 g, 14.43 mmol) in DMF (70 mL). The reaction was stirred for 30 min at room temperature and 3-bromoprop-1-ene (1.37 mL, 15.88 mmol) was added. The reaction was warmed (50° C) and stirring was continued for 3h. The reaction was quenched with minimal methanol, and then water (100 mL) was added. The mixture was extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography (0-5% methanol : dichloromethane) yielding 1.96 of ester intermediate as a white solid that was immediately carried forward.

Potassium hydroxide (1.42 g, 25.4 mmol) in water (10 mL) was added to a solution of methyl 6-allyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxylate (1.96 g, 1.0 equiv., 5.07 mmol) in methanol (25 mL). The reaction was stirred at 45°C for 1h. The reaction was then cooled to room temperature, and the methanol was evaporated under reduced pressure. The aqueous solution was acidified to pH 2 using 3N hydrochloric acid, and the resulting precipitate was collected by filtration. The filter cake was washed with water and dried, yielding title compound (1.18 g, 37%). LCMS M/Z (M+H) 219.

Step 2:

6-allyl-N-methyl-7-oxo-N-[1-[4-(trifluoromethyl)pyrimidin-2-yl]-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



To an 8 mL vial was added 6-allyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (Step 1,50 mg, 0.23 mmol), N,N-dimethylformamide (1 mL), HATU (1.05 equiv., 0.24 mmol), and triethylamine (4 equiv., 0.92 mmol). The reaction vial was capped and vortexed for one minute. N-methyl-1-(4-(trifluoromethyl)pyrimidin-2-yl)piperidin-4-amine hydrochloride (62 mg, 0.27 mmol, as prepared in example **139**) was added and the reaction vial shaken at room temperature overnight. The reaction mixture was diluted with dichloromethane and washed with water. The organic solution was then concentrated under reduced pressure and the residue was purified by HPLC (20-60%ACN/0.1%NH4OH in H2O) yielding title compound (32 mg, 36%). ^{1}H NMR (400 MHz, DMSO-*d6*) δ 12.14 (s, 1H), 8.47 (d, *J* = 1.2 Hz, 1H), 8.15 (d, *J* = 6.2 Hz, 1H), 7.43 – 7.25 (m, 2H), 6.85 (dd, *J* = 6.4, 1.3 Hz, 1H), 6.24 (t, *J* = 2.3 Hz, 1H), 5.99 (ddt, *J* = 17.2, 10.5, 5.3 Hz, 1H), 5.17 (dq, *J* = 10.3, 1.4 Hz, 1H), 5.13 – 5.01 (m, 1H), 4.72 – 4.58 (m, 2H), 4.51 (d, *J* = 13.1 Hz, 2H), 4.33 (s, 1H), 2.79 (s, 5H), 1.72 (td, *J* = 11.4, 10.2, 3.8 Hz, 4H). LCMS M/Z (M+H) 393.

The following compounds were prepared in a similar fashion to Example 159.

Examples 160-168

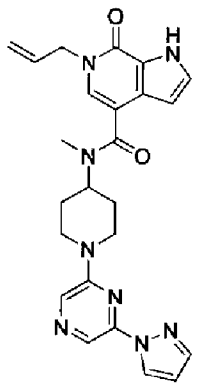
Example	Compound Name	NMR	m/z
160	6-allyl-N-[1-(2-cyanopyrimidin-4-yl)-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.15 (s, 1H), 8.67 (d, J = 4.8 Hz, 1H), 7.43 – 7.22 (m, 2H), 6.99 (d, J = 4.8 Hz, 1H), 6.30 – 6.19 (m, 1H), 6.12 – 5.89 (m, 1H), 5.25 – 5.13 (m, 1H), 5.13 – 5.01 (m, 1H), 4.77 (d, J = 13.0 Hz, 2H), 4.64 (d, J = 5.4 Hz, 2H), 4.36 (s, 1H), 2.93 (s, 2H), 2.80 (s, 3H), 1.90 – 1.60 (m, 4H).	418
161	6-allyl-N-methyl-7-oxo-N-(1-pyrimidin-4-yl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.14 (s, 1H), 8.47 (d, J = 1.2 Hz, 1H), 8.15 (d, J = 6.2 Hz, 1H), 7.43 – 7.25 (m, 2H), 6.85 (dd, J = 6.4, 1.3 Hz, 1H), 6.24 (t, J = 2.3 Hz, 1H), 5.99 (ddt, J = 17.2, 10.5, 5.3 Hz, 1H), 5.17 (dq, J = 10.3, 1.4 Hz, 1H), 5.13 – 5.01 (m, 1H), 4.72 – 4.58 (m, 2H), 4.51 (d, J = 13.1 Hz, 2H), 4.33 (s, 1H), 2.79 (s, 5H), 1.72 (td, J = 11.4, 10.2, 3.8 Hz, 4H).	393
162	6-allyl-N-[1-(6-methoxypyrimidin-4-yl)-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.15 (s, 1H), 8.23 (d, J = 0.8 Hz, 1H), 7.34 (d, J = 2.8 Hz, 1H), 7.30 (s, 1H), 6.24 (d, J = 2.7 Hz, 1H), 6.10 (d, J = 0.9 Hz, 1H), 6.06 – 5.91 (m, 1H), 5.21 – 5.12 (m, 1H), 5.12 – 5.01 (m, 1H), 4.64 (dt, J = 5.5, 1.5 Hz, 2H), 4.45 (d, J = 13.1 Hz, 2H), 4.30 (s, 1H), 3.81 (s, 3H), 3.37 – 3.25 (m, 1H), 2.78 (s, 5H), 1.74 – 1.62 (m, 4H).	423

163	6-allyl-N-[1-(6,7-dihydro-5H-cyclopenta[d]pyrimidin-4-yl)-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.16 (s, 1H), 8.30 (s, 1H), 7.35 (d, J = 2.8 Hz, 1H), 7.29 (s, 1H), 6.23 (d, J = 2.8 Hz, 1H), 6.06 – 5.91 (m, 1H), 5.17 (dq, J = 10.2, 1.4 Hz, 1H), 5.12 – 5.01 (m, 1H), 4.67 – 4.60 (m, 2H), 4.51 (d, J = 13.1 Hz, 2H), 3.30 (s, 2H), 2.99 (t, J = 7.3 Hz, 2H), 2.94 – 2.85 (m, 2H), 2.79 (s, 3H), 2.72 (dd, J = 15.7, 7.8 Hz, 2H), 2.01 – 1.88 (m, 2H), 1.84 – 1.70 (m, 4H).	433
164	6-allyl-N-methyl-7-oxo-N-[1-[6-(trifluoromethyl)pyrimidin-4-yl]-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.16 (s, 1H), 8.61 (d, J = 1.1 Hz, 1H), 7.38 – 7.27 (m, 3H), 6.25 (d, J = 2.7 Hz, 1H), 6.06 – 5.92 (m, 1H), 5.22 – 5.13 (m, 1H), 5.12 – 5.02 (m, 1H), 4.68 – 4.60 (m, 2H), 4.41 – 4.36 (m, 1H), 3.35 – 3.23 (m, 2H), 2.96 (s, 2H), 2.79 (s, 3H), 1.79 – 1.72 (m, 4H).	461
165	6-allyl-N-[1-(2,6-dimethylpyrimidin-4-yl)-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.16 (s, 1H), 7.38 – 7.27 (m, 2H), 6.53 (s, 1H), 6.28 – 6.21 (m, 1H), 6.06 – 5.91 (m, 1H), 5.21 – 5.13 (m, 1H), 5.12 – 5.01 (m, 1H), 4.64 (dt, J = 5.4, 1.6 Hz, 2H), 4.51 (d, J = 13.1 Hz, 2H), 4.31 (s, 1H), 2.81 – 2.76 (m, 5H), 2.31 (s, 3H), 2.20 (s, 3H), 1.75 – 1.61 (m, 4H).	421
166	6-allyl-N-methyl-7-oxo-N-[1-(6-propylpyrimidin-4-yl)-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.15 (s, 1H), 8.39 (d, J = 1.1 Hz, 1H), 7.38 – 7.28 (m, 2H), 6.70 (d, J = 1.3 Hz, 1H), 6.24 (d, J = 2.8 Hz, 1H), 6.06 – 5.91 (m, 1H), 5.21 – 5.13 (m, 1H), 5.12 – 5.01 (m, 1H), 4.67 – 4.60 (m, 2H), 4.52 (d, J = 12.9 Hz, 2H), 3.35 – 3.25 (m, 16H), 2.85 – 2.76 (m, 5H), 2.56 – 2.42 (m, 2H), 1.76 – 1.57 (m, 6H), 0.98 – 0.84 (m, 3H).	435

167	6-allyl-N-[1-(6-isopropylpyrimidin-4-yl)-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.15 (s, 1H), 8.40 (d, J = 1.0 Hz, 1H), 7.38 – 7.28 (m, 2H), 6.68 (d, J = 1.2 Hz, 1H), 6.24 (d, J = 2.8 Hz, 1H), 6.06 – 5.91 (m, 1H), 5.21 – 5.13 (m, 1H), 5.12 – 5.01 (m, 1H), 4.67 – 4.50 (m, 4H), 3.30 (d, J = 19.9 Hz, 16H), 2.86 – 2.71 (m, 5H), 1.77 – 1.66 (m, 4H), 1.17 (d, J = 6.9 Hz, 6H).	435
168	6-allyl-N-[1-(2-cyclopropyl-6-methyl-pyrimidin-4-yl)-4-piperidyl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.15 (s, 1H), 7.37 – 7.27 (m, 2H), 6.47 (s, 1H), 6.24 (d, J = 2.7 Hz, 1H), 5.99 (ddt, J = 17.2, 10.5, 5.4 Hz, 1H), 5.17 (dq, J = 10.3, 1.4 Hz, 1H), 5.06 (dq, J = 17.2, 1.6 Hz, 1H), 4.64 (dt, J = 5.6, 1.6 Hz, 2H), 4.48 (d, J = 13.1 Hz, 2H), 4.30 (s, 0H), 2.90 – 2.67 (m, 5H), 2.18 (s, 3H), 1.89 (tt, J = 7.9, 4.9 Hz, 1H), 1.74 – 1.60 (m, 4H), 0.93 – 0.79 (m, 4H).	447

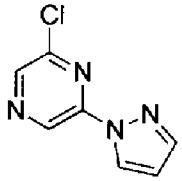
Example 169

6-allyl-N-methyl-7-oxo-N-[1-(6-pyrazol-1-ylpyrazin-2-yl)-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

2-chloro-6-(1H-pyrazol-1-yl)pyrazine

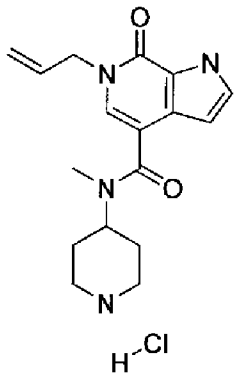


To a 40 mL vial was added 2,6-dichloropyrazine (4.0 g, 26.9 mmol), 1H-pyrazole (1.8 g, 26.9 mmol), potassium carbonate (7.4 g, 53.7 mmol), and 10 mL of N,N-dimethylacetamide. The

reaction was capped and shaken at 50°C for 2 hours, then cooled to room temperature and diluted with ethyl acetate. The organic was then washed with water, and concentrated under reduced pressure. The crude product was purified by flash column (10-35% Ethyl Acetate : Heptanes) yielding title compound as a white solid (1.51 g, 31%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.24 – 9.12 (m, 2H), 8.80 – 8.68 (m, 2H), 8.68 – 8.54 (m, 2H), 7.96 (dd, J = 1.7, 0.7 Hz, 2H), 6.74 – 6.63 (m, 2H), 3.38 – 3.24 (m, 1H). LCMS M/Z (M+H) 281.

Step 2:

6-allyl-N-methyl-7-oxo-N-(piperidin-4-yl)-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide hydrochloride

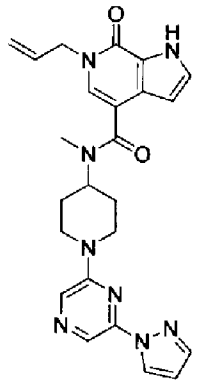


To a round bottom flask was added 6-allyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (2.3 g, 10.5 mmol **Example 159, step 1**) followed by N,N-dimethylformamide (20 mL), HATU (4.3 g, 11.1 mmol), triethylamine (5.9 mL, 42.2 mmol), and tert-butyl 4-(methylamino)-piperidine-1-carboxylate (2.9 g, 13.7 mmol). The reaction was stirred for 1h, then was diluted with ethyl acetate, and washed with water. The organic was concentrated under reduced pressure. The crude product was purified by flash column (0-10% dichloromethane : methanol) yielding boc protected product.

The product was then taken up with 20 mL methanol, and 10 mL of 4N HCl in dioxane was added. The reaction was stirred at r.t. for 1h, at which time mixture was concentrated under reduced pressure yielding product as HCl salt (2.0 g, 55% over two steps). The crude amine was carried on without further purification. LCMS M/Z (M+H) 315.

Step 3:

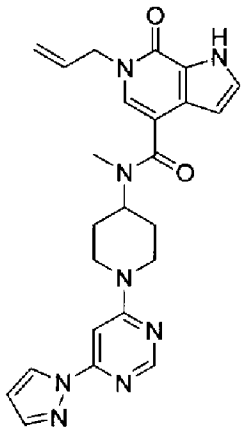
6-allyl-N-methyl-7-oxo-N-[1-(6-pyrazol-1-ylpyrazin-2-yl)-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



To a 4 mL vial was added 6-allyl-N-methyl-7-oxo-N-(4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide hydrochloride (40 mg, 0.11 mmol) followed by 2-chloro-6-pyrazol-1-yl-pyrazine (21mg, 0.11 mmol), diisopropylethylamine (0.08 mL, 0.46 mmol), and 0.16 mL. The reaction was capped and shaken at 90°C overnight. The reaction was cooled to room temperature, diluted with ethyl acetate, and washed with water. The organic was concentrated under reduced pressure, and the residue was purified by HPLC (20-60%ACN/0.1%NH4OH in H2O) yielding title compound (10 mg, 19%). 1H NMR (400 MHz, DMSO-d6) δ 12.15 (s, 1H), 8.59 (dd, J = 2.6, 0.7 Hz, 1H), 8.38 – 8.17 (m, 2H), 7.82 (dd, J = 1.7, 0.7 Hz, 1H), 7.42 – 7.21 (m, 2H), 6.57 (dd, J = 2.6, 1.7 Hz, 1H), 6.25 (dd, J = 2.8, 1.5 Hz, 1H), 6.07 – 5.89 (m, 1H), 5.24 – 5.13 (m, 1H), 5.13 – 5.02 (m, 1H), 4.67 – 4.61 (m, 2H), 4.57 (d, J = 13.2 Hz, 2H), 4.35 (s, 1H), 3.04 – 2.86 (m, 2H), 2.81 (s, 3H), 1.95 – 1.68 (m, 4H). LCMS M/Z (M+H) 459.

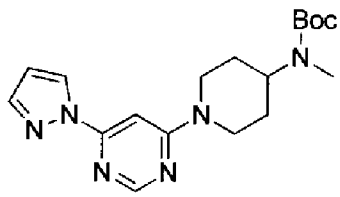
Example 170

6-allyl-*N*-methyl-7-oxo-*N*-[1-(6-pyrazol-1-ylpyrimidin-4-yl)-4-piperidyl]-1*H*-pyrrolo[2,3-*c*]pyridine-4-carboxamide



Step 1

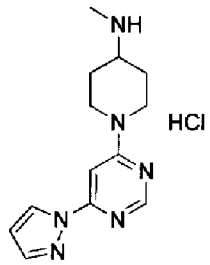
***tert*-butyl (1-(6-(1*H*-pyrazol-1-yl)pyrimidin-4-yl)piperidin-4-yl)(methyl)carbamate**



To a solution of tert-butyl (1-(6-chloropyrimidin-4-yl)piperidin-4-yl)(methyl) carbamate (600 mg, 1.84 mmol) in DMF (10 mL) was added 1*H*-pyrazole (150 mg, 2.20 mmol) and cesium carbonate (1.2 g, 3.67 mmol). After addition, the reaction mixture was heated at 80 °C for 12 h, at which time LCMS indicated the reaction had gone to completion. After cooled, the solid was removed by filtration and the filtrate was concentrated under reduced pressure. The residue was dissolved in ethyl acetate (50 mL), washed with water (2 x 30 mL), dried over sodium sulfate and concentrated to give the crude title compound (500 mg, 76 % yield) as a yellow solid.

Step 2

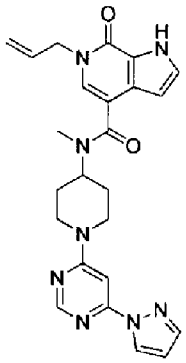
1-(6-(1*H*-pyrazol-1-yl)pyrimidin-4-yl)-N-methylpiperidin-4-amine hydrochloride



To a solution of *tert*-butyl (1-(6-(1*H*-pyrazol-1-yl)pyrimidin-4-yl)piperidin-4-yl)(methyl) carbamate (500 mg, 1.39 mmol) in ethyl acetate (10 mL) was added hydrogen chloride (2 N in ethyl acetate, 10 mL) at 0 °C. After addition, the mixture was stirred at ambient temperature for 2 h, at which time LCMS indicated the reaction had gone to completion. The solution was concentrated under reduced pressure to give the crude title compound (400 mg, 97% yield) as a white solid.

Step 3

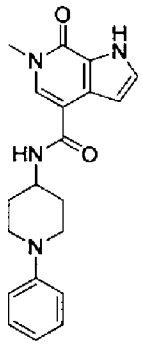
6-allyl-*N*-methyl-7-oxo-*N*-[1-(6-pyrazol-1-ylpyrimidin-4-yl)-4-piperidyl]-1*H*-pyrrolo[2,3-*c*]pyridine-4-carboxamide



To a solution of 1-(6-(1*H*-pyrazol-1-yl)pyrimidin-4-yl)-*N*-methylpiperidin-4-amine hydrochloride (216 mg, 0.73 mmol) in DMF (4 mL) was added 6-allyl-7-oxo -6,7-dihydro-1*H*-pyrrolo[2,3-c]pyridine-4-carboxylic acid (80 mg, 0.37 mmol), *N*-ethyl-*N*-isopropylpropan-2-amine (142 mg, 1.1 mmol) and HATU (181 mg, 0.48 mmol). After addition, the mixture was stirred at ambient temperature for 1.5 h, at which time LCMS indicated that the reaction had gone to completion. The solvent was removed under reduce pressure. The residue was dissolved in ethyl acetate (20 mL), washed with brine (2 x 15 mL) and concentrated. The crude product was purified by reverse phase chromatography (acetonitrile 40% / 0.1% NH_4OH in water) to give the title compound (12.8 mg, 8% yield) as a yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.19 (s, 1 H), 8.68 (s, 1 H), 8.49 (s, 1 H), 7.91 (s, 1 H), 7.34 (d, J = 11.6 Hz, 2 H), 7.24 (s, 1 H), 6.63 (s, 1 H), 6.24 (s, 1 H), 5.99-5.94 (m, 1 H), 5.16 (d, J = 10.0 Hz, 1 H), 5.06 (d, J = 17.2 Hz, 1 H), 4.64-4.40 (m, 5 H), 3.03 (s, 2 H), 2.78 (s, 3 H), 1.79 (s, 4 H). LCMS M/Z (M+H) 459.1.

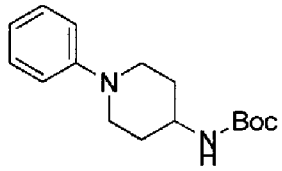
Example 171

6-methyl-7-oxo-N-(1-phenyl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

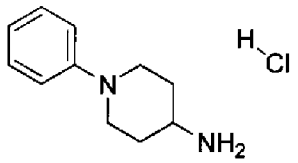
tert-butyl (1-phenylpiperidin-4-yl)carbamate



To a solution of tert-butyl piperidin-4-ylcarbamate (420 mg, 1.96 mmol) in dry xylene (8 mL) was added 1-iodo-4-methylbenzene (400 mg, 1.96 mmol), sodium *tert*-butoxide (564 mg, 5.88 mmol), $Pd_2(dba)_3$ (10 mg) and xantphos (15 mg). With nitrogen protection, the reaction mixture was heated at 120 °C under microwave conditions for 30 min, at which time LCMS indicated the reaction had gone to completion. The mixture was concentrated under reduced pressure and the residue was purified by silica gel chromatography (Hexanes/ethyl acetate=5:1) to give the title compound (100 mg, 17.5% yield) that was used directly in step 2.

Step 2

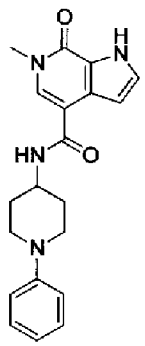
1-phenylpiperidin-4-amine hydrochloride



To a solution of tert-butyl (1-phenylpiperidin-4-yl)carbamate (100 mg, 0.35 mmol) in ethyl acetate (10 mL) was added Hydrogen chloride (2 N in Ethyl acetate, 10 mL). The reaction mixture was stirred at ambient temperature for 30 min and then concentrated under reduced pressure to give the crude title compound as hydrogen chloride salt (60 mg, 78% yield). This material was used directly in the next step.

Step 3

6-methyl-7-oxo-N-(1-phenyl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



To a solution of 1-phenylpiperidin-4-amine hydrochloride (60 mg, 0.28 mmol) in DMF (3 mL) was added 6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid

(**Intermedate C**) (65 mg, 0.34 mmol), HATU (128 mg, 0.34 mmol) and diisopropylethylamine (1 mL). The reaction mixture was stirred at ambient temperature for 4 h, at which time LCMS indicated that the reaction had gone to completion. The mixture was concentrated under reduced pressure. The residue was diluted with ethyl acetate (15 mL) and washed with water (2 x 10 mL). The organic solution was concentrated under reduced pressure and the residue was purified by preparative HPLC (basic - acetonitrile : water (10 nM ammonia)25%-55%) to give the title compound (20 mg, 15% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.03 (s, 1 H), 7.85-7.79(m, 2 H), 7.28 (s, 1 H), 7.19-7.15 (m, 2 H), 6.93-6.91 (m, 2 H), 6.72-6.65 (m, 2 H), 3.92-3.90 (m, 1 H), 3.71-3.68 (m, 2 H), 3.51 (s, 3 H), 2.78 (t, *J* = 11.6 Hz, 2 H), 1.86-1.84 (m, 2 H), 1.63-1.55 (m, 2 H). LCMS M/Z (M+H) 351.1.

The following compounds were prepared in a similar fashion to Example 168.

Examples 172-180

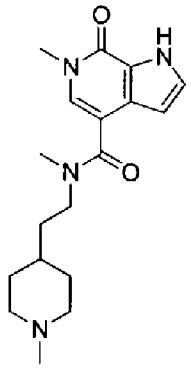
Example	Compound Name	NMR	m/z
172	N,6-dimethyl-7-oxo-N-(1-phenyl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.18-12.10 (br. s., 1 H), 7.41 (s, 1 H), 7.34 (s, 1 H), 7.23-7.17 (m, 2 H), 6.93 (d, *J* = 8.0 Hz, 2 H), 6.75 (t, *J* = 7.4 Hz, 1 H), 6.22 (s, 1 H), 4.28-4.15 (m, 1 H), 3.77-3.71 (m, 2 H), 3.53 (s, 3 H), 2.83 (s, 3 H), 2.68-2.60 (m, 2 H), 1.93-1.85 (m, 2 H), 1.74-1.72 (m, 2 H)	365
173	N,6-dimethyl-N-[1-(m-tolyl)-4-piperidyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 7.43-7.41 (m, 2 H), 7.12 (t, *J* = 7.6 Hz, 1 H), 6.84-6.80 (m, 2 H), 6.70 (d, *J* = 7.2 Hz, 1 H), 6.38 (d, *J* = 2.4 Hz, 1 H), 3.80-3.60 (m, 5 H), 3.00 (s, 3 H), 2.93 - 2.47 (m, 3 H), 2.30 (s, 3 H), 2.13 - 2.02 (m, 2 H), 1.94 - 1.82 (m, 2 H).	379
174	N,6-dimethyl-7-oxo-N-[1-[3-(trifluoromethyl)phenyl]-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 7.90-7.71 (m, 4 H), 7.43-7.39 (m, 2 H), 6.37 (d, *J* = 2.4 Hz, 1 H), 3.86-3.83 (m, 2 H), 3.66 (s, 4 H), 3.03 (s, 3 H), 2.47-2.39 (m, 2 H), 2.16-2.13 (m, 2 H).	432

175	N,6-dimethyl-7-oxo-N-[1-[4-(trifluoromethyl)phenyl]-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 7.39-7.35 (m, 3 H), 7.18-7.14 (m, 2 H), 7.04 (d, J = 7.2 Hz, 1 H), 6.35 (d, J = 2.8 Hz, 1 H), 3.91-3.79 (m, 2 H), 3.65 (s, 3 H), 3.36-3.34 (m, 1 H), 2.97 (s, 3 H), 2.84-2.74 (m, 2 H), 2.07-2.01 (m, 2 H), 1.99-1.87 (m, 2 H).	433
176	N,6-dimethyl-7-oxo-N-[1-(p-tolyl)-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 7.47-7.36 (m, 2 H), 7.06 (d, J = 8.0 Hz, 2 H), 6.91 (d, J = 7.2 Hz, 2 H), 6.38 (d, J = 3.2 Hz, 1 H), 3.70-3.67 (m, 5 H), 3.01 (s, 3 H), 2.87-2.53 (m, 3 H), 2.25 (s, 3 H), 2.13-2.02 (m, 2 H), 1.89-1.83 (m, 2 H).	379
177	N-[1-(3-ethylphenyl)-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 7.43-7.42 (m, 2 H), 7.18 - 7.12 (m, 1 H), 6.87-6.80 (m, 2 H), 6.76 - 6.71 (m, 1 H), 6.38 (d, J = 2.8 Hz, 1 H), 3.85-3.70 (m, 2 H), 3.68 (s, 3 H), 3.01 (s, 3 H), 2.89 - 2.50 (m, 5 H), 2.13-2.03 (m, 2 H), 1.95-1.84 (m, 2 H), 1.22 (t, J = 8.0 Hz, 3 H).	393
178	N-[1-(4-ethylphenyl)-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 7.43-7.41 (m, 2 H), 7.09 (d, J = 8.4 Hz, 2 H), 6.93 (d, J = 6.8 Hz, 2 H), 6.38 (d, J = 2.4 Hz, 1 H), 3.75-3.60 (m, 5 H), 3.01 (s, 3 H), 2.80-2.49 (m, 5 H), 2.10-2.02 (m, 2 H), 1.90-1.79 (m, 2 H), 1.20 (t, J = 7.6 Hz, 3 H).	393
179	N-[1-(3-isopropylphenyl)-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 7.43-7.41 (m, 2 H), 7.16 (t, J = 7.8 Hz, 1 H), 6.87-6.72 (m, 3 H), 6.38 (d, J = 3.2 Hz, 1 H), 3.83-3.71 (m, 2 H), 3.68 (s, 3 H), 3.01 (s, 3 H), 2.97-2.46 (m, 4 H), 2.13-2.03 (m, 2 H), 1.95-1.80 (m, 2 H), 1.24 (d, J = 7.2 Hz, 6 H).	407

180	N-[1-(4-isopropylphenyl)-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 7.47-7.34 (m, 2 H), 7.12 (d, *J* = 8.4 Hz, 2 H), 6.94 (d, *J* = 7.2 Hz, 2 H), 6.38 (d, *J* = 3.2 Hz, 1 H), 3.76-3.60 (m, 5 H), 3.01 (s, 3 H), 2.97-2.45 (m, 4 H), 2.13-2.02 (m, 2 H), 1.90-1.82 (m, 2 H), 1.22 (d, *J* = 6.8 Hz, 6 H).	407

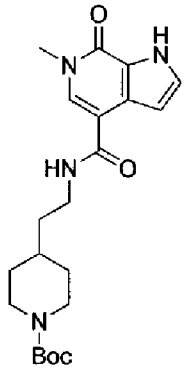
Example 181

N,6-dimethyl-N-[2-(1-methyl-4-piperidyl)ethyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

tert-butyl 4-[2-[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]ethyl]piperidine-1-carboxylate

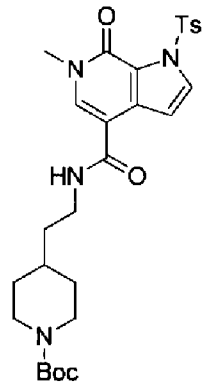


HATU (988 mg, 2.6 mmol) was added to a stirred mixture of 6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (**Intermediate C**) (500 mg, 2.6 mmol), *tert*-butyl 4-(2-aminoethyl)piperidine-1-carboxylate (713 mg, 3.1 mmol), and diisopropylethylamine (1.0 g, 7.8 mmol) in DMF (10 mL). The reaction mixture was stirred at room temperature for 16 h, at which time LCMS indicated that the reaction had gone to completion. The reaction mixture was

partitioned between ethyl acetate (50 mL) and water (15 mL). The separated organic solution was washed with brine (2 x 10 mL), dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel chromatography column (dichloromethane : methanol = 10:1) to afford the title compound (800 mg, 72.4% yield) as a yellow solid. LCMS M/Z (M+H) 402.9.

Step 2:

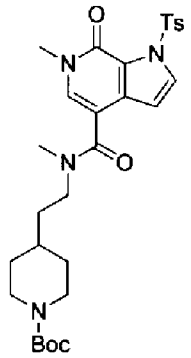
tert-butyl 4-[2-[[6-methyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carbonyl]amino]ethyl]piperidine-1-carboxylate



Sodium hydride (60%, 119 mg, 3.0 mmol) was added to a stirred and cooled (0 °C) solution of tert-butyl 4-[2-[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]ethyl]piperidine-1-carboxylate (800 mg, 2.0 mmol) in DMF (10 mL). Stirring was continued for 1 h at room temperature before 4-methylbenzene-1-sulfonyl chloride (455 mg, 2.4 mmol) was added. The reaction mixture was then stirred at room temperature for 1 h and quenched by addition of saturated aqueous ammonium chloride (2 mL). The reaction mixture was partitioned between ethyl acetate (150 mL) and water (50 mL). The organic layer was washed with brine (10 mL x 2), dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether : ethyl acetate = 1:2) to afford the title compound (500 mg, 45.0% yield) as a white solid. LCMS M/Z (M+H) 556.8.

Step 3:

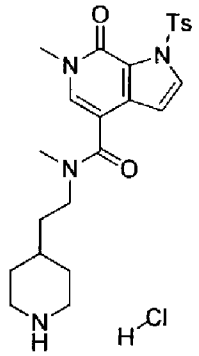
tert-butyl 4-[2-[methyl-[6-methyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carbonyl]amino]ethyl]piperidine-1-carboxylate



Sodium hydride (60%, 54 mg, 1.4 mmol) was added to a stirred and cooled (0 °C) solution of tert-butyl 4-[2-[[6-methyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carbonyl]amino]ethyl]piperidine-1-carboxylate (**Step 2,** 500 mg, 0.9 mmol) in DMF (10 mL). Stirring was continued for 1 h at room temperature before iodomethane (153 mg, 1.1 mmol) was added. The reaction mixture was then stirred at room temperature for 1 h and quenched by addition of saturated aqueous ammonium chloride (2 mL). The reaction mixture was partitioned between ethyl acetate (120 mL) and water (30 mL). The organic layer was washed with brine (10 mL x 2), dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether: ethyl acetate = 1:1) to afford the title compound (350 mg, 68.3% yield) as a yellow solid. LCMS M/Z (M+H) 571.2.

Step 4:

N,6-dimethyl-7-oxo-N-[2-(4-piperidyl)ethyl]-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxamide hydrogen chloride

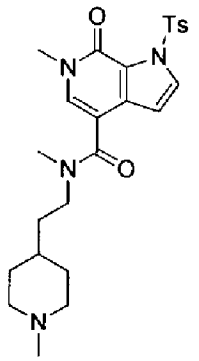


A mixture of tert-butyl 4-[2-[methyl-[6-methyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carbonyl]amino]ethyl]piperidine-1-carboxylate (350 mg, 0.6 mmol) in 4 N Hydrogen chloride/ethyl acetate, (40 mmol, 10 mL) was stirred at room temperature for 2 h. The solvent

was concentrated under reduced pressure to give the crude title compound as a yellow solid that was carried on to the next step. LCMS M/Z (M+H) 471.8.

Step 5:

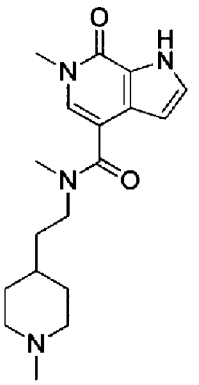
N,6-dimethyl-N-[2-(1-methyl-4-piperidyl)ethyl]-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxamide



A mixture of N,6-dimethyl-7-oxo-N-[2-(4-piperidyl)ethyl]-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxamide hydrogen chloride (100 mg, 0.2 mol) and paraformaldehyde (7 mg, 0.2 mmol) in methanol (5 mL) was heated at 70 °C for 16 h. The solution was cooled to 0 °C and then sodium borohydride (12 mg, 0.3 mmol) was added. After addition, stirring was continued for 1 h at room temperature. The reaction mixture was quenched by addition of saturated aqueous ammonium chloride (5 mL). The resulting mixture was partitioned between ethyl acetate (30 mL) and water (10 mL). The separated organic solution was washed with brine (2 x 5 mL), dried over sodium sulfate and concentrated under reduced pressure to afford the crude title compound (100 mg, 97.1% yield) as a white solid. LCMS M/Z (M+H) 485.1.

Step 6:

N,6-dimethyl-N-[2-(1-methyl-4-piperidyl)ethyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



A mixture of N,6-dimethyl-N-[2-(1-methyl-4-piperidyl)ethyl]-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxamide (100 mg, 0.2 mmol) in methanol (2 mL) and

aqueous sodium hydroxide solution (20% wt/vol, 1 mL) was heated at 100 °C for 16 h. After cooling, the mixture was concentrated under reduced pressure and the residue was purified by preparative HPLC, acetonitrile : water (10 nM ammonia), 10%-40%, to give the title compound (10 mg, 14.5% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.11 (s, 1 H), 7.38-7.30 (m, 2 H), 6.16 (d, *J* = 3.2 Hz, 1 H), 3.50 (s, 3 H), 2.90 (s, 3 H), 2.65-2.64 (m, 2 H), 2.06 (s, 3 H), 1.73-1.49 (m, 7 H), 1.06-1.05 (m, 4 H). LCMS M/Z (M+H) 331.2.

The following compounds were prepared in a similar fashion to Example 181.

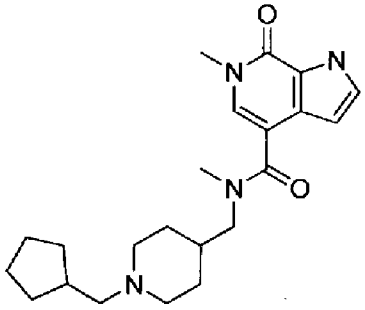
Examples 182-186

Example	Compound Name	NMR	m/z
182	N-[2-(1-ethyl-4-piperidyl)ethyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 8.52 (s, 1 H), 7.41 (d, *J* = 3.6 Hz, 2 H), 6.37 (d, *J* = 2.4 Hz, 1 H), 3.68-3.50 (m, 7 H), 3.13-3.32 (m, 5 H), 3.00-2.70 (m, 2 H), 2.14-2.10 (m, 1 H), 1.82-1.42 (m, 5 H), 1.34-1.21 (m, 4 H)	345
183	N-[2-(1-isopropyl-4-piperidyl)ethyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 8.51 (s, 1 H), 7.48-7.37 (m, 2 H), 6.38 (s, 1 H), 3.70-3.33 (m, 7 H), 3.10-2.75 (m, 6 H), 2.20-2.00 (m, 1 H), 1.85-1.40 (m, 5 H), 1.38-1.10 (m, 7 H)	359
184	N-[2-(1-cyclobutyl-4-piperidyl)ethyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 8.48 (s, 1 H), 7.39- 7.38 (m, 2 H), 6.34 (d, *J* = 3.0 Hz, 1 H), 3.84-3.32 (m, 7 H), 3.06 (s, 3 H), 2.82 -2.52 (m, 2 H), 2.37 -2.25 (m, 2 H), 2.19 -2.10 (m, 2 H), 2.08-1.96 (m, 2 H), 1.91-1.77 (m, 2 H), 1.73- 1.51 (m, 4 H), 1.44 -1.16 (m, 2 H).	371
185	N-[2-[1-(2-methoxyethyl)-4-piperidyl]ethyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 8.52 (s, 1 H), 7.39 (d, *J* = 2.8 Hz, 2 H), 6.34 (d, *J* = 2.0 Hz, 1 H), 3.76-3.44 (m, 8 H), 3.37 (s, 3 H), 3.22-3.18 (m, 2 H), 3.06 (s, 3 H), 2.99-2.53 (m, 3 H), 2.25-1.90 (m, 1 H), 1.75-1.25 (m, 6 H).	375

186	N-[2-(1-cyclopropyl-4-piperidyl)ethyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400MHz, DMSO-*d6*): δ 11.40 (s, 1 H), 8.86 (s, 1 H), 8.30 (s, 1 H), 8.22 (s, 1 H), 4.03 (s, 3 H), 2.50 (q, *J* = 1.6 Hz, 2 H), 2.44 (s, 3 H), 1.05 (t, *J* = 7.6 Hz, 3 H).	301

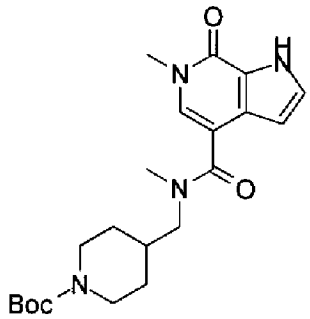
Example 187

N-[[1-(cyclopentylmethyl)-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

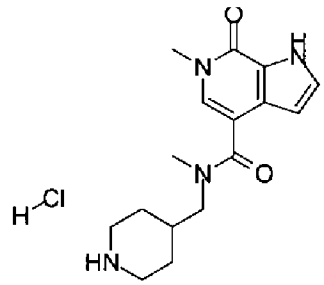
tert-butyl 4-[[methyl-(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]methyl]piperidine-1-carboxylate



HATU (4.4 g, 11.7 mmol) was added to a stirred mixture of 6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (**Intermediate C**) (1.5 g, 7.8 mmol), *tert*-butyl 4-(2-aminoethyl)piperidine-1-carboxylate (2.1 g, 9.4 mmol), and diisopropylethylamine (2.0 g, 15.6 mmol) in DMF (50 mL). After addition, the reaction mixture was stirred at room temperature for 2 h, at which time LCMS showed the completion of the reaction. The reaction mixture was diluted with ethyl acetate (200 mL), and then washed with water (50 mL), brine (20 mL x 2), dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography (dichloromethane:methanol = 10:1) to afford the title compound (2.3 g, 74.2% yield) as a white solid. LCMS M/Z (M+H) 402.9.

Step 2:

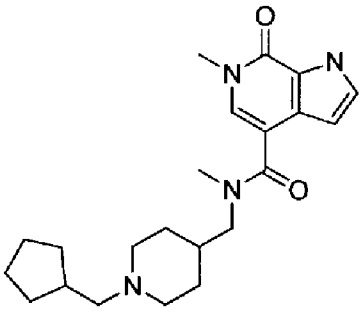
N,6-dimethyl-7-oxo-N-(4-piperidylmethyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide hydrogen chloride



A mixture of tert-butyl 4-[[methyl-(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]methyl]piperidine-1-carboxylate (2.3 g, 5.7 mmol) in 4 N hydrogen chloride/ethyl acetate (20 mL) was stirred at room temperature for 2 h. The solvent was evaporated to give the crude title compound (1.5 g, 88.2% yield) as a colorless oil. LCMS M/Z (M+H) 303.1.

Step 3:

N-[[1-(cyclopentylmethyl)-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Sodium triacetoxyborohydride (112 mg, 0.53 mmol) was added to a stirred mixture of N,6-dimethyl-7-oxo-N-(piperidin-4-ylmethyl)-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide hydrochloride (80 mg, 0.24 mmol), cyclopentanecarbaldehyde (39 mg, 0.40 mmol) in dichloromethane (10 mL). After addition, the reaction mixture was stirred at room temperature for 20 h, at which time LCMS showed the completion of the conversion. The reaction mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by preparative HPLC, acetonitrile : water (10 nM ammonia), 55%-85%, to give the title compound (8.7 mg, 7.8% yield) as a white solid. ^{1}H NMR (400 MHz, CD_3OD): δ 7.40 (s, 2 H), 6.35 (d, J = 2.4 Hz, 1 H), 3.67 (s, 3 H), 3.50-3.45 (m, 2 H), 2.92 (s, 3 H), 2.91-2.89

(m, 2 H), 2.39-2.32 (m, 2 H), 2.20-2.11 (m, 4 H), 1.81-1.58 (m, 10 H), 1.19-1.12 (m, 2 H).

LCMS M/Z (M+H) 385.20.

The following compounds were prepared in a similar fashion to Example 187.

Examples 188-206

Example	Compound Name	NMR	m/z
188	N,6-dimethyl-N-[(1-methyl-4-piperidyl)methyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.14 (s, 1 H), 7.40 (s, 1 H), 7.33 (d, *J* = 2.4 Hz, 1 H), 6.17 (d, *J* = 2.4 Hz, 1 H), 3.52 (s, 3 H), 3.32-3.30 (m, 2 H), 2.98 (s, 3 H), 2.75-2.70 (m, 2 H), 2.10 (s, 3 H), 1.78-1.75 (m, 3 H), 1.69-1.45 (m, 3 H), 1.20-0.80 (m, 2 H)	317
189	N-[(1-cyclobutyl-4-piperidyl)methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 8.50 (s, 1 H), 7.41-7.39 (m, 2 H), 6.34 (d, *J* = 2.8 Hz, 1 H), 3.66 (s, 3 H), 3.53-3.34 (m, 5 H), 3.09 (s, 3 H), 2.75-2.65 (m, 2 H), 2.40-1.75 (m, 9 H), 1.70-1.45 (m, 2H)	357
190	N-[(1-isopropyl-4-piperidyl)methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 8.52 (s, 1 H), 7.40-7.38 (m, 2 H), 6.33 (d, *J* = 2.8 Hz, 1 H), 3.64 (s, 3 H), 3.53-3.34 (m, 4 H), 3.08 (s, 3 H), 3.06-2.88 (m, 2 H), 2.30-1.80 (m, 2 H), 1.60 (m, 2 H), 1.40-1.25 (m, 6 H)	345
191	N-[(1-ethyl-4-piperidyl)methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400MHz, DMSO-*d6*): δ 12.07 (s, 1 H), 8.24 (s, 1 H), 7.91 (t, *J* = 5.2 Hz, 1 H), 7.77 (s, 1 H), 7.30 (s, 1 H), 6.67 (s, 1 H), 3.52 (s, 3 H), 3.26-3.23 (m, 2 H), 2.91 (d, *J* = 11.2 Hz, 2 H), 2.52 (s, 3 H), 2.34-2.31 (m, 1 H), 1.96 (t, *J* = 10.8 Hz, 2 H), 1.69 (d, *J* = 11.6Hz, 2 H), 1.46 - 1.40 (m, 2 H), 1.21-1.14 (m, 2 H), 0.99 (t, *J* = 7.2 Hz, 3 H).	331

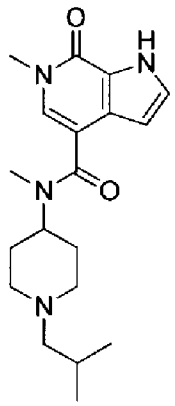
192	N-[(1-cyclopropyl-4-piperidyl)methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 11.90 (s, 1 H), 7.16 (s, 1 H), 7.10 (s, 1 H), 5.95 (s, 1 H), 3.30 (s, 3 H), 3.07-3.00 (m, 3 H), 2.71 (s, 3 H), 2.69-2.64 (m, 2 H), 1.88-1.65 (m, 2 H), 1.49 - 1.26 (m, 5 H), 0.16-0.13 (m, 2 H), 0.04-0.01 (m, 2 H).	343
193	N-[[1-(2-methoxyethyl)-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR(400 MHz, DMSO-*d6*): δ 12.08 (s, 1 H), 7.91-7.85 (m, 1 H), 7.79 (s, 1 H), 7.31 (d, *J* = 2.8 Hz, 1 H), 6.69 (d, *J* = 2.8 Hz, 1 H), 3.54 (s, 3 H), 3.40 (t, *J* = 6.4 Hz, 2 H), 3.26 (d, *J* = 5.2 Hz, 2 H), 3.21 (s, 3 H), 2.82 (d, *J* = 11.6 Hz, 2 H), 2.41 (t, *J* = 6.4 Hz, 2 H), 1.89 (t, *J* = 10.8 Hz, 2 H), 1.65 (d, *J* = 11.6 Hz, 2 H), 1.47-1.41 (m, 2 H), 1.24-1.21 (m, 1 H), 1.18-1.09 (m, 2 H).	361
194	N-[(1-benzyl-4-piperidyl)methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR(400 MHz, CD_3OD): δ 7.40 (s, 1 H), 7.39 (s, 1 H),7.31-7.28 (m, 5 H), 6.34 (d, *J* = 2.4 Hz, 1 H), 3.67 (s, 3 H), 3.52-3.50 (m, 4 H), 3.06 (s, 3 H), 2.93-2.85 (m, 2 H), 2.10-2.04 (m, 2 H), 1.67-1.02 (m, 5 H).	393
195	N,6-dimethyl-N-[[1-(o-tolylmethyl)-4-piperidyl]methyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR(400 MHz, CD_3OD): δ 7.40-7.38 (m, 2H), 7.23-7.15 (m, 4 H), 6.34 (d, *J* = 2.8 Hz, 1 H), 3.66 (s, 3 H), 3.49-3.45 (m, 4 H), 3.08 (s, 3 H), 2.96-2.93 (m, 2 H), 2.35 (s, 3 H), 2.06-2.00 (m, 2 H), 1.76-1.24 (m, 5 H).	407
196	N,6-dimethyl-7-oxo-N-[[1-(p-tolylmethyl)-4-piperidyl]methyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR(400 MHz, DMSO-*d6*): δ 12.13 (s, 1 H), 7.38 (s, 1 H), 7.32 (d, *J* = 2.4 Hz, 1 H), 7.12-7.08 (m, 4 H), 6.17 (d, *J* = 3.2 Hz, 1 H), 3.52 (s, 3 H), 3.33-3.30 (m, 4 H), 2.93 (s, 3 H), 2.74-2.71 (m, 2 H), 2.26 (s, 3 H), 1.88-1.85 (m, 2 H), 1.66-1.54 (m, 3 H), 1.09-1.05 (m, 2 H).	407

197	N,6-dimethyl-7-oxo-N-[[1-(1-phenylethyl)-4-piperidyl]methyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.09 (s, 1 H), 7.33 (s, 1 H), 7.27-7.22 (m, 6 H), 6.12 (d, *J* = 2.4 Hz, 1 H), 3.48 (s, 3 H), 3.27-3.25 (m, 2 H), 2.86 (s, 3 H), 2.65-2.63 (m, 1 H), 2.50-2.47 (m, 4 H), 1.83-1.80 (m, 3 H), 1.77-1.56 (m, 2 H), 1.22-1.20 (m, 3 H)	406
198	N-[[1-[(2-chlorophenyl)methyl]-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.13 (s, 1 H), 7.44-7.39 (m, 3 H), 7.32-7.24 (m, 3 H), 6.18 (d, *J* = 2.4 Hz, 1 H), 3.53 (s, 5 H), 2.94 (s, 3 H), 2.78-2.75 (m, 2 H), 2.50-2.47 (m, 2 H), 2.02-1.98 (m, 2 H), 1.70-1.57 (m, 3 H), 1.24-1.20 (m, 2 H).	427
199	N-[[1-[(3-chlorophenyl)methyl]-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 7.40-7.29 (m, 6 H), 6.34 (d, *J* = 2.4 Hz, 1 H), 3.67 (s, 3 H), 3.52-3.42 (m, 4 H), 3.08 (s, 3 H), 2.90-2.86 (m, 2 H), 2.04-1.98 (m, 2 H), 1.77-1.63 (m, 5 H).	427
200	N-[[1-[(4-chlorophenyl)methyl]-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.08 (s, 1 H), 7.34-7.25 (m, 6 H), 6.12 (s, 1 H), 3.48 (s, 3 H), 3.36-3.31 (m, 2 H), 2.89 (s, 3 H), 2.70-2.68 (m, 2 H), 2.50-2.47 (m, 2 H), 1.86-1.84 (m, 2 H), 1.63-1.51 (m, 3 H), 1.13-1.10 (m, 2 H).	427
201	N-[[1-[(2-fluorophenyl)methyl]-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.12 (s, 1 H), 7.38-7.28 (m, 4 H), 7.17-7.11 (m, 2 H), 6.17 (s, 1 H), 3.52-3.48 (m, 5 H), 2.93 (s, 3 H), 2.75-2.71 (m, 2 H), 2.50-2.47 (m, 2 H), 1.97-1.92 (m, 2 H), 1.66-1.56 (m, 3 H), 1.10-1.08 (m, 2 H).	411

202	N-[[1-[(3-fluorophenyl)methyl]-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.13 (s, 1 H), 7.39-7.31 (m, 3 H), 7.12-7.07 (m, 3 H), 6.17 (s, 1 H), 3.52 (s, 3 H), 3.44 (s, 2 H), 2.93 (s, 3 H), 2.76-2.71 (m, 2 H), 2.50-2.47 (m, 2 H), 1.91-1.89 (m, 2 H), 1.68-1.56 (m, 3 H), 1.18-1.15 (m, 2 H).	411
203	N-[[1-[(4-fluorophenyl)methyl]-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-*d6*): δ 12.13 (s, 1 H), 7.38-7.29 (m, 4 H), 7.13-7.09 (m, 2 H), 6.17 (s, 1 H), 3.52 (s, 3 H), 3.40 (s, 2 H), 2.93 (s, 3 H), 2.74-2.71 (m, 2 H), 2.50-2.47 (m, 2 H), 1.88-1.82(m, 2 H), 1.66-1.57 (m, 3 H), 1.15-1.08 (m, 2 H).	411
204	N,6-dimethyl-N-[[1-(m-tolylmethyl)-4-piperidyl]methyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 12.13 (s, 1 H), 7.38 (s, 1 H), 7.32 (s, 1 H), 7.19-7.15 (m, 1 H), 7.06-7.02 (m, 3 H), 6.17 (s, 1 H), 3.52 (s, 3 H), 3.36 (s, 2 H), 2.93 (s, 3 H), 2.74-2.71 (m, 2 H), 2.27 (s, 3 H), 1.88-1.85 (m, 2 H), 1.67-1.55 (m, 3 H), 1.15-1.08 (m, 2 H).	406
205	N-[(1-cyclopentyl-4-piperidyl)methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 7.40 (s, 2 H), 6.35 (d, J = 3.2 Hz, 1 H), 3.67 (s, 3 H), 3.49-3.45 (m, 2 H), 3.09-2.93 (m, 5 H), 2.55-2.52 (m, 1 H), 1.91-1.40 (m, 15 H).	371
206	N-[[1-(cyclohexylmethyl)-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 7.43 (s, 1 H), 7.42 (s, 1 H), 6.36 (s, 1 H), 3.68 (s, 3 H), 3.50-3.45 (m, 4 H), 3.11 (s, 3 H), 2.90-2.85 (m, 4 H), 2.12-1.71 (m, 10 H), 1.37-1.22 (m, 4 H), 1.10-1.06 (m, 2 H).	399

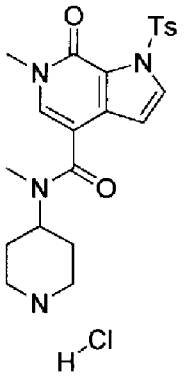
Example 207

N-(1-isobutyl-4-piperidyl)-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

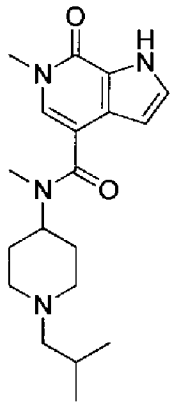
N,6-dimethyl-7-oxo-N-(4-piperidyl)-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxamide hydrochloride



To a 40 mL vial was added 6-methyl-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxylic acid (**Intermediate E**, 1.24 g, 2.6 mmol) N,N-dimethylformamide (10 mL), HATU (1.1 g, 2.9 mmol), and triethylamine (1.09 mL 7.8 mmol). The reaction was stirred for 15 minutes. *Tert*-butyl 4-(methylamino)piperidine-1-carboxylate (1.5 equiv., 3.9 mmol) was then added, and the reaction was shaken at room temperature for 4h. The reaction was then diluted with ethyl acetate, and then washed with water. The aqueous solution was further extracted 2 times with ethyl acetate. The combined organic extracts were dried over sodium sulfate, and concentrated under reduced perssure to affort 1.09 g of crude product. The crude material was up in methanol (20 mL) and 4N hydrogen chloride in dioxane (20 mL). The reaction was stirred at room temperature for 1h and then concentrated under reduced pressure to yield 965 mg of product that was 80% pure by LCMS. LCMS M/Z (M+H) 443. This material was used without further purification.

Step 2:

N-(1-isobutyl-4-piperidyl)-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



MP-Cyanoborohydride (0.2g, 2.39 mmol/g, 0.48 mmol) was added to a mixture of N,6-dimethyl-7-oxo-N-(4-piperidyl)-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxamide hydrochloride (75 mg, 0.16 mmol), methanol (0.75 mL), 1,2-dichloroethane (0.75 mL), isobutyraldehyde (23 mg, 0.32 mmol) and triethylamine (0.043 mL, 0.31 mmol). The reaction was shaken at room temperature overnight and the mixture was filtered, washing the resin with methanol. The filtrate was concentrated under reduced pressure and the residue was purified by preperative HPLC (5-85%MeOH/0.1%NH4OH in H20) to give N-(1-isobutyl-4-piperidyl)-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (11.2 mg, 20%). ^{1}H NMR (400 MHz, DMSO-*d6*) δ 12.12 (s, 2H), 7.39 – 7.29 (m, 3H), 6.18 (d, *J* = 2.8 Hz, 2H), 3.72 – 3.67 (m, 1H), 3.52 (s, 5H), 2.91 – 2.78 (m, 2H), 2.28 – 2.23 (m, 3H), 2.05 – 1.95 (m, 3H), 1.84 – 1.65 (m, 4H), 1.63 – 1.56 (m, 2H), 0.88 – 0.80 (m, 6H). LCMS M/Z (M+H) 345.

The following compounds were prepared in a similar fashion to Example 207.

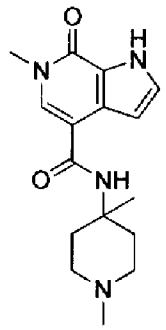
Examples 208-209

Example	Compound Name	NMR	m/z
208	N-[1-(cyclopropylmethyl)-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.39 – 7.29 (m, 2H), 6.19 (d, *J* = 2.7 Hz, 1H), 3.52 (s, 3H), 3.30 (s, 31H), 3.03 – 2.98 (m, 2H), 2.83 (s, 3H), 2.29 – 2.24 (m, 2H), 1.86 – 1.81 (m, 2H), 1.81 – 1.73 (m, 1H), 1.60 (d, *J* = 10.8 Hz, 2H), 0.80 (d, *J* = 8.1 Hz, 1H), 0.49 – 0.39 (m, 2H), 0.13 – 0.02 (m, 2H).	343

209	Trans-N-(3-fluoro-1-isopropyl-4-piperidyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (s, 1H), 8.02 (d, J = 8.3 Hz, 1H), 7.80 (s, 1H), 7.37 – 7.26 (m, 1H), 6.69 (dd, J = 2.8, 1.6 Hz, 1H), 4.52 (dtd, J = 50.3, 9.6, 5.0 Hz, 1H), 3.91 (d, J = 7.1 Hz, 1H), 3.56 (s, 3H), 3.21 – 3.06 (m, 1H), 2.94 – 2.60 (m, 2H), 2.29 – 2.08 (m, 2H), 1.89 (d, J = 14.6 Hz, 1H), 1.50 (tt, J = 12.5, 6.1 Hz, 1H), 0.98 (dd, J = 6.6, 3.3 Hz, 6H).	335

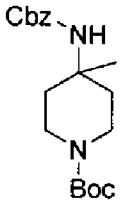
Example 210

N-(1,4-dimethyl-4-piperidyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

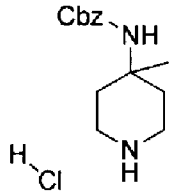
tert-butyl 4-(((benzyloxy)carbonyl)amino)-4-methylpiperidine-1-carboxylate



A mixture of 1-(tert-butoxycarbonyl)-4-methylpiperidine-4-carboxylic acid **(Intermediate C**, 5.0 g, 20.5 mmol), triethylamine (4.3 mL, 30.8 mmol) and diphenylphosphoryl azide (6.0 mL, 29.8 mmol) in toluene (100 mL) was stirred at room temperature for 1 h. Benzyl alcohol (5.4 mL, 51.3 mmol) was added into the reaction mixture and the reaction mixture was heated at 80 °C for 18 h, at which time TLC showed the completion of the reaction. The solvent was evaporated and the residue was dissolved in ethyl acetate (100 mL). The solution was washed with water (30 mL x 2), dried over sodium sulfate and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (petroleum ether : ethyl acetate = 3:1) to give the title compound (1.8 g, 25.2% yield) as colorless oil. LCMS M/Z (M+H) 349.1.

Step 2:

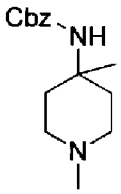
benzyl (4-methylpiperidin-4-yl)carbamate hydrochloride



tert-Butyl 4-(((benzyloxy)carbonyl)amino)-4-methylpiperidine-1-carboxylate (1.3 g, 3.73 mmol) in dioxane (30 mL) was treated with hydrogen chloride (4 N in dioxane, 10 mL). The reaction mixture was stirred at room temperature for 2 h, at which time TLC indicated that the reaction had gone to completion. The mixture was concentrated under reduced pressure to give the crude title compound (1.0 g, 100% yield) as colorless oil. This material was used into next step without further treatment. LCMS M/Z (M+H) 248.9.

Step 3:

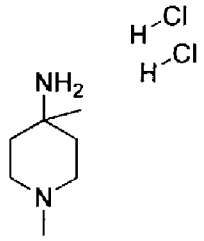
benzyl (1,4-dimethylpiperidin-4-yl)carbamate



A mixture of benzyl (4-methylpiperidin-4-yl)carbamate hydrochloride (650 mg, 2.3 mmol), formaldehyde (aq. 35-40%, 1 mL) and sodium cyanoborohydride (289 mg, 4.6 mmol) in methanol (30 mL) was stirred at 90 °C for 3 h, at which time LCMS indicated the reaction had gone to completion. The reaction was quenched by addition of saturated aqueous ammonium chloride (5 mL). This mixture was adjusted to pH 8-9 using saturated aqueous sodium bicarbonate and the resulting mixture was extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced pressure to give the crude title compound (300 mg, 49.7% yield) as colorless oil. LCMS M/Z (M+H) 263.1.

Step 4:

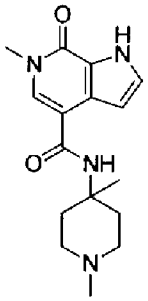
1,4-dimethylpiperidin-4-amine di-hydrochloride



A mixture of benzyl (1,4-dimethylpiperidin-4-yl)carbamate (300 mg, 1.16 mmol) and palladium on charcoal (50 mg) in methanol (50 mL) and concentrated hydrochloric acid (one drop) was stirred under a hydrogen atmosphere (balloon) for 18 h, at which time LCMS indicated the reaction had gone to completion. The mixture was filtered through a short pad of Celite and rinsed with methanol (10 mL). The combined organic filtrates were concentrated under reduced pressure to give the crude title compound (100 mg, 43% yield) as light yellow oil. This crude material was used directly in the next step.

Step 5

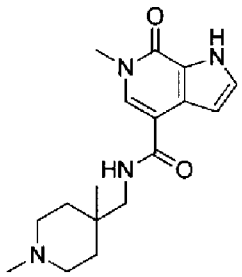
N-(1,4-dimethyl-4-piperidyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



HATU (305 mg, 0.80 mmol) was added to a mixture of 6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (**Intermediate C**) (141 mg, 0.73 mmol), 1,4-dimethylpiperidin-4-amine di-hydrochloride (189 mg, 1.47 mmol), and diisopropylethylamine (300 mg, 2.32 mmol) in DMF (2 mL). The resulting mixture was stirred at room temperature for 2 h, at which time LCMS indicated that the reaction had gone to completion. The mixture was diluted with water (10 mL) and extracted with ethyl acetate (2 x 20 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by preparative HPLC, acetonitrile : water (10 nM ammonia bicarbonate), 0%-30%, to give the title compound (49 mg, 22.3% yield) as a white solid. ^{1}H NMR (400 MHz, CD_3OD): δ 7.68 (s, 1 H), 7.37 (d, J = 2.8 Hz, 1 H), 6.68 (d, J = 2.8 Hz, 1 H), 3.67 (s, 3 H), 2.69-2.60 (m, 2 H), 2.46-2.32 (m, 7 H), 1.8-1.65 (m, 2 H), 1.48 (s, 3 H). LCMS M/Z (M+H) 303.1.

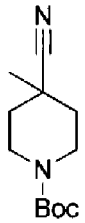
Example 211

N-[(1,4-dimethyl-4-piperidyl)methyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

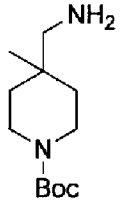
***tert*-butyl 4-cyano-4-methylpiperidine-1-carboxylate**



Under nitrogen protection, LDA (1M in THF, 26.2 mL, 26.2 mmol) was added dropwise to a stirred and cooled (-78 °C) solution of *tert*-butyl 4-cyanopiperidine-1-carboxylate (5.0 g, 23.8 mmol) in THF (100 mL). After addition, the reaction mixture was stirred at -78 °C for 1 h, and then methyl iodide (1.48 mL, 23.8 mmol) was added dropwise. The resulting mixture was allowed warm to room temperature and stirring was continued for 2 h. The reaction was quenched by addition of saturated aqueous ammonium chloride (50 mL), and extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were washed with brine, dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether : ethyl acetate 4:1) to give the title compound (4.3 g, 81% yield) as light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.10-3.95 (m, 2 H), 3.10-2.95 (m, 2 H), 1.90-1.85 (d, J = 12 Hz, 2 H), 1.45-1.32 (m, 14 H).

Step 2:

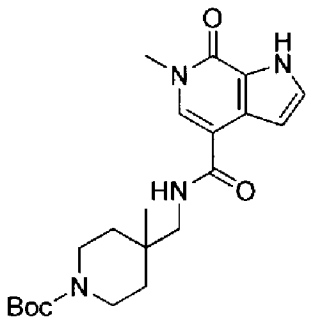
***tert*-butyl 4-(aminomethyl)-4-methylpiperidine-1-carboxylate**



Raney-Ni (3.0 g) was carefully added to a solution of *tert*-butyl 4-cyano-4-methylpiperidine-1-carboxylate (4.3 g, 19.2 mmol) in methanol under nitrogen. After addition, the mixture was stirred under hydrogen (50 psi) for 2 h at room temperature. The resulting mixture was filtered through a short pad of Celite using dichloromethane to rinse. The filtrate was concentrated under reduced pressure to give the title compound (4.0 g, 91.5% yield) as light brown oil. This crude material was used directly in the next step. LCMS M/Z (M+H) 229.1.

Step 3:

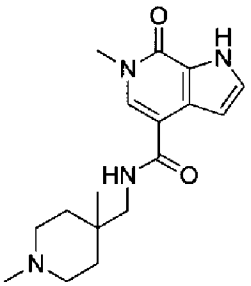
tert-butyl 4-methyl-4-[[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]methyl]piperidine-1-carboxylate



HATU (294 mg, 0.8 mmol) was added to the mixture of 6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (**Intermediate C**) (135 mg, 0.7 mmol), *tert*-butyl 4-(aminomethyl)-4-methylpiperidine-1-carboxylate (160 mg, 0.7 mmol), and diisopropylethylamine (181 mg, 1.4 mmol) in DMF (3 mL). After addition, the reaction mixture was stirred at room temperature for 2 h, at which time LCMS indicated that the reaction had gone to completion. The mixture was quenched by addition of water (5 mL) and extracted with ethyl acetate (2 x 10 mL). The combined organic extracts were washed with brine, dried over sodium sulfate and concentrated under reduced pressure to give the crude title compound (275 mg, 94% yield) as light brown oil. This crude material was used directly in the next step. LCMS M/Z (M+H) 402.9.

Step 4:

N-((1,4-dimethylpiperidin-4-yl)methyl)-6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



tert-Butyl 4-methyl-4-[[(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)amino]methyl]piperidine-1-carboxylate (275 mg, 0.7 mmol) was treated with 4N hydrogen chloride in ethyl acetate (10 mL) for 1 h at room temperature. The mixture was concentrated under reduced pressure and the residue was mixed with paraformaldehyde (18 mg, 0.6 mmol), triethylamine (90 mg, 0.9 mmol), and methanol (5 mL). The resulting mixture was heated at 90 °C for 2 h and then cooled to 0 °C. Sodium borohydride (45 mg, 1.2 mmol) was added to the mixture in one portion and stirring was continued for 30 min at room temperature, at which time LCMS indicated the reaction had gone to completion. The mixture was concentrated under reduced pressure and the residue was purified by preparative HPLC (acetonitrile : water (0.3% formic acid), 1%-30%) to give the title compound (30.1 mg, 32.3%) as a white solid. ^{1}H NMR (400 MHz, CD_3OD): δ 7.78 (s, 1 H), 7.38 (d, J = 2.8 Hz, 1 H), 6.73 (d, J = 2.8 Hz, 1 H) , 3.67 (s, 3 H), 3.49-3.20 (m, 6 H), 2.87 (s, 3 H), 1.83-1.81 (m, 2 H), 1.68-1.65 (m, 2 H), 1.13 (s, 3H). LCMS M/Z (M+H) 317.2.

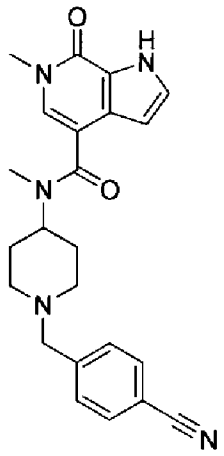
The following compound was prepared in a similar fashion to Example 211.

Examples 212

Example	Compound Name	NMR	m/z
212	N-[(1-isopropyl-4-methyl-4-piperidyl)methyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, CD_3OD): δ 8.34 (s, 1 H), 7.76 (s, 1 H), 7.38 (d, J = 2.8 Hz, 1 H), 6.73 (d, J = 2.4 Hz, 1 H) , 3.67 (s, 3 H), 3.50-3.10 (m, 7 H), 1.86-1.83 (m, 2 H), 1.71-1.67 (m, 2 H), 1.37 (d, J = 8.0 Hz, 6 H), 1.12 (s, 3H).	345

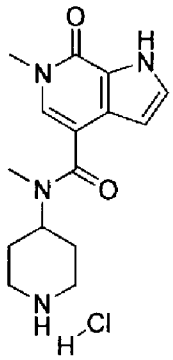
Example 213

N-[1-[(4-cyanophenyl)methyl]-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

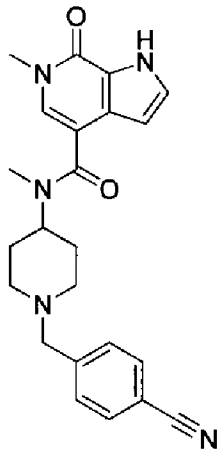
N,6-dimethyl-7-oxo-N-(4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide hydrochloride



To a 40 mL vial was added 6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (**Intermediate C**, 690 mg, 3.6 mmol) followed by N,N-dimethylformamide (10 mL), HATU (1.67 g, 4.4 mmol), triethylamine (2.02 mL, 14.5 mmol) and *tert*-butyl 4-(methylamino)piperidine-1-carboxylate (900 mg., 4.2 mmol). The reaction was capped and shaken at room temperature for 2h. The resulting precipitate was collected by filtration, washed with ethyl acetate, and dried to afford the desired boc-protected amine intermediate (513 mg, 36%). This material was suspended in methanol (4 mL) and hydrogen chloride (4 N in dioxane, 4 mL) was added. The reaction was shaken at room temperature for 1h and then concentrated under reduced pressure to afford N,6-dimethyl-7-oxo-N-(4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide hydrochloride (425 mg, 36%). This material was used directly in the next step.

Step 2:

N-[1-[(4-cyanophenyl)methyl]-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



To a 4 mL vial was added N,6-dimethyl-7-oxo-N-(4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide hydrochloride (43 mg, 0.13 mmol) followed by N,N-dimethylformamide (0.5 mL), diisopropylethylamine (3 equiv., 0.40 mmol), and 4-(bromomethyl)benzonitrile (1.1 equiv., 0.15 mmol). The reaction was capped and shaken at 50°C overnight. After cooling, the mixture was diluted with dichloromethane, washed with water and concentrated under reduced pressure. The residue was purified by preparative HPLC (5-85%MeOH/0.1%NH4OH in H20) to yield N-[1-[(4-cyanophenyl)methyl]-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (25 mg, 48%). 1H NMR (400 MHz, DMSO-d6) δ 12.11 (s, 1H), 7.82 – 7.74 (m, 2H), 7.50 (dd, J = 8.2, 3.4 Hz, 2H), 7.39 – 7.28 (m, 2H), 6.18 (d, J = 2.8 Hz, 1H), 4.01 (s, 1H), 3.53 (d, J = 5.4 Hz, 5H), 2.83 (s, 5H), 1.99 (d, J = 15.0 Hz, 2H), 1.89 – 1.70 (m, 2H), 1.61 (d, J = 11.5 Hz, 2H). LCMS M/Z (M+H) 404.

The following compounds were prepared in a similar fashion to Example 213.

Examples 214-243

Example	Compound Name	NMR	m/z
214	N,6-dimethyl-7-oxo-N-[1-(1-phenylethyl)-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 7.41 – 7.12 (m, 7H), 6.16 (d, J = 2.7 Hz, 1H), 3.51 (s, 3H), 3.48 – 3.37 (m, 1H), 3.09 – 2.59 (m, 4H), 1.94 – 1.59 (m, 6H), 1.33 – 1.23 (m, 3H).	393

215	N-[1-[(2-cyanophenyl)methyl]-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.80 (ddd, J = 8.0, 4.0, 1.3 Hz, 1H), 7.72 – 7.62 (m, 1H), 7.60 – 7.52 (m, 1H), 7.51 – 7.41 (m, 1H), 7.39 – 7.29 (m, 2H), 6.19 (d, J = 2.7 Hz, 1H), 3.61 (d, J = 5.8 Hz, 2H), 3.52 (s, 3H), 2.82 (s, 5H), 2.12 – 2.01 (m, 2H), 1.86 – 1.72 (m, 2H), 1.66 – 1.58 (m, 2H).	404
216	N-[1-[(2-fluorophenyl)methyl]-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.44 – 7.25 (m, 4H), 7.21 – 7.09 (m, 2H), 6.18 (d, J = 2.7 Hz, 1H), 3.99 (s, 1H), 3.54 – 3.44 (m, 5H), 2.92 – 2.80 (m, 5H), 2.01 – 1.93 (m, 3H), 1.87 – 1.69 (m, 3H), 1.65 – 1.56 (m, 2H).	397
217	N-(1-isopentyl-4-piperidyl)-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.38 – 7.28 (m, 2H), 6.18 (t, J = 2.1 Hz, 1H), 3.96 (s, 1H), 3.52 (s, 3H), 3.30 (d, J = 18.3 Hz, 1H), 2.89 (d, J = 8.6 Hz, 2H), 2.82 (s, 3H), 2.27 – 2.19 (m, 2H), 1.82 – 1.69 (m, 5H), 1.63 – 1.47 (m, 3H), 1.28 (q, J = 7.2 Hz, 2H), 0.85 (d, J = 6.6 Hz, 6H).	359
218	N,6-dimethyl-7-oxo-N-[1-(p-tolylmethyl)-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.33 (d, J = 18.8 Hz, 2H), 7.19 – 7.07 (m, 4H), 6.18 (d, J = 2.7 Hz, 1H), 3.99 (s, 1H), 3.52 (s, 3H), 3.40 – 3.23 (m, 5H), 2.88 – 2.80 (m, 5H), 2.27 (s, 3H), 1.91 – 1.86 (m, 2H), 1.85 – 1.71 (m, 2H), 1.63 – 1.55 (m, 2H).	393
219	N-[1-(cyclopentylmethyl)-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.38 – 7.28 (m, 2H), 6.21 – 6.15 (m, 1H), 3.96 (s, 1H), 3.52 (s, 3H), 2.91 (d, J = 8.9 Hz, 2H), 2.82 (s, 3H), 2.17 – 2.10 (m, 2H), 2.08 – 1.95 (m, 1H), 1.83 – 1.72 (m, 5H), 1.69 – 1.41 (m, 9H), 1.21 – 1.08 (m, 2H).	371

220	N-[1-[(3-cyanophenyl)methyl]-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.75 – 7.68 (m, 2H), 7.64 (d, J = 7.9 Hz, 1H), 7.54 (t, J = 7.9 Hz, 1H), 7.39 – 7.28 (m, 2H), 6.18 (d, J = 2.7 Hz, 1H), 4.01 (s, 1H), 3.51 (d, J = 6.5 Hz, 5H), 2.84 (s, 5H), 2.72 (d, J = 10.8 Hz, 0H), 1.99 – 1.94 (m, 2H), 1.88 – 1.75 (m, 2H), 1.65 – 1.57 (m, 2H).	404
221	N-[1-[(4-methoxyphenyl)methyl]-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.38 – 7.28 (m, 2H), 7.21 – 7.14 (m, 2H), 6.91 – 6.83 (m, 2H), 6.18 (d, J = 2.7 Hz, 1H), 3.98 (s, 1H), 3.73 (s, 3H), 3.52 (s, 3H), 3.35 (s, 2H), 2.82 (s, 5H), 1.87 (s, 2H), 1.84 – 1.70 (m, 2H), 1.63 – 1.55 (m, 2H).	409
222	N-[1-[(3-methoxyphenyl)methyl]-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.39 – 7.28 (m, 2H), 7.22 (t, J = 7.8 Hz, 1H), 6.89 – 6.76 (m, 3H), 6.18 (d, J = 2.8 Hz, 1H), 4.00 (s, 1H), 3.73 (s, 3H), 3.52 (s, 3H), 3.40 (s, 2H), 2.83 (s, 5H), 1.94 – 1.89 (m, 2H), 1.87 – 1.73 (m, 2H), 1.64 – 1.56 (m, 2H).	409
223	N-[1-[(2-chlorophenyl)methyl]-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.52 – 7.43 (m, 1H), 7.45 – 7.23 (m, 5H), 6.19 (d, J = 2.8 Hz, 1H), 4.07 (s,1H), 3.56 – 3.50 (m, 5H), 2.92 – 2.81 (m, 5H), 2.06 – 2.01 (m, 2H), 1.88 – 1.74 (m, 2H), 1.66 – 1.58 (m, 2H).	413
224	N-[1-[(3-chlorophenyl)methyl]-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.39 – 7.21 (m, 8H), 6.18 (d, J = 2.8 Hz, 1H), 4.00 (s, 1H), 3.52 (s, 3H), 3.44 (s, 3H), 2.86 – 2.81 (m, 5H), 2.02 – 1.91 (m, 3H), 1.88 – 1.70 (m, 3H), 1.65 – 1.57 (m, 2H).	413

225	N-[1-(2-methoxyethyl)-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 7.38 – 7.28 (m, 2H), 6.18 (dd, J = 2.7, 1.4 Hz, 1H), 3.96 (s, 1H), 3.52 (s, 3H), 3.39 (t, J = 5.8 Hz, 2H), 3.21 (s, 3H), 2.91 (d, J = 10.9 Hz, 2H), 2.82 (s, 3H), 2.53 (s, 1H), 2.43 (t, J = 5.9 Hz, 2H), 1.95 – 1.90 (m, 2H), 1.84 – 1.70 (m, 2H), 1.62 – 1.54 (m, 2H).	347
226	N-[1-(2-cyclopropylethyl)-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.39 – 7.28 (m, 2H), 6.19 (t, J = 2.3 Hz, 1H), 3.99 (s, 1H), 3.52 (s, 3H), 2.96 – 2.91 (m, 2H), 2.82 (s, 4H), 2.35 (s, 2H), 1.90 – 1.85 (m, 2H), 1.83 – 1.75 (m, 2H), 1.65 – 1.60 (m, 2H), 1.36 – 1.26 (m, 2H), 0.70 – 0.57 (m, 1H), 0.42 – 0.31 (m, 2H), 0.01 (d, J = 5.9 Hz, 2H).	357
227	N-ethyl-N-(1-isopropyl-4-piperidyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.13 (s, 1H), 7.31 (d, J = 6.1 Hz, 2H), 6.15 (d, J = 2.8 Hz, 1H), 3.69 (s, 1H), 3.52 (s, 3H), 3.38 – 3.25 (m, 2H), 2.77 (d, J = 10.8 Hz, 2H), 2.63 (p, J = 6.6 Hz, 1H), 2.48 (s, 1H), 1.91 (s, 2H), 1.80 – 1.59 (m, 4H), 1.09 (t, J = 6.9 Hz, 3H), 0.89 (d, J = 6.5 Hz, 6H).	345
228	N-(3-isopropyl-3-azabicyclo[3.1.0]hexan-6-yl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 7.93 (d, J = 4.2 Hz, 1H), 7.76 (s, 1H), 7.33 – 7.27 (m, 1H), 6.72 – 6.66 (m, 1H), 3.53 (s, 3H), 3.06 (d, J = 8.7 Hz, 2H), 2.95 (d, J = 3.8 Hz, 1H), 2.42 – 2.32 (m, 3H), 1.57 (s, 2H), 0.98 (d, J = 6.2 Hz, 6H).	315

229	N-[[1-(2-cyclohexylethyl)-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.39 (s, 1H), 7.32 (t, J = 2.7 Hz, 1H), 6.20 – 6.14 (m, 1H), 3.53 (s, 3H), 3.32 – 3.27 (m, 2H), 2.93 (s, 3H), 2.80 – 2.75 (m, 2H), 2.26 – 2.17 (m, 2H), 1.81 – 1.76 (m, 2H), 1.66 – 1.61 (m, 5H), 1.59 – 1.54 (m, 3H), 1.32 – 1.22 (m, 2H), 1.21 – 1.05 (m, 6H), 0.92 – 0.81 (m, 2H).	413
230	N,6-dimethyl-7-oxo-N-[[1-(tetrahydropyran-3-ylmethyl)-4-piperidyl]methyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.39 (s, 1H), 7.35 – 7.29 (m, 1H), 6.17 (t, J = 2.4 Hz, 1H), 3.79 – 3.66 (m, 2H), 3.53 (s, 3H), 3.32 – 3.20 (m, 2H), 3.03 – 2.91 (m, 4H), 2.83 – 2.78 (m, 1H), 2.13 – 1.96 (m, 2H), 1.84 – 1.76 (m, 1H), 1.74 – 1.66 (m, 5H), 1.56 – 1.39 (m, 4H), 1.14 – 1.06 (m, 4H).	401
231	N,6-dimethyl-7-oxo-N-[[1-(tetrahydrofuran-2-ylmethyl)-4-piperidyl]methyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.39 (s, 1H), 7.32 (t, J = 2.5 Hz, 1H), 6.17 (dd, J = 2.9, 1.4 Hz, 1H), 3.86 (d, J = 9.1 Hz, 1H), 3.70 (q, J = 7.3 Hz, 1H), 3.53 (s, 4H), 3.30 (t, J = 4.9 Hz, 2H), 2.93 (s, 3H), 2.79 (s, 1H), 2.33 – 2.27 (m, 2H), 1.97 – 1.81 (m, 3H), 1.81 – 1.68 (m, 2H), 1.66 – 1.61 (m, 2H), 1.55 – 1.50 (m, 2H), 1.49 – 1.35 (m, 2H), 1.07 – 1.02 (m, 3H).	387
232	N-[[1-(3-methoxypropyl)-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.39 (s, 1H), 7.35 – 7.29 (m, 1H), 6.17 (d, J = 2.7 Hz, 1H), 3.53 (s, 3H), 3.32 – 3.25 (m, 2H), 3.19 (s, 3H), 2.93 (s, 3H), 2.81 – 2.74 (m, 2H), 2.29 – 2.21 (m, 2H), 1.86 – 1.75 (m, 2H), 1.68 – 1.52 (m, 6H), 1.08 – 1.03 (m, 3H).	375

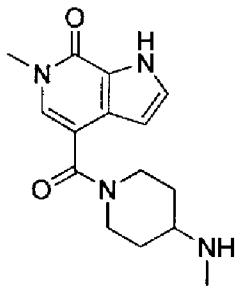
233	N-[[1-(cyclobutylmethyl)-4-piperidyl]methyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.38 (s, 1H), 7.35 – 7.29 (m, 1H), 6.17 (d, J = 2.8 Hz, 1H), 3.53 (s, 3H), 3.32 – 3.25 (m, 2H), 2.93 (s, 3H), 2.71 (s, 2H), 2.48 – 2.38 (m, 1H), 2.26 (d, J = 7.0 Hz, 2H), 1.96 (d, J = 9.8 Hz, 2H), 1.87 – 1.70 (m, 4H), 1.65 – 1.53 (m, 4H), 1.05 – 1.00 (m, 3H).	371
234	N,6-dimethyl-7-oxo-N-[[1-(tetrahydropyran-4-ylmethyl)-4-piperidyl]methyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.39 (s, 1H), 7.32 (t, J = 2.6 Hz, 1H), 6.17 (t, J = 2.1 Hz, 1H), 3.79 (d, J = 10.8 Hz, 2H), 3.53 (s, 3H), 3.32 – 3.20 (m, 2H), 2.93 (s, 3H), 2.76 (s, 2H), 2.10 – 2.03 (m, 2H), 1.83 – 1.75 (m, 2H), 1.70 – 1.65 (m, 2H), 1.59 – 1.50 (m, 4H), 1.13 – 1.02 (m, 4H).	401
235	N,6-dimethyl-7-oxo-N-[[1-(tetrahydropyran-2-ylmethyl)-4-piperidyl]methyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.39 (s, 1H), 7.35 – 7.29 (m, 1H), 6.20 – 6.14 (m, 1H), 3.80 (d, J = 11.2 Hz, 1H), 3.53 (s, 3H), 3.38 – 3.22 (m, 2H), 2.93 (s, 3H), 2.82 – 2.77 (m, 2H), 2.33 – 2.23 (m, 1H), 2.22 – 2.13 (m, 1H), 1.94 – 1.84 (m, 2H), 1.75 – 1.70 (m, 1H), 1.66 – 1.61 (m, 2H), 1.58 – 1.50 (m, 3H), 1.47 – 1.33 (m, 4H), 1.10 – 1.05 (m, 3H).	401
236	N,6-dimethyl-7-oxo-N-[[1-(tetrahydrofuran-3-ylmethyl)-4-piperidyl]methyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.39 (s, 1H), 7.32 (t, J = 2.7 Hz, 1H), 6.18 (t, J = 2.2 Hz, 1H), 3.72 – 3.50 (m, 6H), 3.36 – 3.27 (m, 1H), 2.93 (s, 3H), 2.82 (s, 1H), 2.41 – 2.33 (m, 1H), 2.23 – 2.16 (m, 2H), 1.92 – 1.79 (m, 4H), 1.68 – 1.63 (m, 1H), 1.57 – 1.52 (m, 2H), 1.51 – 1.41 (m, 2H), 1.08 – 1.03 (m, 3H).	387

237	N-cyclobutyl-N-(1-isopropyl-4-piperidyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.13 (d, J = 3.6 Hz, 1H), 7.34 – 7.25 (m, 2H), 6.14 (t, J = 2.3 Hz, 1H), 4.13 (p, J = 8.8 Hz, 1H), 3.52 (s, 3H), 3.32 (s, 11H), 2.79 (d, J = 10.9 Hz, 2H), 2.67 (p, J = 8.3, 7.4 Hz, 1H), 2.52 – 2.35 (m, 3H), 2.31 (d, J = 12.7 Hz, 2H), 2.11 – 1.90 (m, 4H), 1.52 (ddd, J = 38.7, 21.9, 9.9 Hz, 4H), 0.93 (d, J = 6.5 Hz, 6H).	371
238	Cis-N-(1-isopropyl-3-methyl-4-piperidyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 7.80 (s, 1H), 7.56 – 7.49 (m, 1H), 7.31 (d, J = 2.8 Hz, 1H), 6.64 (d, J = 2.8 Hz, 1H), 4.01 – 3.90 (m, 1H), 3.56 (s, 3H), 2.65 (dq, J = 12.3, 6.2, 5.7 Hz, 2H), 2.38 – 2.25 (m, 2H), 2.12 – 1.99 (m, 1H), 1.81 – 1.67 (m, 1H), 1.62 – 1.51 (m, 1H), 1.00 – 0.88 (m, 9H).	331
239	Trans-N-(1-isopropyl-3-methyl-4-piperidyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H), 7.81 (s, 1H), 7.74 (d, J = 8.6 Hz, 1H), 7.33 – 7.28 (m, 1H), 6.68 (d, J = 2.7 Hz, 1H), 3.56 (s, 3H), 3.47 (dd, J = 13.7, 6.0 Hz, 1H), 2.91 – 2.75 (m, 3H), 2.33 – 2.22 (m, 1H), 1.99 (t, J = 11.1 Hz, 1H), 1.86 – 1.67 (m, 2H), 1.60 – 1.46 (m, 1H), 1.01 (d, J = 6.5 Hz, 7H), 0.87 (d, J = 6.5 Hz, 3H).	331
240	Cis-N-(3-fluoro-1-isopropyl-4-piperidyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 7.92 (s, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.34 – 7.28 (m, 1H), 6.72 – 6.66 (m, 1H), 4.77 (d, J = 49.9 Hz, 1H), 4.03 – 3.86 (m, 1H), 3.55 (s, 3H), 3.09 – 2.99 (m, 1H), 2.85 – 2.67 (m, 2H), 2.50 – 2.42 (m, 1H), 2.25 (t, J = 11.3 Hz, 1H), 1.94 – 1.79 (m, 1H), 1.69 – 1.60 (m, 1H), 0.97 (dd, J = 6.6, 4.0 Hz, 6H).	335

241	N-(1-isopropylazepan-4-yl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.06 (s, 1H), 7.80 (s, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.34 – 7.28 (m, 1H), 6.67 (d, J = 2.7 Hz, 1H), 4.09 (ddd, J = 13.2, 8.8, 4.6 Hz, 1H), 3.55 (s, 3H), 3.30 (d, J = 19.0 Hz, 1H), 2.92 – 2.77 (m, 1H), 2.68 – 2.50 (m, 4H), 1.93 – 1.81 (m, 1H), 1.80 – 1.60 (m, 4H), 1.60 – 1.47 (m, 1H), 0.94 (dd, J = 6.6, 2.1 Hz, 6H).	331
242	N-(8-isopropyl-8-azabicyclo[3.2.1]octan-3-yl)-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H), 7.31 (d, J = 2.6 Hz, 2H), 6.17 – 6.11 (m, 1H), 4.48 (s, 1H), 3.52 (s, 3H), 3.47 (d, J = 9.1 Hz, 2H), 2.75 (s, 3H), 2.28 – 2.08 (m, 3H), 1.92 – 1.82 (m, 2H), 1.51 – 1.41 (m, 2H), 1.38 – 1.27 (m, 2H), 0.90 (d, J = 5.7 Hz, 6H).	357
243	N-cyclopropyl-N-(1-isopropyl-4-piperidyl)-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.02 (s, 1H), 7.45 (s, 1H), 7.35 – 7.17 (m, 1H), 6.32 – 6.17 (m, 1H), 4.01 – 3.72 (m, 1H), 3.53 (s, 3H), 2.95 – 2.77 (m, 2H), 2.77 – 2.57 (m, 2H), 2.22 – 2.06 (m, 2H), 2.06 – 1.89 (m, 2H), 1.89 – 1.69 (m, 2H), 0.95 (dd, J = 11.4, 6.6 Hz, 6H), 0.65 – 0.50 (m, 2H), 0.50 – 0.37 (m, 2H).	357

Example 244

6-methyl-4-(4-(methylamino)piperidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7(6H)-one

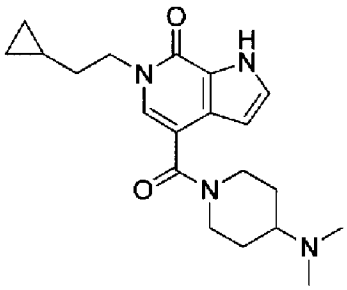


A mixture of 6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (**Intermediate C**) (60 mg, 0.3 mmol), triethylamine (90 mg, 0.9 mmol), HATU (200 mg, 0.5

mmol) and *tert*-butyl N-methyl-N-(4-piperidyl)carbamate (110 mg, 0.5 mmol) in DMF (1 mL) was stirred at 50 °C for 2h. The reaction mixture was added to water (10 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced pressure to yield *tert*-butyl N-methyl-N-[1-(6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)-4-piperidyl]carbamate (100 mg). This intermediate was dissolved in dichloromethane (2 mL) and trifluoroacetic acid (0.1 mL) was then added. The mixture was stirred for 1h at room temperature at which time LCMS indicated that the reaction had gone to completion. The mixture was concentrated under reduced pressure and the residue was purified by SFC chromatography (10-20% CO2 / 0.1% NH4OH in MeOH) to give the title compound (54 mg, 60% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.40 (s, 1H), 7.33 (d, *J* = 2.8 Hz, 1H), 6.24 (d, *J* = 2.8 Hz, 1H), 3.98 (s, 1H), 3.53 (s, 3H), 3.06 – 2.95 (m, 2H), 2.88 (m, *J* = 15.9 Hz, 2H), 2.36 (s, 3H), 2.07 (s, 1H), 1.85 (d, *J* = 12.8 Hz, 2H), 1.25 (d, *J* = 11.3 Hz, 2H). LCMS M/Z (M+H) 289.2.

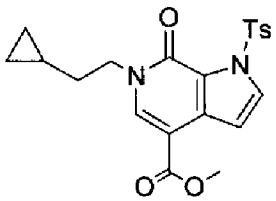
Example 245

6-(2-cyclopropylethyl)-4-(4-(dimethylamino)piperidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7(6H)-one



Step 1

methyl 6-(2-cyclopropylethyl)-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxylate

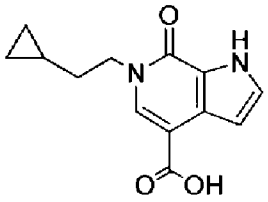


Sodium hydride, 60% in mineral oil (35 mg, 0.87 mmol) was added to a cooled (0° C) mixture of methyl 7-oxo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridine-4-carboxylate (**Intermediate B,** 200 mg, 0.58 mmol) in N,N-dimethylformamide (4 mL). The mixture was stirred for 15 min at 0°C and then 2-bromoethylcyclopropane (100 mg, 0.69 mmol) was added. The reaction was allowed to warm to room temperature and stirring was continued for 18h. The reaction was

diluted with water (20 mL) and then extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were washed with brine (2 x 20 mL), dried over sodium sulfate and concentrated under reduced pressure to yield the title compound (200 mg, 100% yield). This crude was used directly in the next step. LCMS M/Z (M+H) 415.4.

Step 2

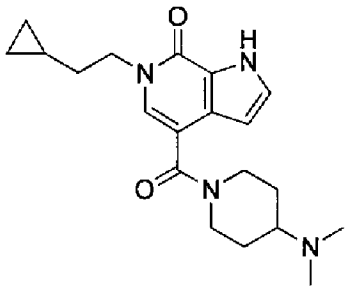
6-(2-cyclopropylethyl)-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid



A mixture of methyl 6-(2-cyclopropylethyl)-7-oxo-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine-4-carboxylate (200 mg, 0.5 mmol) and lithium hydroxide (50 mg, 2 mmol) in dichloromethane (4 mL), methanol (6 mL) and water (1 mL) was stirred at 45°C for 5h. The mixture was concentrated under reduced pressure and the residue was dissolved in water (4 mL). The aqueous solution was acidified to pH 1 with 1N hydrochloric acid. The resulting precipitate was collected by filtration, washed with water, and dried to yield the title compound (100 mg, 80% yield) as a brown solid. LCMS M/Z (M+H) 247.2.

Step 3

6-(2-cyclopropylethyl)-4-(4-(dimethylamino)piperidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7(6H)-one



A mixture of 6-(2-cyclopropylethyl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (50 mg, 0.2 mmol), triethylamine (80 mg, 0.8 mmol), HATU (90 mg, 0.3 mmol) and N,N-dimethylpiperidin-4-amine (30 mg, 0.3 mmol) in N,N-dimethylformamide (1 mL) was stirred at 50 °C for 1 h. The reaction mixture was added to water (5 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by preparative HPLC (0-25%ACN/0.1%NH4OH in H2O) to give 6-(2-cyclopropylethyl)-4-(4-

(dimethylamino)piperidine-1-carbonyl)-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (22 mg, 30% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d6) δ 12.09 (s, 1H), 7.41 (s, 1H), 7.33 (d, *J* = 2.8 Hz, 1H), 6.24 (d, *J* = 2.8 Hz, 1H), 4.06 (t, *J* = 7.1 Hz, 2H), 3.03 – 2.80 (m, 2H), 2.30 (dd, *J* = 12.7, 8.9 Hz, 1H), 2.16 (s, 6H), 1.75 (d, *J* = 12.3 Hz, 2H), 1.56 (q, *J* = 7.0 Hz, 2H), 1.30 (d, *J* = 11.9 Hz, 2H), 0.77 – 0.58 (m, 1H), 0.44 – 0.30 (m, 2H). LCMS M/Z (M+H) 357.5.

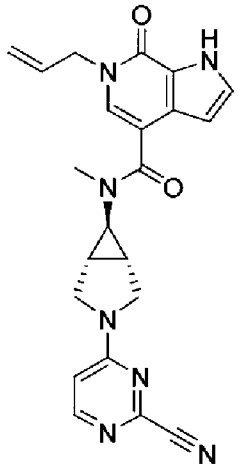
The following compound was prepared in a similar fashion to Example 245.

Examples 246-249

Example	Compound Name	NMR	m/z
246	6-but-2-enyl-4-[4-(dimethylamino)piperidine-1-carbonyl]-1H-pyrrolo[2,3-c]pyridin-7-one	^{1}H NMR (400 MHz, DMSO-d6) δ 12.14 (s, 1H), 7.45 – 7.25 (m, 2H), 6.25 (t, *J* = 2.3 Hz, 1H), 5.77 –5.50 (m, 2H), 4.55 (d, *J* = 5.4 Hz, 2H), 2.91 (t, *J* = 12.5 Hz, 2H), 2.32 (d, *J* = 3.9 Hz, 1H), 2.17 (s, 6H), 1.75 (dd, *J* = 13.1, 4.0 Hz, 2H), 1.69 – 1.62 (m, 3H), 1.30 (dd, *J* = 11.6, 3.9 Hz, 2H).	343.2
247	6-but-3-enyl-4-[4-(dimethylamino)piperidine-1-carbonyl]-1H-pyrrolo[2,3-c]pyridin-7-one	. ^{1}H NMR (400 MHz, DMSO-d6) δ 12.11 (s, 1H), 7.36 (s, 1H), 7.33 (d, J = 2.7 Hz, 1H), 6.23 (d, J = 2.7 Hz, 1H), 5.93 – 5.73 (m, 1H), 5.07 – 4.93 (m, 2H), 4.07 (t, J = 7.0 Hz, 2H), 3.02 – 2.83 (m, 3H), 2.44 (t, J = 6.9 Hz, 2H), 2.30 (m, 1H), 2.17 (s, 6H), 1.75 (d, J = 12.6 Hz, 2H), 1.42 – 1.22 (m, 2H).	343.2
248	6-butyl-N-[(1-methyl-4-piperidyl)methyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO) δ 12.01 (s, 1H), 7.94 (t, J = 5.7 Hz, 1H), 7.78 (s, 1H), 7.31 (d, J = 2.7 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 4.08 – 3.91 (m, 2H), 3.13 (t, J = 6.3 Hz, 2H), 2.74 (d, J = 11.5 Hz, 2H), 2.12 (d, J = 5.4 Hz, 3H), 1.89 – 1.74 (m, 2H), 1.74 – 1.59 (m, 4H), 1.59 – 1.41 (m, 1H), 1.41 – 1.27 (m, 2H), 1.27 – 1.11 (m, 2H), 0.98 – 0.84 (m, 3H).	345

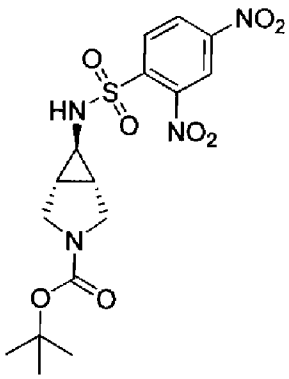
Example 249

6-allyl-N-[(1S,5R)-3-(2-cyanopyrimidin-4-yl)-3-azabicyclo[3.1.0]hexan-6-yl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

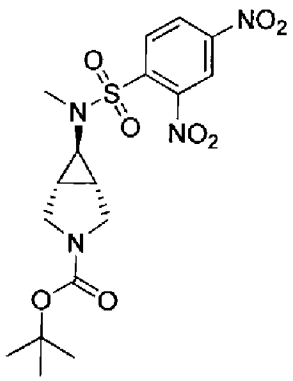
***tert*-butyl (1R,5S)-6-[(2,4-dinitrophenyl)sulfonylamino]-3-azabicyclo[3.1.0]hexane-3-carboxylate**



To a flask was added *tert*-butyl (1R,5S)-6-amino-3-azabicyclo[3.1.0]hexane-3-carboxylate (500 mg, 2.50 mmol) and dichloromethane (50 mL). The solution was cooled to 0°C and 2,6-lutidine (2.9 mL, 25.0 mmol) and 2,4-dinitrobenzenesulfonyl chloride (0.67 g, 2.50 mmol) were then added. The reaction was stirred at 0°C for 30 minutes, then allowed to warm to room temperature and stirred overnight. The reaction was diluted with water (100 mL). This mixture was acidified to pH 2.5 using 5% potassium hydrogen sulfate in water. The organic phase was separated, washed with brine, dried over sodium sulfate, and concentrated under reduced pressure to afford crude title compound. This material was used directly in the next step assuming theoretical yield. LCMS M/Z (M - H) 427.

Step 2:

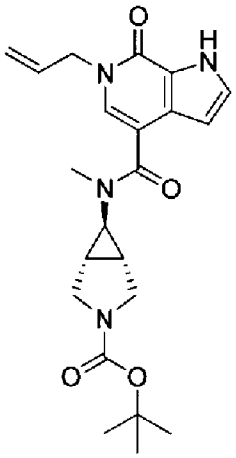
***tert*-butyl (1R,5S)-6-[(2,4-dinitrophenyl)sulfonyl-methyl-amino]-3-azabicyclo[3.1.0]hexane-3-carboxylate**



The crude *tert*-butyl (1R,5S)-6-[(2,4-dinitrophenyl)sulfonylamino]-3-azabicyclo[3.1.0]hexane-3-carboxylate (107 mg, 0.25 mmol) was dissolved in N,N-dimethylformamide (20 mL), and cooled to 0°C. Sodium hydride (60% in mineral oil, 15 mg, 0.38 mmol) was then added and the reaction was stirred at 0°C for 10 minutes. Iodomethane (0.047 mL, 0.75 mmol) was added. The reaction was allowed to warm to room temperature, and stirred for an additional 4 h. The reaction was then diluted with dichloromethane (100 mL), and washed with water. The organic solution was concentrated under reduced pressure and the residue was purified by silica gel chromatography (0-5% methanol:dichloromethane) yielding title compound *(715* mg, 65% for 2 steps). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.02 (d, J = 2.3 Hz, 1H), 8.61 (dd, J = 8.7, 2.3 Hz, 1H), 8.29 (d, J = 8.7 Hz, 1H), 3.49 (d, J = 11.0 Hz, 2H), 3.35 – 3.27 (m, 4H), 2.90 (s, 3H), 2.10 – 2.01 (m, 3H), 1.35 (s, 9H).

Step 3:

***tert*-butyl (1R,5S)-6-[(6-allyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)-methyl-amino]-3-azabicyclo[3.1.0]hexane-3-carboxylate**

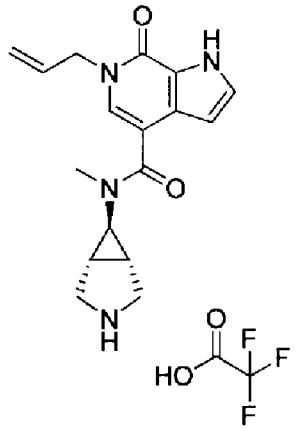


To a 40 mL vial was added *tert*-butyl (1R,5S)-6-[(2,4-dinitrophenyl)sulfonyl-methyl-amino]-3-azabicyclo[3.1.0]hexane-3-carboxylate (650 mg, 1.47 mmol), dichloromethane (10 mL), and propan-1-amine (0.36 mL, 4.41 mmol). The reaction was stirred at room temperature for 4 h at which point LCMS showed loss of starting material. The reaction was concentrated under reduced pressure. This crude was carried on without purification.

To a 20 mL vial was added 6-allyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (**Example 159, step 1**, 200 mg, 0.92 mmol), N,N-dimethylformamide (4 mL), HATU (365 mg, 0.96 mmol), and triethylamine (0.51 mL, 3.66 mmol). The reaction was capped and shaken at room temperature for 15 minutes. *tert*-Butyl (1R,5S)-6-(methylamino)-3-azabicyclo[3.1.0]hexane-3-carboxylate (1.3 equiv., 1.19 mmol) was then added, and the reaction was shaken for 1 h. The reaction was then diluted water (100 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel chromatography (2-5% methanol:dichloromethane), yielding title compound (127 mg, 34%). LCMS M/Z (M + H) Minor: 413, Major: 357 (loss of t-butyl fragment).

Step 4:

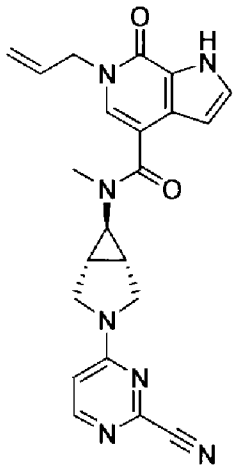
6-allyl-N-[(1R,5S)-3-azabicyclo[3.1.0]hexan-6-yl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide; 2,2,2-trifluoroacetic acid



To a 4 mL vial was added *tert*-butyl (1R,5S)-6-[(6-allyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carbonyl)-methyl-amino]-3-azabicyclo[3.1.0]hexane-3-carboxylate (87 mg, 0.21 mmol), dichloromethane (0.5 mL), and trifluoroacetic acid (0.08 mL, 1.04 mmol). The reaction was capped and shaken at room temperature for 1h, then concentrated under reduced pressure. The residue was azeotroped with ethanol (3x) and dichloromethane (3x) to afford the desired product, which was taken directly to the next step. LCMS M/Z (M + H) 313.

Step 5:

6-allyl-N-[(1S,5R)-3-(2-cyanopyrimidin-4-yl)-3-azabicyclo[3.1.0]hexan-6-yl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



To a 4 mL vial was added 6-allyl-N-[(1S,5R)-3-azabicyclo[3.1.0]hexan-6-yl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide; 2,2,2-trifluoroacetic acid (40 mg, 0.094 mmol), acetonitrile (0.25 mL), diisopropylethylamine (0.049 mL, 0.28 mmol), and 4-chloropyrimidine-2-carbonitrile (14 mg, 0.10 mmol). The reaction was capped and shaken at 75°C for 1 h. The

reaction was concentrated under reduced pressure and the residue was purified by preparative HPLC (0-25%ACN/0.1%NH4OH in H2O) yielding 6-allyl-N-[(1S,5R)-3-(2-cyanopyrimidin-4-yl)-3-azabicyclo[3.1.0]hexan-6-yl]-N-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (35 mg, 89%). ^{1}H NMR (400 MHz, DMSO-*d6*) δ 12.12 (s, 1H), 8.22 (d, *J* = 6.4 Hz, 1H), 7.46 (s, 1H), 7.33 (t, *J* = 2.7 Hz, 1H), 6.67 (d, *J* = 6.4 Hz, 1H), 6.34 – 6.28 (m, 1H), 6.01 (ddt, *J* = 16.2, 10.7, 5.5 Hz, 1H), 5.20 – 5.05 (m, 2H), 4.69 – 4.61 (m, 2H), 3.61 – 3.30 (m, 4H), 3.00 (s, 3H), 2.68 (s, 1H), 1.97 – 1.86 (m, 2H). LCMS M/Z (M + H) 416.

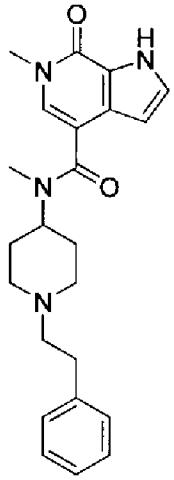
The following compounds were prepared in a similar fashion to Example 249:

Examples 250-251

Example	Compound Name	NMR	m/z
250	6-allyl-N-methyl-7-oxo-N-[(1S,5R)-3-[4-(trifluoromethyl)pyrimidin-2-yl]-3-azabicyclo[3.1.0]hexan-6-yl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.10 (d, J = 3.8 Hz, 1H), 8.63 (dd, J = 5.0, 2.7 Hz, 1H), 7.45 (d, J = 2.6 Hz, 1H), 7.31 (q, J = 2.5 Hz, 1H), 7.00 (dd, J = 4.9, 2.7 Hz, 1H), 6.30 (d, J = 3.4 Hz, 1H), 6.08 – 5.85 (m, 1H), 5.24 – 4.95 (m, 2H), 4.64 (d, J = 10.9 Hz, 2H), 3.52 (d, J = 10.8 Hz, 2H), 3.44 – 3.32 (m, 2H), 3.01 (d, J = 2.8 Hz, 3H), 2.69 (d, J = 2.7 Hz, 1H), 1.86 (s, 2H).	459
251	6-allyl-N-methyl-7-oxo-N-(3-pyrimidin-4-yl-3-azabicyclo[3.1.0]hexan-6-yl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 2H), 8.42 (d, *J* = 1.1 Hz, 1H), 8.11 (d, *J* = 6.0 Hz, 1H), 7.46 (s, 1H), 7.35 – 7.29 (m, 1H), 6.40 – 6.28 (m, 2H), , 6.08 – 5.85 (m, 1H), 5.18 – 5.03 (m, 2H), 4.64 (d, *J* = 5.6 Hz, 2H), 3.31 (s, 4H), 3.01 (s, 3H), 2.69 – 2.63 (m, 1H), 1.89 (s, 2H).	391

Example 252

N,6-dimethyl-7-oxo-N-(1-phenethyl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



To a microwave vial was added N,6-dimethyl-7-oxo-N-(4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide hydrochloride (**Example 210, Step 1**, 45 mg, 0.14 mmol), acetonitrile (0.2 mL), diisopropylethylamine (0.071 mL, 0.42 mmol), water (0.10 mL), and 2-bromoethylbenzene (39 mg, 0.21 mmol). The reaction was sealed and stirred under microwave irradiation for 30 minutes at 150 °C. The reaction was then concentrated under reduced pressure and the residue was purified by preparative HPLC (5-50%ACN/0.1%NH4OH in H2O) yielding N,6-dimethyl-7-oxo-N-(1-phenethyl-4-piperidyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide (22 mg, 41%).

The following compound was prepared in a similar fashion to Example 252.

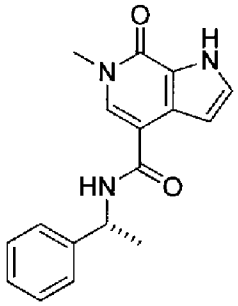
Examples 253-255

Example	Compound Name	NMR	m/z
253	N-[1-[2-(2-fluorophenyl)ethyl]-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.14 (s, 1H), 7.40 – 7.18 (m, 4H), 7.17 – 7.07 (m, 2H), 6.22 – 6.16 (m, 1H), 3.74 (s, 1H), 3.52 (s, 3H), 3.02 – 2.95 (m, 2H), 2.82 (s, 3H), 2.74 (t, J = 7.7 Hz, 2H), 2.46 (d, J = 7.5 Hz, 2H), 1.97 – 1.92 (m, 2H), 1.85 – 1.71 (m, 2H), 1.65 – 1.58 (m, 2H).	411

254	N-[1-[2-(4-chlorophenyl)ethyl]-4-piperidyl]-N,6-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.13 (s, 1H), 7.39 – 7.20 (m, 6H), 6.19 (dd, J = 2.8, 1.6 Hz, 1H), 3.99 (s, 1H), 3.52 (s, 3H), 3.01 – 2.93 (m, 2H), 2.82 (s, 3H), 2.70 (t, J = 7.5 Hz, 2H), 1.95 – 1.90 (m, 2H), 1.84 – 1.70 (m, 2H), 1.65 – 1.57 (m, 2H).	427
255	N,6-dimethyl-7-oxo-N-[1-(2-phenylpropyl)-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 12.13 (s, 1H), 7.39 – 7.12 (m, 7H), 6.18 (dd, J = 2.8, 1.3 Hz, 1H), 3.96 (s, 1H), 3.52 (s, 3H), 2.96 – 2.86 (m, 3H), 2.81 (s, 3H), 2.39 – 2.32 (m, 2H), 1.94 – 1.89 (m, 1H), 1.82 – 1.68 (m, 3H), 1.63 – 1.54 (m, 2H), 1.17 (d, J = 6.8 Hz, 3H).	407

Example 256

(R)-6-methyl-7-oxo-N-(1-phenylethyl)-6,7-dihydro-1Hpyrrolo[2,3-c]pyridine-4-carboxamide



A vial was charged with 4-bromo-6-methyl-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-7-one (**Intermediate D**, 45 mg, 0.118 mmol), palladium acetate (2.65 mg, 0.012 mmol), and Xantphos (6.83 mg, 0.012 mmol) before being evacuated and purged with carbon monoxide (3x). Toluene (2 mL) was added, followed by (R)-1-phenylethanamine (28.6 mg, 0.236 mmol), and triethylamine (82 µl, 0.590 mmol), and the reaction mixture was stirred at 90 °C for 2 h. After cooling, the mixture was diluted with ethyl acetate and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and the residue was purified by silica gel chromatography (eluting with hexanes and ethyl acetate) to afford crude intermediate.

This material was dissolved in methanol (6 mL) and then potassium hydroxide (33.1 mg, 0.590 mmol) in water (1 mL) was added. The reaction was stirred at room temperature 18 h. The reaction was filtered through Celite, using methanol to rinse and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (eluting with hexanes and ethyl acetate) to give the title compound as a white, amorphous solid (10 mg, 29%) after lyophilization from dioxane. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 12.02 - 12.10 (m, 1H), 8.34 (d, *J* = 7.69 Hz, 1H), 7.94 (s, 1H), 7.40 (d, *J* = 7.06 Hz, 2H), 7.28 - 7.36 (m, 3H), 7.23 (d, *J* = 7.27 Hz, 1H), 6.67 (t, *J* = 2.29 Hz, 1H), 5.14 (s, 1H), 3.57 (s, 3H), 1.46 (d, *J* = 7.27 Hz, 3H). LCMS M/Z (M+H) 296.

The following compounds were prepared in a similar fashion to Example 256:

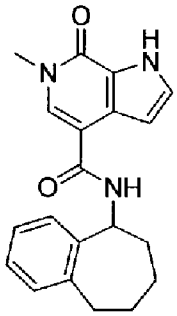
Examples 257-264

Example	Compound Name	NMR	m/z
257	N-benzyl-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 12.10 (br. s., 1H), 8.52 (t, J = 6.02 Hz, 1H), 7.91 (s, 1H), 7.34 (s, 1H), 7.30 - 7.34 (m, 2H), 7.20 - 7.28 (m, 1H), 6.70 - 6.77 (m, 1H), 4.46 (d, J = 6.02 Hz, 1H), 3.55 (s, 3H).	282
258	6-methyl-7-oxo-N-(2-phenylethyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.08 (br. s., 1H), 8.03 (br. s., 1H), 7.79 (s, 1H), 7.18 - 7.34 (m, 4H), 6.66 (t, J = 2.39 Hz, 1H), 3.54 (s, 3H), 3.43 - 3.51 (m, 2H), 2.84 (t, J = 7.48 Hz, 2H).	296
259	N-benzyl-6-butyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.02 - 12.10 (m, 1H), 8.47 - 8.58 (m, 1H), 7.88 (s, 1H), 7.31 - 7.37 (m, 4H), 7.21 - 7.28 (m, 1H), 6.73 - 6.77 (m, 1H), 4.47 (d, J = 6.02 Hz, 2H), 3.93 - 4.04 (m, 2H), 1.62 - 1.75 (m, 2H), 1.25 - 1.39 (m, 2H), 0.87 - 0.96 (m, 3H).	324
260	N-benzyl-6-[(E)-but-2-enyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 11.98 - 12.21 (m, 2H), 8.46 - 8.58 (m, 1H), 7.82 (s, 1H), 7.31 - 7.38 (m, 5H), 7.20 - 7.28 (m, 1H), 6.72 - 6.77 (m, 1H), 5.63 (s, 2H), 4.64 - 4.72 (m, 1H), 4.52 - 4.59 (m, 2H), 4.47 (d, J = 5.82 Hz, 2H), 1.75 - 1.81 (m, 1H), 1.66 (d, J = 4.36 Hz, 3H).	322

261	N-[(4-methoxyphenyl)methyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.09 (br. s., 1H), 8.42 (t, J = 6.02 Hz, 1H), 7.88 (s, 1H), 7.32 (t, J = 2.80 Hz, 1H), 7.26 (d, J = 8.72 Hz, 2H), 6.86 - 6.92 (m, 2H), 6.73 (t, J = 2.39 Hz, 1H), 4.38 (d, J = 5.82 Hz, 2H), 3.73 (s, 3H), 3.54 (s, 3H).	312
262	6-methyl-7-oxo-N-(2-thienylmethyl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.10 (br. s., 1H), 8.59 (s, 1H), 7.87 (s, 1H), 7.39 (d, J = 4.99 Hz, 1H), 7.33 (t, J = 2.80 Hz, 1H), 7.02 (br. s., 1H), 6.94 - 7.00 (m, 1H), 6.74 (s, 1H), 4.61 (d, J = 5.82 Hz, 3H), 3.54 (s, 3H).	288
263	N-[(4-fluorophenyl)methyl]-6-methyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.10 (br. s., 1H), 8.52 (t, J = 5.92 Hz, 1H), 7.90 (s, 1H), 7.34 - 7.42 (m, 2H), 7.33 (t, J = 2.80 Hz, 1H), 7.11 - 7.20 (m, 2H), 6.74 (t, J = 2.49 Hz, 1H), 4.44 (d, J = 5.82 Hz, 2H), 3.55 (s, 3H).	300
264	6-methyl-7-oxo-N-[(1S)-1-phenylethyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d6) δ 12.06 (br. s., 1H), 8.34 (d, J = 7.89 Hz, 1H), 7.94 (s, 1H), 7.37 - 7.45 (m, 2H), 7.28 - 7.36 (m, 3H), 7.23 (d, J = 7.48 Hz, 1H), 6.67 (s, 1H), 5.06 - 5.21 (m, 1H), 3.57 (s, 3H), 1.47 (d, J = 7.06 Hz, 3H).	296

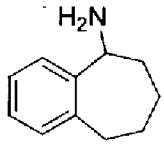
Example 265

6-methyl-7-oxo-N-(6,7,8,9-tetrahydro-5Hbenzo[7]annulen-5-yl)-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

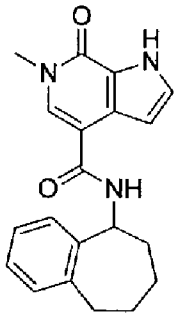
6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-amine



A round bottomed flask was charged with 6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (1 ml, 6.68 mmol), isopropanol (70 mL), sodium cyanoborohydride (2.94 g, 46.8 mmol), and ammonium acetate (15.46 g, 201 mmol). The mixture was stirred at room temperature for 4 h and then heated to reflux overnight. After cooling, the reaction was quenched with 1 N sodium hydroxide (100 mL) and extracted with dichloromethane (3 x 50 mL). The combined organic extracts were washed with water, dried with sodium sulfate, and concentrated under reduced pressure to give a crude residue that contained 6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-amine. This material was used directly in the following amide bond formation.

Step 2:

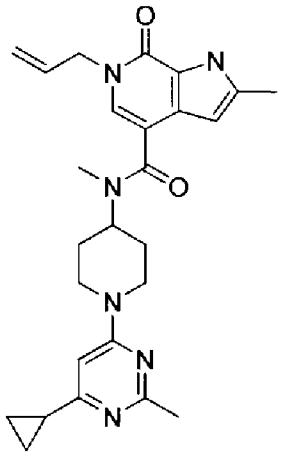
6-methyl-7-oxo-N-(6,7,8,9-tetrahydro-5Hbenzo[7]annulen-5-yl)-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



The following example was prepared in a similar fashion to Example 256 using 6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-amine (synthesis step 1). ^{1}H NMR (400 MHz, DMSO-*d6*) δ 12.00 - 12.13 (m, 1H), 8.37 - 8.46 (m, 1H), 8.07 (s, 1H), 7.29 - 7.33 (m, 1H), 7.22 - 7.28 (m, 1H), 7.13 (d, J = 4.57 Hz, 3H), 6.66 - 6.72 (m, 1H), 5.17 - 5.27 (m, 1H), 3.60 (s, 3H), 2.78 - 2.94 (m, 2H), 1.60 - 2.01 (m, 4H), 1.21 - 1.36 (m, 2H). LCMS M/Z (M+H) 336.

Example 266

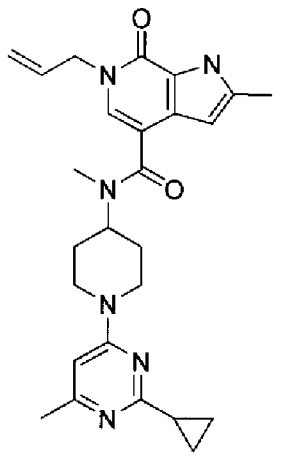
6-methyl-7-oxo-N-(6,7,8,9-tetrahydro-5Hbenzo[7]annulen-5-yl)-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



The following example was prepared in a similar fashion to Example 159 using 6-allyl-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (**Intermediate F**). 1H NMR (400 MHz, DMSO-d6) δ 11.91 (s, 1H), 7.24 (s, 1H), 6.57 (s, 1H), 6.05 – 5.90 (m, 2H), 5.16 (dq, J = 10.3, 1.5 Hz, 1H), 5.04 (dq, J = 17.1, 1.6 Hz, 1H), 4.61 (dd, J = 4.3, 2.7 Hz, 2H), 4.52 (d, J = 13.2 Hz, 2H), 2.82 – 2.74 (m, 5H), 2.37 – 2.21 (m, 7H), 1.91 – 1.79 (m, 1H), 1.73 – 1.63 (m, 4H), 0.98 – 0.80 (m, 4H). LCMS M/Z (M+H) 461.

Example 267

6-allyl-N-(1-(2-cyclopropyl-6-methylpyrimidin-4-yl)piperidin-4-yl)-N,2-dimethyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxamide

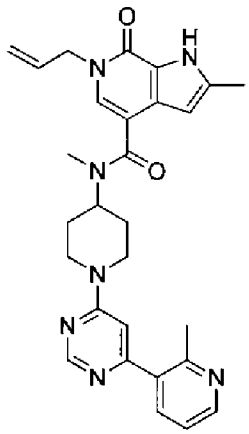


The following example was prepared in a similar fashion to Example 159 using 6-allyl-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4-carboxylic acid (**Intermediate F**). 1H NMR (400 MHz, DMSO-d6) δ 11.90 (s, 1H), 7.24 (s, 1H), 6.48 (s, 1H), 6.05 – 5.90 (m, 2H), 5.16 (dq, J = 10.3, 1.4 Hz, 1H), 5.04 (dq, J = 17.0, 1.6 Hz, 1H), 4.61 (dt, J = 5.8, 1.5 Hz, 2H),

4.48 (d, J = 13.1 Hz, 2H), 4.31 (s, 0H), 2.92 – 2.71 (m, 5H), 2.32 (s, 3H), 2.18 (s, 3H), 1.89 (tt, J = 7.9, 4.8 Hz, 1H), 1.73 – 1.61 (m, 4H), 0.93 – 0.77 (m, 4H). LCMS M/Z (M+H) 461.

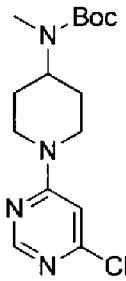
Example 268

6-allyl-*N*,2-dimethyl-*N*-[1-[6-(2-methyl-3-pyridyl)pyrimidin-4-yl]-4-piperidyl]-7-oxo-1*H*-pyrrolo[2,3-*c*]pyridine-4-carboxamide



Step 1

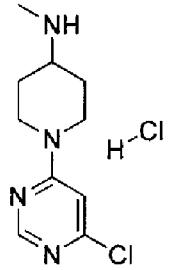
***tert*-butyl (1-(6-chloropyrimidin-4-yl)piperidin-4-yl)(methyl)carbamate**



To a solution of 4,6-dichloropyrimidine (5.2 g, 35.0 mmol) in DMF (100 mL) were added *tert*-butyl methyl(piperidin-4-yl)carbamate (5.0 g, 23.3 mmol) and cesium carbonate (15.2 g, 46.7 mmol). After addition, the reaction mixture was heated at 80°C for 16 h, at which time LCMS indicated the reaction had gone to completion. The solution was poured into ice water, and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were concentrated under reduced pressure. The crude product was purified by silica gel chromatography column (Hexanes/ethyl acetate = 5:1) to give the title compound (7.0 g, 92% yield) as a colorless oil.

Step 2

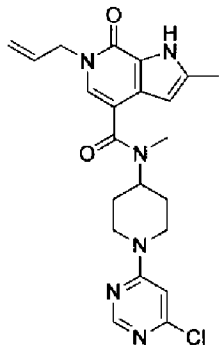
1-(6-chloropyrimidin-4-yl)-N-methylpiperidin-4-amine hydrochloride



To a solution of *tert*-butyl (1-(6-chloropyrimidin-4-yl)piperidin-4-yl)(methyl) carbamate (7.0 g, 21.4 mmol) in ethyl acetate (25 mL) was added a solution of hydrogen chloride (2 N in ethyl acetate, 10 mL). After addition, the mixture was stirred at room temperature for 3 h, at which time LCMS indicated the reaction had gone to completion. The solution was concentrated under reduced pressure to give the crude title compound (4.5 g, 80% yield) as a yellow oil.

Step 3

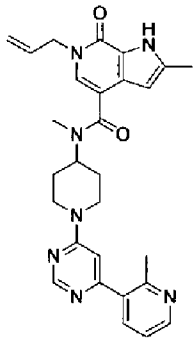
6-allyl-*N*-(1-(6-chloropyrimidin-4-yl)piperidin-4-yl)-N,2-dimethyl-7-oxo-6,7-dihydro-1*H*-pyrrolo[2,3-*c*]pyridine-4-carboxamide



To a solution of 6-allyl-2-methyl-7-oxo-6,7-dihydro-1*H*-pyrrolo[2,3-*c*]pyridine -4-carboxylic acid (3.0 g, 12.92 mmol) (**Intermediate F**) in DMF (100 mL) was added 1-(6-chloropyrimidin-4-yl)-N-methylpiperidin-4-amine hydrochloride (4.4 g, 16.7 mmol), HATU (5.9 g, 15.5 mmol) and triethylamine (2.6 g, 25.8 mmol). The resulting mixture was stirred at ambient temperature for 16 h, at which time LCMS indicated the reaction had gone to completion. The solution was poured into water (20 mL) and then extracted with ethyl acetate (3 x 100 mL). The combined organic layers were concentrated under reduced pressure. The crude product was purified by silica gel chromatography column (Hexanes/ethyl acetate = 1:2) to give the title compound (2.8 g, 49% yield) as a yellow oil.

Step 4

6-allyl-*N*,2-dimethyl-*N*-[1-[6-(2-methyl-3-pyridyl)pyrimidin-4-yl]-4-piperidyl]-7-oxo-1*H*-pyrrolo[2,3-*c*]pyridine-4-carboxamide



A mixture of 6-allyl-*N*-(1-(6-chloropyrimidin-4-yl)piperidin-4-yl)-*N*,2-dimethyl-7-oxo- 6,7-dihydro-1*H*-pyrrolo[2,3-*c*]pyridine-4-carboxamide (100 mg, 0.23 mmol), (2-methylpyridin-3-yl)boronic acid (47 mg, 0.34 mmol), cesium carbonate (148 mg, 0.45 mmol) and $Pd(dppf)Cl_2$ (20 mg, 0.03 mmol) in dioxane/H_2O (5:1, 3 mL) was heated at 85 °C under microwave conditions for 0.5 h, at which time LCMS indicated the reaction had gone to completion. The solvent was evaporated under reduced pressure and the crude product was purified by reverse phase chromatography (acetonitrile 30-50% / 0.1% NH_4OH in water) to give the title compound (24 mg, 21% yield) as a yellow solid. ^1H NMR (400 MHz, DMSO-d_6): δ 11.95 (s, 1 H), 8.58 (s, 1 H), 8.51-8.50 (m, 1 H), 7.81-7.78 (m, 1 H), 7.34-7.31 (m, 1 H), 7.26 (s, 1 H), 7.03 (s, 1 H), 6.02-5.93 (m, 2 H), 5.17-5.14 (m, 1 H), 5.06-5.02 (m, 1 H), 4.62-4.61 (m, 4 H), 4.35-4.32 (s, 1 H), 3.93-3.89 (m, 2 H), 2.90 (s, 3 H), 2.79 (s, 3 H), 2.32 (s, 3 H), 1.76-1.72 (m, 4 H). LCMS M/Z (M+H) 498.

The following compounds were prepared in a similar fashion to Example 268:

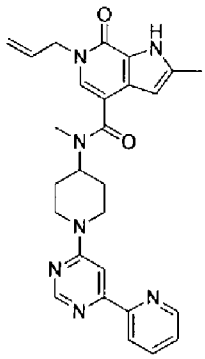
Examples 269-270

Example	Compound Name	NMR	m/z
269	6-allyl-N-[1-[6-(2-furyl)pyrimidin-4-yl]-4-piperidyl]-N,2-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^1H NMR (400 MHz, DMSO-d_6): δ 8.47 (s, 1 H), 7.88-7.87 (m, 1 H), 7.26 (s, 1 H), 7.20-7.19 (m, 1 H), 7.06 (s, 1 H), 6.68-6.66 (m, 1 H), 6.03-5.93 (m, 1 H), 5.18-5.15 (m, 1 H), 5.07-5.02 (m, 1 H), 4.63-4.61 (m, 4 H), 4.37-4.35 (s, 1 H), 2.94-2.90 (m, 2 H), 2.78 (s, 3 H), 2.32 (s, 3 H), 1.76-1.72 (m, 4 H).	473

270	6-allyl-N-[1-[6-(2-chlorophenyl)pyrimidin-4-yl]-4-piperidyl]-N,2-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6): δ 11.94 (s, 1 H), 8.58 (s, 1 H), 7.56-7.54 (m, 2 H), 7.47-7.45 (m, 2 H), 7.26 (s, 1 H), 7.04 (s, 1 H), 6.01-5.94 (m, 2 H), 5.17-5.14 (m, 1 H), 5.06-5.01 (m, 1 H), 4.62-4.61 (m, 4 H), 4.36-4.33 (s, 1 H), 3.93-3.89 (m, 2 H), 2.78 (s, 3 H), 2.32 (s, 3 H), 1.76-1.72 (m, 4 H).	517

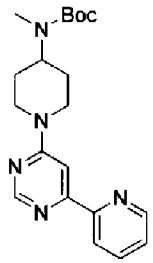
Example 271

6-allyl-*N*,2-dimethyl-7-oxo-*N*-[1-[6-(2-pyridyl)pyrimidin-4-yl]-4-piperidyl]-1*H*-pyrrolo[2,3-*c*]pyridine-4-carboxamide



Step 1

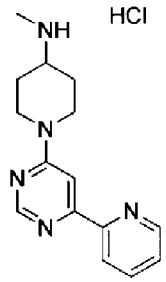
***tert*-butyl methyl(1-(6-(pyridin-2-yl)pyrimidin-4-yl)piperidin-4-yl)carbamate**



A mixture of tert-butyl (1-(6-chloropyrimidin-4-yl)piperidin-4-yl)(methyl)carbamate (500 mg, 1.53 mmol), 2-(tributylstannyl)pyridine (845 mg, 2.30 mmol), $Pd(OAc)_2$ (200 mg, 0.89 mmol) and X-Phos (100 mg, 0.21 mmol) in dioxane (10 mL) was heated at 120°C under microwave conditions for 30 min, at which time LCMS indicated the reaction had gone to completion. After cooled, the reaction mixture was quenched by addition of water (30 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic layers were concentrated under reduced pressure. The crude product was purified by silica gel chromatography (Hexanes/ethyl acetate = 3:1) to give the title compound (300 mg, 53% yield) as a colorless oil.

Step 2

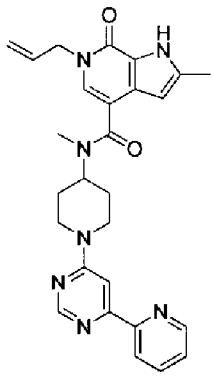
***N*-methyl-1-(6-(pyridin-2-yl)pyrimidin-4-yl)piperidin-4-amine hydrochloride**



To a solution of *tert*-butyl methyl(1-(6-(pyridin-2-yl)pyrimidin-4-yl)piperidin-4-yl) carbamate (300 mg, 0.81 mmol) in ethyl acetate (10 mL) was added hydrogen chloride (2 N in Ethyl acetate, 10 mL). After addition, the reaction mixture was stirred at ambient temperature for 2 h, at which time LCMS indicated the reaction had gone to completion. The solvent was evaporated under reduced pressure to give the title compound (200 mg, 81% yield) as a yellow solid.

Step 3:

6-allyl-N,2-dimethyl-7-oxo-N-[1-[6-(2-pyridyl)pyrimidin-4-yl]-4-piperidyl]-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



To a solution of 6-allyl-2-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridine-4- carboxylic acid (100 mg, 0.43 mmol) in DMF (5 mL) was added N-methyl-1- (6-(pyridin-2-yl)pyrimidin-4-yl)piperidin-4-amine hydrochloride (158 mg, 0.52 mmol), HATU (213 mg, 0.56 mmol) and N-ethyl-N-isopropylpropan-2-amine (178 mg, 1.38 mmol). After addition, the reaction mixture was stirred at ambient temperature for 8 h, at which time LCMS indicated the reaction had gone to completion. The reaction mixture was diluted with H_2O (10 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were concentrated under reduced pressure. The crude product was purified by reverse phase chromatography (acetonitrile 45-75% / 0.1% NH_4OH in water) to give title compound (26 mg, 12%) as a yellow solid. ^1H NMR (400 MHz,

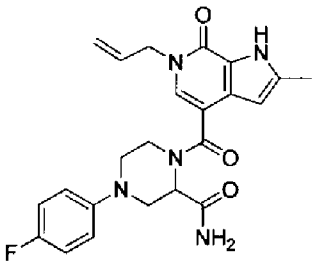
CD_3OD): δ 8.67 (d, J = 4.4 Hz, 1 H), 8.57 (s, 1 H), 8.27 (d, J = 8.0 Hz, 1 H), 8.01-7.90 (m, 1 H), 7.67 (s, 1 H), 7.51-7.43 (m, 1 H), 7.31 (s, 1 H), 6.10-5.97 (m, 2 H), 5.22 (d, J = 10.4 Hz, 1 H), 5.14 (d, J = 17.2 Hz, 1 H), 4.85-4.62(m, 5H), 3.25-3.01 (m, 2 H), 2.91 (s, 3 H), 2.43 (s, 3 H), 1.95-1.82 (m, 4 H). LCMS M/Z (M+H) 484.

The following compound was prepared in a similar fashion to Example 271:

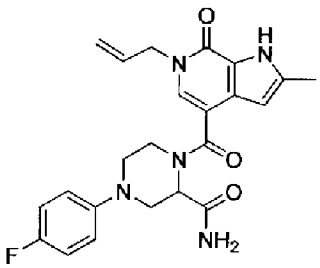
Example	Compound Name	NMR	m/z
272	6-allyl-N,2-dimethyl-N-[1-[6-(3-methyl-2-pyridyl)pyrimidin-4-yl]-4-piperidyl]-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6): δ 11.94 (s, 1 H), 8.58 (s, 1 H), 8.50-8.49 (m, 1 H), 7.74-7.72 (m, 1 H), 7.40-7.37 (m, 1 H), 7.27 (s, 1 H), 7.17 (s, 1 H), 6.01-5.94 (m, 2 H), 5.18-5.15 (m, 1 H), 5.07-5.02 (m, 1 H), 4.63-4.61 (m, 4 H), 4.38-4.34 (s, 1 H), 3.93-3.89 (m, 2 H), 2.79 (s, 3 H), 2.45 (s, 3 H), 2.32 (s, 3 H), 2.32 (s, 3 H), 1.76-1.72 (m, 4 H).	498

Example 273 and Example 274

1-(6-allyl-2-methyl-7-oxo-6,7-dihydro-1*H*-pyrrolo[2,3-*c*]pyridine-4-carbonyl)-4-(4-fluorophenyl)piperazine-2-carboxamide



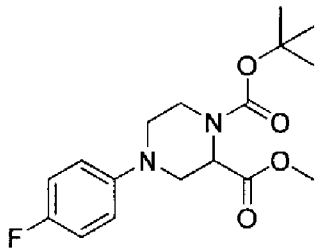
Cis peak 1



Cis peak 2

Step 1

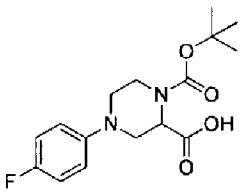
1-*tert*-butyl 2-methyl 4-(4-fluorophenyl)piperazine-1,2-dicarboxylate



In 9 parallel batches, A mixture of tert-butyl 2-methyl piperazine-1,2-dicarboxylate (1.0 g, 4.09 mmol), (4-fluorophenyl)boronic acid (1.72 g, 12.28 mmol), Copper(II) acetate (1.5 g, 8.19 mmol), pyridine (647 mg, 8.19 mmol) and sodium bicarbonate (688 mg, 8.19 mmol) in dichloromethane (50 ml) was stirred at ambient temperature under O_2 (balloon) for 60 h, at which time LCMS indicated the reaction had gone to completion. The combined solutions were concentrated under reduced pressure. The residue was dissolved in ethyl acetate (50 mL), washed with water (2 x 40 mL) and concentrated. The crude product was purified by silica gel chromatography column (Hexanes/ethyl acetate = 5:1) to give the title compound (9.8 g, yield 79%) as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.91-6.80 (m, 2 H), 6.80-6.62 (m, 2 H), 4.86-4.68 (m, 1 H), 4.05-3.88 (m, 2 H), 3.77 (s, 3 H), 3.37-3.15 (m, 2 H), 2.90-2.86 (m, 1 H), 2.77-2.68 (m, 1 H), 1.49-1.40 (m, 9 H). LCMS M/Z (M+H) 338.

Step 2

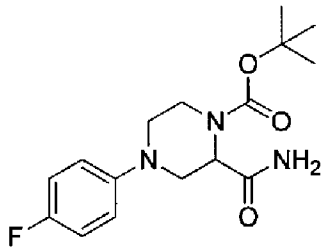
1-(*tert*-butoxycarbonyl)-4-(4-fluorophenyl)piperazine-2-carboxylic acid



To a solution of 1-tert-butyl 2-methyl 4-(4-fluorophenyl) piperazine-1,2-dicarboxylate (5.8 g, 17.14 mmol) in MeOH (80 mL) was added a solution of lithium hydroxide (1.64 g, 68.56 mmol) in water (10 mL). After addition, the reaction mixture was stirred at 30 °C for 2 h, at which time LCMS indicated the reaction had gone to completion. The solvent was evaporated under reduced pressure. The residue was diluted with water (20 mL), adjusted to pH = 4-5 with 1 N aqueous hydrochloric acid and then extracted with ethyl acetate (2 x 30 mL). The combined organic layers were concentrated to give the crude title compound (5.6 g, 99% yield) as a brown oil.

Step 3

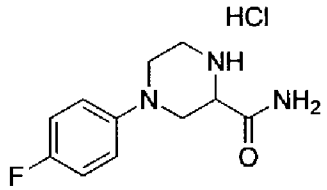
***tert*-butyl 2-carbamoyl-4-(4-fluorophenyl)piperazine-1-carboxylate**



To a solution of 1-(*tert*-butoxycarbonyl)-4-(4-fluorophenyl) piperazine-2-carboxylic acid (5.6 g, 17.3 mmol) in DMF (100 mL) was added N-ethyl-N-isopropylpropan-2- amine (12.3 mL, 69.1 mmol), HATU (9.8 g, 25.9 mmol) and NH_4Cl (2.77 g, 51.8 mmol). The reaction mixture was stirred at ambient temperature for 18 h, at which time LCMS indicated the reaction had gone to completion. The solvent was evaporated under reduced pressure. The residue was dissolved in ethyl acetate (200 mL), washed with water (2 x 70 mL) and concentrated. The crude product was purified by silica gel chromatography (Hexanes/ethyl acetate = 1:1) to give the title compound (4.8 g, 86% yield) as a white solid. ^{1}H NMR (400MHz, $CDCl_3$): δ 6.96-6.86 (m, 4 H), 6.04 (br., s, 2 H), 4.85-4.65 (m, 1 H), 4.20-4.08 (m, 2 H), 3.37-3.14 (m, 2 H), 2.83-2.65 (m, 2 H), 1.49 (s, 9 H).

Step 4

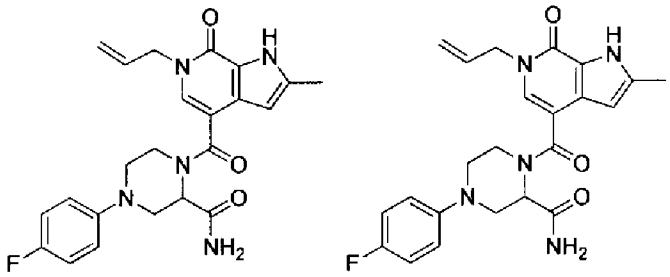
4-(4-fluorophenyl)piperazine-2-carboxamide hydrochloride



To a solution of *tert*-butyl 2-carbamoyl-4-(4-fluorophenyl)piperazine-1-carboxylate (980 mg, 3.03 mmol) in methanol (10 mL) was added hydrogen chloride (2 N in ethyl acetate, 10 mL). The resulting mixture was stirred at ambient temperature for 2 h, at which time LCMS indicated the reaction had gone to completion. The solvent was evaporated under reduced pressure to give the crude title compound (700 mg, 89% yield) as a white solid.

Step 5

1-(6-allyl-2-methyl-7-oxo-6,7-dihydro-1*H*-pyrrolo[2,3-*c*]pyridine-4-carbonyl)-4-(4-fluorophenyl)piperazine-2-carboxamide (fraction 1) and 1-(6-allyl-2-methyl-7-oxo-6,7-dihydro-1*H*-pyrrolo[2,3-*c*]pyridine-4-carbonyl)-4-(4-fluorophenyl)piperazine-2-carboxamide (fraction 2)



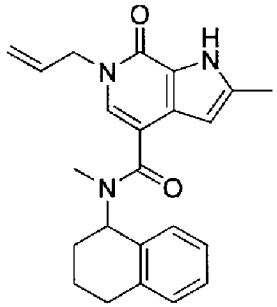
To a solution of 6-allyl-2-methyl-7-oxo-6,7-dihydro-1*H*-pyrrolo[2,3-*c*]pyridine- 4-carboxylic acid (**Intermediate F**) (2.5 g, 12.14 mmol) in DMF (50 mL) was added 4-(4-fluorophenyl)piperazine-2-carboxamide (4.0 g, 15.78 mmol), HATU (4.8 g, 12.75 mmol) and *N*-ethyl-*N*-isopropylpropan-2-amine (6.3 g, 48.56 mmol). The resulting mixture was heated at 60 °C for 18 h, at which time LCMS indicated the reaction had gone to completion. The mixture was quenched by addition of water (80 mL) and the precipitate was collected by filtration. The solid was washed with water and dried in vacuum to give the mixture of enantiomers (3.1 g, 59% yield) as a brown solid. The enantiomers were separated by using chiral SFC (SFC80; Chiralpak AD 300×50mm I.D.,5um; Supercritical CO_2 / EtOH+NH_3:H_2O= 55/45; 200 ml/min) to give the title compounds as white solids.

Fraction 1 (976 mg, 18% yield). ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.98 (s, 1 H), 7.54 (s, 1 H), 7.41-7.16 (m, 2 H), 7.14-7.00 (m, 2 H), 6.97-6.85 (m, 2 H), 6.18 (br. s, 1 H), 6.00-5.92 (m, 1 H), 5.16 (d, J = 10.4, 1 H), 5.05 (d, J = 17.2, 1 H), 4.61 (s, 2 H), 4.12-4.03 (m, 1 H), 3.75-3.37 (m, 4 H), 2.89 (d, J = 9.6, 1 H), 2.70-2.58 (m, 1 H), 2.32 (s, 3 H). LCMS M/Z (M+H) 438. SFC retention time: 0.63 min.

Fraction 2 (833 mg, 16% yield). ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.97 (s, 1 H), 7.53 (s, 1 H), 7.40-7.15 (m, 2 H), 7.13-7.01 (m, 2 H), 6.95-6.86 (m, 2 H), 6.17 (br. s, 1 H), 5.99-5.92 (m, 1 H), 5.15 (d, J = 10.0, 1 H), 5.05 (d, J = 16.8, 1 H), 4.61 (s, 2 H), 4.10-4.01 (m, 1 H), 3.70-3.37 (m, 4 H), 2.89 (d, J = 9.6, 1 H), 2.69-2.58 (m, 1 H), 2.31 (s, 3 H). LCMS M/Z (M+H) 438. SFC retention time: 2.15 min.

Example 275

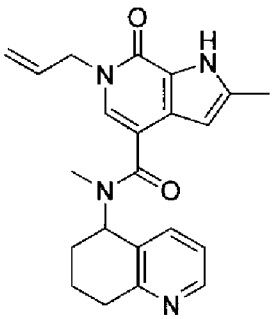
6-allyl-N,2-dimethyl-7-oxo-N-tetralin-1-yl-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Title compound was prepared in a similar fashion as **Example 244** using **Intermediate F**. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.93 (s, 1H), 7.36 (s, 1H), 7.24 – 7.08 (m, 4H), 6.06 (s, 1H), 6.03 – 5.93 (m, 1H), 5.22 – 4.94 (m, 3H), 4.77 – 4.48 (m, 2H), 2.62 (s, 5H), 2.33 (s, 3H), 2.14 – 1.80 (m, 4H). LCMS M/Z (M+H) 376.

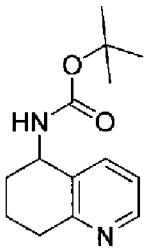
Example 276

6-allyl-N,2-dimethyl-7-oxo-N-tetralin-1-yl-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

tert-butyl N-(5,6,7,8-tetrahydroquinolin-5-yl)carbamate

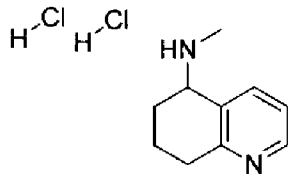


To a 20 mL vial was added 5,6,7,8-tetrahydroquinolin-5-amine (500 mg, 3.4 mmol) followed by tert-butoxycarbonyl tert-butyl carbonate (773 mg , 3.5 mmol), 6 mL of tetrahydrofuran, and 6 mL of saturated sodium bicarbonate. The reaction was shaken at room temperature for 1h. LCMS showed product formation. The reaction was diluted with ethyl acetate, and washed with

water. Organic phase was then concentrated under reduced pressure. The crude product was carried on directly without purification. LCMS M/Z (M+H) 249.

Step 2:

N-methyl-5,6,7,8-tetrahydroquinolin-5-amine dihydrochloride



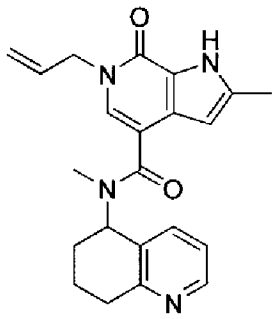
Tert-butyl N-(5,6,7,8-tetrahydroquinolin-5-yl)carbamate (110 mg, 0.44 mmol) was taken up with 3 mL of N,N-dimethylformamide, and sodium hydride 60% in mineral oil (53 mg , 1.33 mmol) was then added. The reaction was stirred for 15 minutes, then iodomethane (0.028 mL, 0.44 mmol) was added. The reaction was capped and shaken at room temperature for 30 min. LCMS showed single addition.

The reaction was diluted with ethyl acetate, and quenched with water. The phases were separated, and the aqueous further extracted with ethyl acetate. The combined organics were concentrated under reduced pressure. LCMS M/Z (M+H) 263.

The crude product was then taken up with 5 mL of methanol followed by 5 mL of 4N HCl/dioxane. The reaction was stirred at room temperature for 1h then concentrated under reduced pressure. The crude was carried on to the next reaction without purification.

Step 3:

6-allyl-N,2-dimethyl-7-oxo-N-tetralin-1-yl-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Title compound was prepared in a similar fashion to **Example 244**, using **Intermediate F**. 1H NMR (400 MHz, DMSO-d6) δ 11.94 (s, 1H), 8.37 (d, J = 4.9 Hz, 1H), 7.52 – 7.46 (m, 1H), 7.39 (s, 1H), 7.24 (dd, J = 7.8, 4.7 Hz, 1H), 6.07 (s, 1H), 5.97 (ddd, J = 15.8, 10.5, 5.2 Hz, 1H), 5.14

(d, J = 10.3 Hz, 1H), 5.03 (d, J = 17.3 Hz, 1H), 4.63 (s, 2H), 2.89 (d, J = 0.5 Hz, 2H), 2.64 (s, 3H), 2.33 (s, 3H), 2.16 – 1.88 (m, 3H). LCMS M/Z (M+H) 377.

The following compounds were prepared in a similar fashion to Example 276:

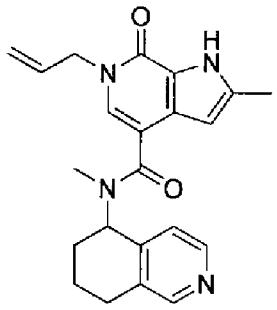
Examples 277-282

Example	Compound Name	NMR	m/z
277	6-allyl-N-chroman-4-yl-N,2-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 11.94 (s, 1H), 7.39 (s, 1H), 7.20 – 7.10 (m, 1H), 7.09 – 7.02 (m, 1H), 6.93 (td, J = 7.5, 1.2 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H), 6.07 (s, 1H), 5.98 (ddt, J = 16.1, 10.5, 5.4 Hz, 1H), 5.14 (d, J = 10.1 Hz, 1H), 5.10 – 5.00 (m, 1H), 4.63 (s, 2H), 4.31 (s, 1H), 4.15 (s, 1H), 2.64 (s, 3H), 2.33 (d, J = 0.8 Hz, 3H), 2.31 – 2.18 (m, 1H), 2.17 – 2.03 (m, 1H).	378
278	6-allyl-N-(7-fluorochroman-4-yl)-N,2-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	1H NMR (400 MHz, DMSO-d6) δ 11.95 (s, 1H), 7.44 (s, 1H), 7.06 – 6.96 (m, 1H), 6.87 – 6.78 (m, 2H), 6.12 – 6.02 (m, 1H), 5.97 (ddd, J = 17.2, 10.4, 5.3 Hz, 1H), 5.14 (dd, J = 10.0, 1.7 Hz, 1H), 5.05 (dd, J = 17.1, 1.8 Hz, 1H), 4.63 (d, J = 5.4 Hz, 2H), 4.32 (d, J = 11.1 Hz, 1H), 4.14 (s, 1H), 2.67 (s, 3H), 2.34 (d, J = 0.9 Hz, 3H), 2.30 – 2.15 (m, 1H), 2.14 – 2.05 (m, 1H).	396
279	6-allyl-N-(4,4-dimethyltetralin-1-yl)-N,2-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide Enantiomer 1	1H NMR (400 MHz, DMSO-d6) δ 11.93 (s, 1H), 7.39 (s, 2H), 7.19 (q, J = 6.8 Hz, 2H), 7.05 (s, 1H), 6.02 (d, J = 39.7 Hz, 2H), 5.09 (d, J = 40.2 Hz, 2H), 4.66 (s, 2H), 2.63 (s, 3H), 2.39 – 2.28 (m, 3H), 2.06 (d, J = 5.2 Hz, 1H), 1.91 (dp, J = 13.1, 5.1, 4.5 Hz, 1H), 1.74 (s, 2H), 1.25 (s, 6H).	404

280	6-allyl-N-(4,4-dimethyltetralin-1-yl)-N,2-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide Enantiomer 2	1H NMR (400 MHz, DMSO-d6) δ 11.93 (s, 1H), 7.39 (s, 2H), 7.19 (q, J = 6.8 Hz, 2H), 7.05 (s, 1H), 6.02 (d, J = 39.7 Hz, 2H), 5.09 (d, J = 40.2 Hz, 2H), 4.66 (s, 2H), 2.63 (s, 3H), 2.39 – 2.28 (m, 3H), 2.06 (d, J = 5.2 Hz, 1H), 1.91 (dp, J = 13.1, 5.1, 4.5 Hz, 1H), 1.74 (s, 2H), 1.25 (s, 6H).	404
281	6-allyl-N-(6-methoxytetralin-1-yl)-N,2-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide, Enantiomer 1	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.94 (s, 1H), 7.44 – 7.20 (m, 1H), 7.12 – 6.91 (m, 1H), 6.84 – 6.72 (m, 1H), 6.72 – 6.57 (m, 1H), 6.14 – 5.88 (m, 2H), 5.86 – 5.60 (m, 1H), 5.24 – 4.83 (m, 3H), 4.80 – 4.47 (m, 2H), 3.72 (s, 3H), 2.87 – 2.57 (m, 5H), 2.33 (s, 3H), 2.19 – 1.75 (m, 4H).	406
282	6-allyl-N-(6-methoxytetralin-1-yl)-N,2-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide, Enantiomer 2	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.94 (s, 1H), 7.44 – 7.20 (m, 1H), 7.12 – 6.91 (m, 1H), 6.84 – 6.72 (m, 1H), 6.72 – 6.57 (m, 1H), 6.14 – 5.88 (m, 2H), 5.86 – 5.60 (m, 1H), 5.24 – 4.83 (m, 3H), 4.80 – 4.47 (m, 2H), 3.72 (s, 3H), 2.87 – 2.57 (m, 5H), 2.33 (s, 3H), 2.19 – 1.75 (m, 4H).	406

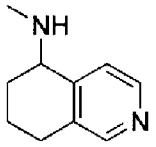
Example 283

6-allyl-N,2-dimethyl-7-oxo-N-(5,6,7,8-tetrahydroisoquinolin-5-yl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Step 1:

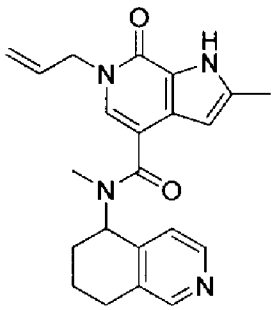
N-methyl-5,6,7,8-tetrahydroisoquinolin-5-amine



To a 20 mL vial was added 7,8-dihydro-6H-isoquinolin-5-one (200 mg, 1.36 mmol) followed by methanamine hydrochloride (275 mg, 4.08 mmol,), diisopropylethylamine (527mg, 4.08 mmol), and 4 mL of 1,2-dichloroethane. The reaction was capped and shaken at 50°C for 1h. Sodium cyanoborohydride (261 mg, 4.08 mmol) was then added, and the reaction was capped and shaken at 50°C for 72h. LCMS shows desired product. The reaction was then diluted with DCM, and washed with 1N NaOH. The organic phase was concentrated under reduced pressure yielding crude product, which was carried on without purification. LCMS M/Z (M+H) 162.

Step 2:

6-allyl-N,2-dimethyl-7-oxo-N-(5,6,7,8-tetrahydroisoquinolin-5-yl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide



Title compound was prepared in a similar fashion to **Example 244**, using **Intermediate F**. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.94 (s, 1H), 8.36 (d, J = 5.2 Hz, 2H), 7.40 (s, 1H), 7.08 (d, J = 4.9 Hz, 1H), 6.08 (s, 1H), 5.97 (s, 1H), 5.21 – 4.98 (m, 2H), 4.63 (s, 2H), 2.74 (s, 2H), 2.66 (s, 3H), 2.34 (s, 3H), 2.16 – 1.75 (m, 4H). LCMS M/Z (M+H) 377.

The following compounds were prepared in a similar fashion to Example 283:

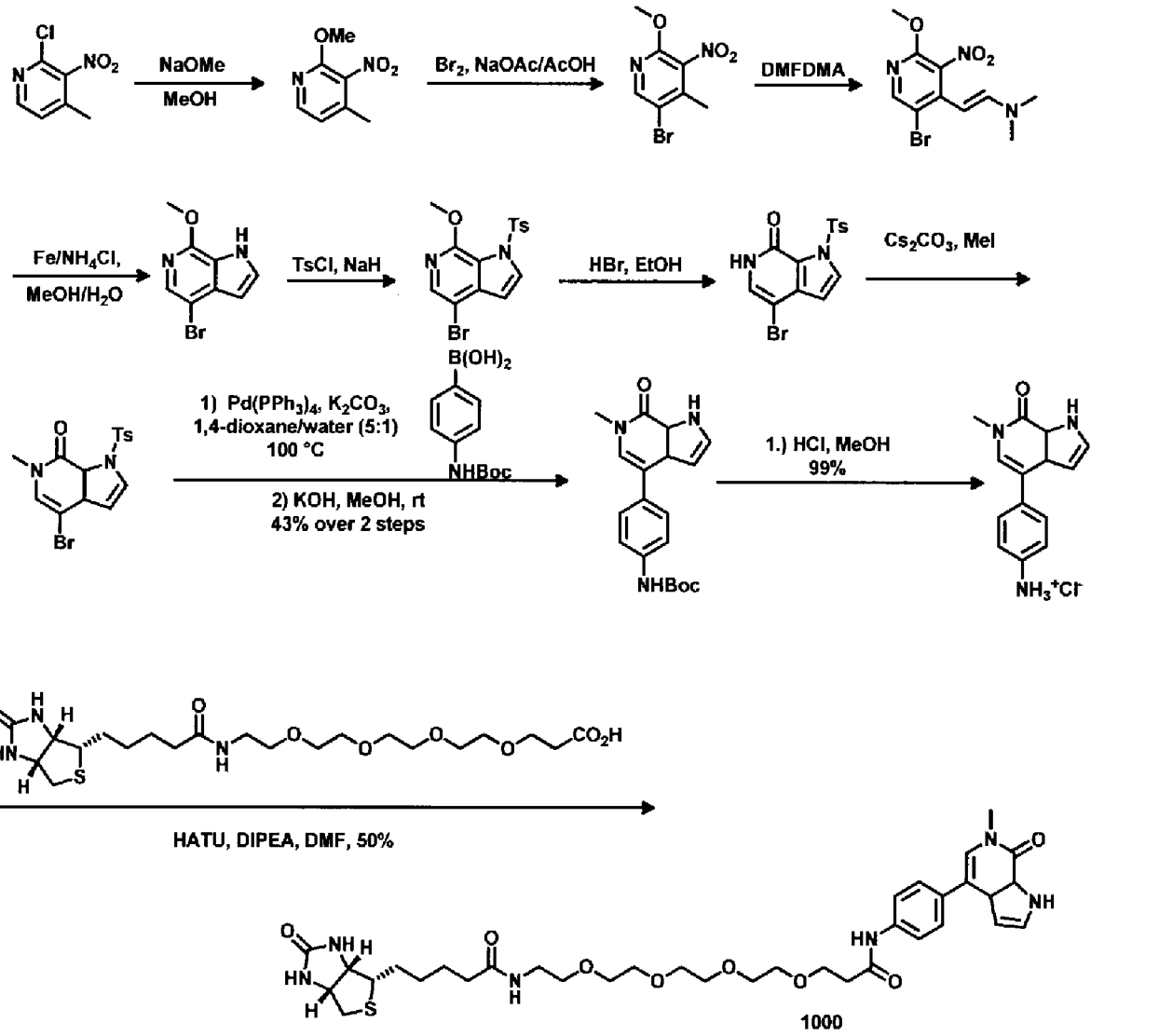
Examples 284-291

Example	Compound Name	NMR	m/z
284	6-allyl-N-(7-fluorotetralin-1-yl)-N,2-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 7.42 (s, 1H), 7.27 – 7.12 (m, 1H), 7.08 – 6.96 (m, 1H), 6.90 – 6.72 (m, 1H), 6.12 – 5.90 (m, 2H), 5.83 – 5.55 (m, 1H), 5.22 – 4.97 (m, 2H), 4.64 (s, 2H), 2.81 – 2.59 (m, 5H), 2.33 (s, 3H), 2.23 – 1.81 (m, 4H).	394
285	6-allyl-N,2-dimethyl-N-(5-methyltetralin-1-yl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 7.32 (d, J = 32.2 Hz, 1H), 7.13 – 6.81 (m, 3H), 6.01 (d, J = 38.2 Hz, 2H), 5.77 (s, 1H), 5.07 (d, J = 43.4 Hz, 3H), 4.65 (s, 2H), 2.65 (d, J = 19.5 Hz, 5H), 2.33 (s, 3H), 2.26 (s, 4H), 2.10 – 1.81 (m, 4H).	390
286	6-allyl-N-(5-fluorotetralin-1-yl)-N,2-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide Enantiomer 1	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.38 (s, 1H), 7.32 – 7.17 (m, 1H), 7.12 – 6.86 (m, 2H), 6.15 – 5.86 (m, 2H), 5.77 (s, 1H), 5.24 – 4.92 (m, 2H), 4.65 (s, 2H), 2.86 – 2.56 (m, 5H), 2.33 (s, 3H), 2.16 – 1.73 (m, 4H).	394
287	6-allyl-N,2-dimethyl-N-(7-methyltetralin-1-yl)-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide Enantiomer 2	1H NMR (400 MHz, DMSO-d6) δ 12.00 – 11.86 (m, 1H), 7.35 (s, 1H), 7.07 (dd, J = 22.6, 7.4 Hz, 2H), 6.94 (s, 1H), 6.01 (d, J = 35.4 Hz, 2H), 5.79 (s, 1H), 5.23 – 4.88 (m, 2H), 4.65 (s, 2H), 2.60 (s, 4H), 2.33 (s, 3H), 2.18 (s, 3H), 2.10 – 1.78 (m, 4H).	390
288	6-allyl-N-(5-methoxytetralin-1-yl)-N,2-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide Enantiomer 1	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.94 (s, 1H), 7.36 (s, 1H), 7.25 – 7.12 (m, 1H), 6.89 – 6.76 (m, 1H), 6.76 – 6.64 (m, 1H), 6.13 – 5.88 (m, 2H), 5.88 – 5.69 (m, 1H), 5.25 – 4.87 (m, 3H), 4.78 – 4.48 (m, 2H), 3.85 – 3.63 (m, 3H), 2.83 – 2.56 (m, 5H), 2.33 (s, 3H), 2.06 – 1.73 (m, 4H).	406

289	6-allyl-N-(5-methoxytetralin-1-yl)-N,2-dimethyl-7-oxo-1H-pyrrolo[2,3-c]pyridine-4-carboxamide Enantiomer 2	^{1}H NMR (400 MHz, DMSO-d_6) δ 11.94 (s, 1H), 7.36 (s, 1H), 7.25 – 7.12 (m, 1H), 6.89 – 6.76 (m, 1H), 6.76 – 6.64 (m, 1H), 6.13 – 5.88 (m, 2H), 5.88 – 5.69 (m, 1H), 5.25 – 4.87 (m, 3H), 4.78 – 4.48 (m, 2H), 3.85 – 3.63 (m, 3H), 2.83 – 2.56 (m, 5H), 2.33 (s, 3H), 2.06 – 1.73 (m, 4H).	406
290	6-allyl-N,2-dimethyl-7-oxo-N-(5,6,7,8-tetrahydroisoquinolin-8-yl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide Enantiomer 1	1H NMR (400 MHz, DMSO-d6) δ 11.96 (s, 1H), 8.48 – 8.20 (m, 2H), 7.43 (s, 1H), 7.14 (d, J = 4.8 Hz, 1H), 6.20 – 5.86 (m, 2H), 5.76 (s, 1H), 5.09 (dd, J = 39.2, 13.5 Hz, 2H), 4.65 (s, 2H), 2.67 (s, 5H), 2.34 (s, 3H), 2.24 – 1.78 (m, 4H).	377
291	6-allyl-N,2-dimethyl-7-oxo-N-(5,6,7,8-tetrahydroisoquinolin-8-yl)-1H-pyrrolo[2,3-c]pyridine-4-carboxamide Enantiomer 2	1H NMR (400 MHz, DMSO-d6) δ 11.96 (s, 1H), 8.48 – 8.20 (m, 2H), 7.43 (s, 1H), 7.14 (d, J = 4.8 Hz, 1H), 6.20 – 5.86 (m, 2H), 5.76 (s, 1H), 5.09 (dd, J = 39.2, 13.5 Hz, 2H), 4.65 (s, 2H), 2.67 (s, 5H), 2.34 (s, 3H), 2.24 – 1.78 (m, 4H).	377

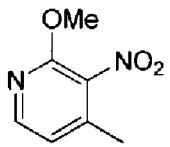
Example 292

Synthesis of biotinylated probe compound (1000) for TAF assay described below.



Step 1:

2-methoxy-4-methyl-3-nitropyridine

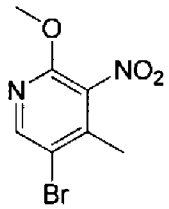


A solution of 2-chloro-4-methyl-3-nitropyridine (250 g, 1.45 mol) in methanol (1.0 L) was added dropwise (2 h) to a stirred and cooled (0 °C) solution of sodium methoxide (250 g, 4.63 mol) in methanol (850 mL). After addition, the mixture was heated to reflux for 23 h, at which time TLC indicated the reaction had gone to completion. The mixture was concentrated under reduced pressure to a volume of approximately 900 mL, and quenched by addition of water (1.5

L). The resulting solid was collected by filtration, washed with water and dried under reduced pressure to give the title compound (250 g, 100% yield) as a brown solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.22 (d, *J* = 5.2 Hz, 1 H), 7.10 (d, *J* = 5.6 Hz, 1 H), 3.92 (s, 3 H), 2.26 (s, 3 H).

Step 2:

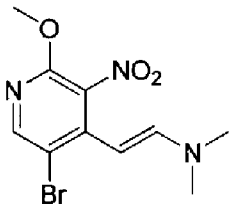
5-bromo-2-methoxy-4-methyl-3-nitropyridine



Sodium acetate (365 g, 5.37 mol) was added to a stirred solution of 2-methoxy-4-methyl-3-nitropyridine (250 g, 1.49 mol) in acetic acid (1.5 L) at ambient temperature and then Br_2 (639 g, 4.00 mol) was added dropwise (30 min). After addition, the mixture was heated at 80 °C for 12 h, at which time TLC indicated the reaction had gone to completion. The mixture was cooled (0 °C) and quenched by sequential addition of 10% aqueous (1.5 L) and saturated aqueous Na_2SO_3 (1.5 L). The resulting solid was collected by filtration washed with water, and dried under reduced pressure to give the title compound (302 g, 82.2% yield) as a light yellow solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.25 (s, 1 H), 3.94 (s, 3 H), 2.29 (s, 3 H).

Step 3:

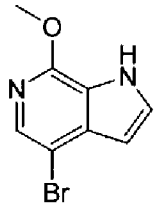
(E)-2-(5-bromo-2-methoxy-3-nitro-4-pyridyl)-N,N-dimethyl-ethenamine



DMF-DMA (600 mL) was slowly added to a stirred and heated (80 °C) solution of 5-bromo-2-methoxy-4-methyl-3-nitropyridine (134 g, 0.54 mol) in DMF (1.1 L). After addition, the mixture was heated at 95 °C for 5 h, at which time TLC indicated the reaction had gone to completion. The mixture was cooled to room temperature and poured into ice-cold water (3 L). The resulting red solid was collected by filtration, washed with water, and dried under reduced pressure to give the title compound (167 g, 100% yield) as red solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.24 (s, 1 H), 7.05 (d, *J* = 13.6 Hz, 1 H), 7.05 (d, *J* = 13.6 Hz, 1 H), 4.80 (d, *J* = 13.2 Hz, 1 H), 3.88 (s, 3 H), 2.90 (s, 6 H).

Step 4:

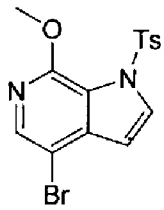
4-bromo-7-methoxy-1H-pyrrolo[2,3-c]pyridine



A mixture of 2-(5-bromo-2-methoxy-3-nitropyridin-4-yl)-N,N-dimethylethenamine (50.0 g, 165 mmol), Fe (50.0 g, 893 mmol) and NH_4Cl (50.0 g, 943 mmol) in methanol/H_2O (1900/250 mL) was heated at reflux for 7 h, at which time LCMS indicated that the reaction had gone to completion. The mixture was filtered while hot and the cake was washed with methanol (3 x 200 mL). The combined filtrate was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography (petroleum ether : Ethyl acetate=5:1) to give the crude product. This crude material was triturated with acetonitrile to give the title compound (37.4 g, 99.5% yield) as a light brown solid. LCMS M/Z (M+H) 226.7, 228.7.

Step 5:

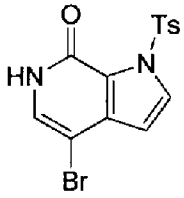
4-bromo-7-methoxy-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine



A solution of 4-bromo-7-methoxy-1H-pyrrolo[2,3-c]pyridine (34.3 g, 0.15 mol) in THF (700 mL) was added dropwise to a stirred and cooled (0 °C) solution of sodium hydride (60%, 19.2 g, 0.48 mol) in THF (700 mL). After addition, the mixture was stirred at room temperature for 1 h, and then cooled again to 0 °C. Tosyl chloride (38.0 g, 0.20 mol) in THF (700 mL) was added dropwise and the resulting mixture was stirred at ambient temperature for 2 h. The reaction was quenched by addition of saturated aqueous ammonium chloride (1.0 L), and then extracted with ethyl acetate (3 x 600 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was triturated with acetonitrile to give the title compound (51.2 g, 88.9% yield) as a brown solid. This crude material was used in the next step without further purification.

Step 6:

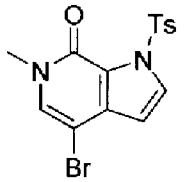
4-bromo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridin-7-one



HBr (40% aqueous, 1.1 L) was added to a solution of 4-bromo-7-methoxy-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine (102.5 g, 0.27 mol) in ethanol (200 mL). After addition, the mixture was heated at 90 °C for 2h, at which time TLC indicated that the reaction had gone to completion. The mixture was cooled to 0 °C and the resulting white solid was collected by filtration. This solid was washed with water and dried under vacuum to give the title compound (87.5 g, 88.6% yield) as a light brown solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 11.48 (s, 1 H), 8.01 (d, *J* = 3.6 Hz, 1 H), 8.90 (d, *J* = 8.0 Hz, 2 H), 7.38 (d, *J* = 8.0 Hz, 2 H), 7.32 (s, 1 H), 6.57 (d, *J* = 3.2 Hz, 1 H), 2.34 (s, 3 H).

Step 7:

4-bromo-6-methyl-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-7-one



Methyl iodide (24.5 g, 172.8 mmol) was added dropwise to a stirred suspension of 4-bromo-1-tosyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (Intermediate A) (16.7 g, 45.5 mmol) and cesium carbonate (17.8 g, 54.6 mmol) in dioxane (250 mL). After addition, the reaction mixture was stirred at room temperature for 18 h, at which time LCMS indicated the reaction had gone to completion. The solvent was evaporated under reduced pressure, and the residue was diluted with water (200 mL). The mixture was extracted with EtOAc (3 x 200 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/ethyl acetate = 3:1) to give the title compound (14.0 g, 81.4% yield) as a brown solid. ^{1}H NMR (400MHz, DMSO-*d6*): δ 8.03 (d, *J* = 3.6 Hz, 1 H), 7.92 (d, *J* = 8.4 Hz, 2 H), 7.78 (s, 1 H), 7.39 (d, *J* = 8.4 Hz, 2 H), 6.57 (d, *J* = 3.6 Hz, 1 H), 3.35 (s, 3 H), 2.35 (s, 3 H).

Step 8:

A 50 mL vial was charged with a magnetic stir bar, 4-bromo-6-methyl-1-tosyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (0.281 g, 0.737 mmol), 1,4-dioxane (3.69 ml, 0.737 mmol), water (0.5 ml, 27.8 mmol), K_2CO_3 (0.306 g, 2.211 mmol), 4-(tertbutoxycarbonylamino)phenylboronic acid (0.227 g, 0.958 mmol), and $Pd(PPh_3)_4$ (0.085 g, 0.074 mmol). The vial was purged, placed under an atmosphere of nitrogen and heated to 95 °C with stirring for 12 h before being allowed to cool to room temperature. The reaction was then diluted with water (20 ml). A precipitate formed which was collected via vacuum filtration using a Buchner funnel. The solids were washed with additional water (2 x 25 mL), dried, and collected. This material was suspended in methanol (~ 5 mL) and treated with KOH (200 mg). After 2 h the MeOH was removed in vacuo and the crude material was suspended in water (~ 20 mL) and the resulting solids were collected via vacuum filtration using a Buchner funnel. The solids were washed with additional water, were collected, and dried in vacuo to afford tert-butyl 4-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenylcarbamate (362 mg, 0.907 mmol) as a light yellow solid. LCMS M/Z (M+H) 494.

Step 9:

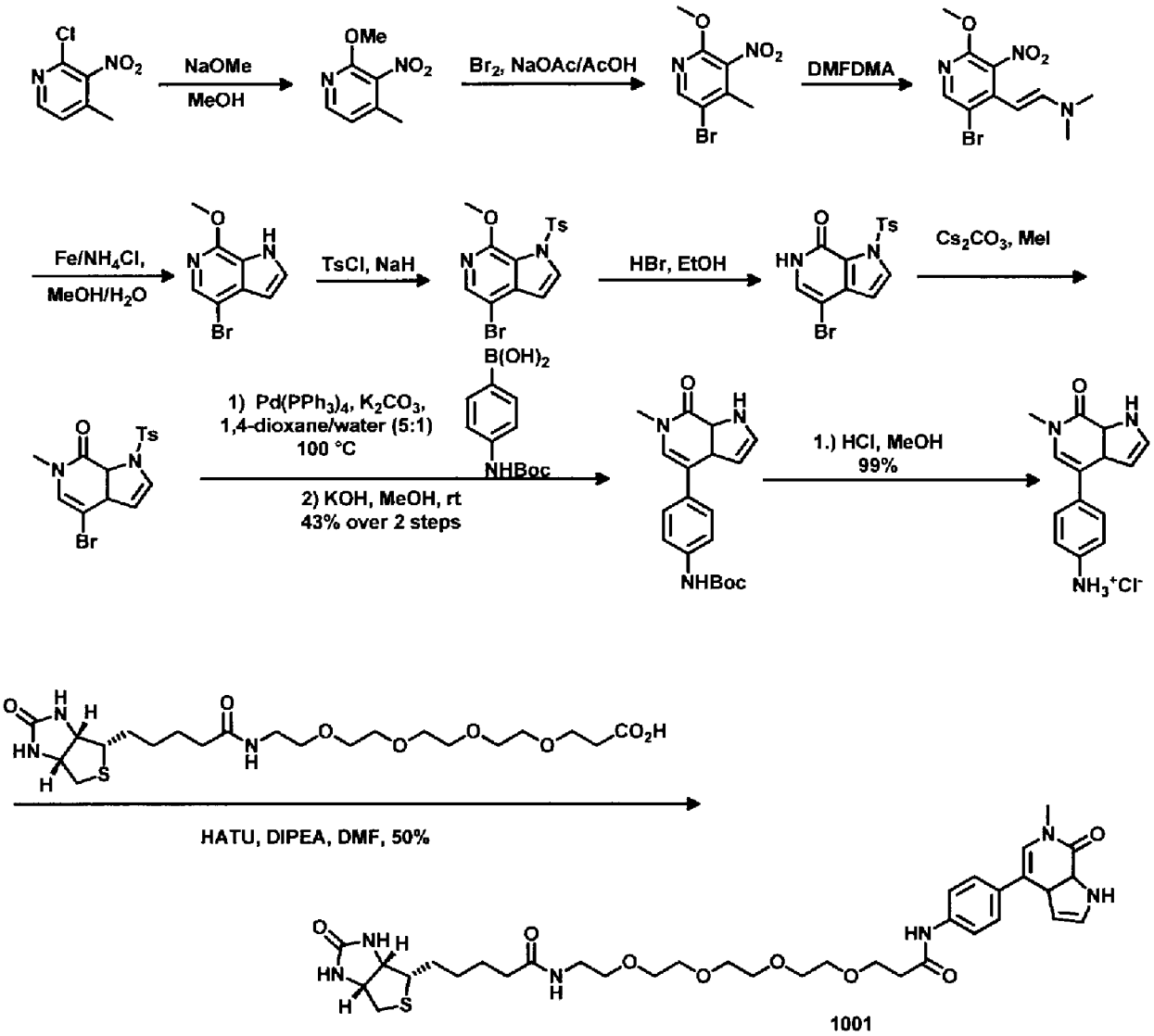
A 50 mL round bottom flask was charged with a magnetic stir bar, tert-butyl 4-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenylcarbamate (350 mg, 1.031 mmol), MeOH (2.062 mL, 1.031 mmol), and HCl (1.031 mL, 4.12 mmol) (4N in dioxane). The reaction was then allowed to stir at rt for 4 h before being diluted with dioxane (25 mL). A precipitate formed which was collected via vacuum filtration using a Buchner funnel, washed with additional dioxane, and dried in vacuo to afford 4-(4-aminophenyl)-6-methyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (188 mg, 0.786 mmol, 76 % yield) as a white solid. LCMS M/Z (M+H) 240.

Step 10:

A 25 mL vial was charged with a magnetic stir bar, 4-(4-aminophenyl)-6-methyl-1Hpyrrolo[2,3-c]pyridin-7(6H)-one (0.038 g, 0.159 mmol), anhydrous DMF (0.794 ml, 0.159 mmol), DIPEA (0.139 ml, 0.794 mmol), 17-oxo-21-((3aS,4S,6aR)-2-oxohexahydro-1Hthieno[3,4-d]imidazol-4-yl)-4,7,10,13-tetraoxa-16-azahenicosan-1-oic acid (0.078 g, 0.159 mmol), and HATU (0.075 g, 0.199 mmol). The crude reaction mixture was directly purified via reverse phase HPLC to afford N-(4-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl)-1-(5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamido)-3,6,9,12-tetraoxapentadecan-15-amide (31 mg, 0.041 mmol, 26.0 % yield). LCMS M/Z (M+2H)/2 357.

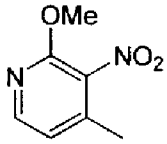
Example 293

Synthesis of biotinylated probe compound (1001) for CECR2 assay described below.



Step 1:

2-methoxy-4-methyl-3-nitropyridine

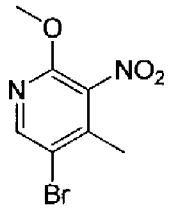


A solution of 2-chloro-4-methyl-3-nitropyridine (250 g, 1.45 mol) in methanol (1.0 L) was added dropwise (2 h) to a stirred and cooled (0 °C) solution of sodium methoxide (250 g, 4.63 mol) in methanol (850 mL). After addition, the mixture was heated to reflux for 23 h, at which time TLC indicated the reaction had gone to completion. The mixture was concentrated under reduced pressure to a volume of approximately 900 mL, and quenched by addition of water (1.5

L). The resulting solid was collected by filtration, washed with water and dried under reduced pressure to give the title compound (250 g, 100% yield) as a brown solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.22 (d, *J* = 5.2 Hz, 1 H), 7.10 (d, *J* = 5.6 Hz, 1 H), 3.92 (s, 3 H), 2.26 (s, 3 H).

Step 2:

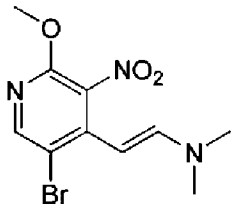
5-bromo-2-methoxy-4-methyl-3-nitropyridine



Sodium acetate (365 g, 5.37 mol) was added to a stirred solution of 2-methoxy-4-methyl-3-nitropyridine (250 g, 1.49 mol) in acetic acid (1.5 L) at ambient temperature and then Br_2 (639 g, 4.00 mol) was added dropwise (30 min). After addition, the mixture was heated at 80 °C for 12 h, at which time TLC indicated the reaction had gone to completion. The mixture was cooled (0 °C) and quenched by sequential addition of 10% aqueous (1.5 L) and saturated aqueous Na_2SO_3 (1.5 L). The resulting solid was collected by filtration washed with water, and dried under reduced pressure to give the title compound (302 g, 82.2% yield) as a light yellow solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.25 (s, 1 H), 3.94 (s, 3 H), 2.29 (s, 3 H).

Step 3:

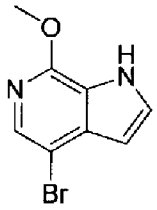
(E)-2-(5-bromo-2-methoxy-3-nitro-4-pyridyl)-N,N-dimethyl-ethenamine



DMF-DMA (600 mL) was slowly added to a stirred and heated (80 °C) solution of 5-bromo-2-methoxy-4-methyl-3-nitropyridine (134 g, 0.54 mol) in DMF (1.1 L). After addition, the mixture was heated at 95 °C for 5 h, at which time TLC indicated the reaction had gone to completion. The mixture was cooled to room temperature and poured into ice-cold water (3 L). The resulting red solid was collected by filtration, washed with water, and dried under reduced pressure to give the title compound (167 g, 100% yield) as red solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 8.24 (s, 1 H), 7.05 (d, *J* = 13.6 Hz, 1 H), 7.05 (d, *J* = 13.6 Hz, 1 H), 4.80 (d, *J* = 13.2 Hz, 1 H), 3.88 (s, 3 H), 2.90 (s, 6 H).

Step 4:

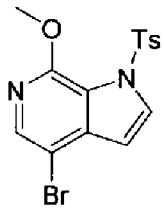
4-bromo-7-methoxy-1H-pyrrolo[2,3-c]pyridine



A mixture of 2-(5-bromo-2-methoxy-3-nitropyridin-4-yl)-N,N-dimethylethenamine (50.0 g, 165 mmol), Fe (50.0 g, 893 mmol) and NH_4Cl (50.0 g, 943 mmol) in methanol/H_2O (1900/250 mL) was heated at reflux for 7 h, at which time LCMS indicated that the reaction had gone to completion. The mixture was filtered while hot and the cake was washed with methanol (3 x 200 mL). The combined filtrate was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography (petroleum ether : Ethyl acetate=5:1) to give the crude product. This crude material was triturated with acetonitrile to give the title compound (37.4 g, 99.5% yield) as a light brown solid. LCMS M/Z (M+H) 226.7, 228.7.

Step 5:

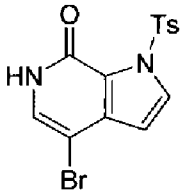
4-bromo-7-methoxy-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine



A solution of 4-bromo-7-methoxy-1H-pyrrolo[2,3-c]pyridine (34.3 g, 0.15 mol) in THF (700 mL) was added dropwise to a stirred and cooled (0 °C) solution of sodium hydride (60%, 19.2 g, 0.48 mol) in THF (700 mL). After addition, the mixture was stirred at room temperature for 1 h, and then cooled again to 0 °C. Tosyl chloride (38.0 g, 0.20 mol) in THF (700 mL) was added dropwise and the resulting mixture was stirred at ambient temperature for 2 h. The reaction was quenched by addition of saturated aqueous ammonium chloride (1.0 L), and then extracted with ethyl acetate (3 x 600 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was triturated with acetonitrile to give the title compound (51.2 g, 88.9% yield) as a brown solid. This crude material was used in the next step without further purification.

Step 6:

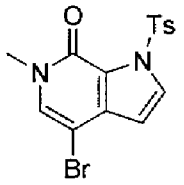
4-bromo-1-(p-tolylsulfonyl)-6H-pyrrolo[2,3-c]pyridin-7-one



HBr (40% aqueous, 1.1 L) was added to a solution of 4-bromo-7-methoxy-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridine (102.5 g, 0.27 mol) in ethanol (200 mL). After addition, the mixture was heated at 90 °C for 2h, at which time TLC indicated that the reaction had gone to completion. The mixture was cooled to 0 °C and the resulting white solid was collected by filtration. This solid was washed with water and dried under vacuum to give the title compound (87.5 g, 88.6% yield) as a light brown solid. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 11.48 (s, 1 H), 8.01 (d, *J* = 3.6 Hz, 1 H), 8.90 (d, *J* = 8.0 Hz, 2 H), 7.38 (d, *J* = 8.0 Hz, 2 H), 7.32 (s, 1 H), 6.57 (d, *J* = 3.2 Hz, 1 H), 2.34 (s, 3 H).

Step 7:

4-bromo-6-methyl-1-(p-tolylsulfonyl)pyrrolo[2,3-c]pyridin-7-one



Methyl iodide (24.5 g, 172.8 mmol) was added dropwise to a stirred suspension of 4-bromo-1-tosyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (Intermediate A) (16.7 g, 45.5 mmol) and cesium carbonate (17.8 g, 54.6 mmol) in dioxane (250 mL). After addition, the reaction mixture was stirred at room temperature for 18 h, at which time LCMS indicated the reaction had gone to completion. The solvent was evaporated under reduced pressure, and the residue was diluted with water (200 mL). The mixture was extracted with EtOAc (3 x 200 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/ethyl acetate = 3:1) to give the title compound (14.0 g, 81.4% yield) as a brown solid. ^{1}H NMR (400MHz, DMSO-*d6*): δ 8.03 (d, *J* = 3.6 Hz, 1 H), 7.92 (d, *J* = 8.4 Hz, 2 H), 7.78 (s, 1 H), 7.39 (d, *J* = 8.4 Hz, 2 H), 6.57 (d, *J* = 3.6 Hz, 1 H), 3.35 (s, 3 H), 2.35 (s, 3 H).

Step 8:

A 50 mL vial was charged with a magnetic stir bar, 4-bromo-6-methyl-1-tosyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (0.281 g, 0.737 mmol), 1,4-dioxane (3.69 ml, 0.737 mmol), water (0.5 ml, 27.8 mmol), K_2CO_3 (0.306 g, 2.211 mmol), 4-(tertbutoxycarbonylamino)phenylboronic acid (0.227 g, 0.958 mmol), and $Pd(PPh_3)_4$ (0.085 g, 0.074 mmol). The vial was purged, placed under an atmosphere of nitrogen and heated to 95 °C with stirring for 12 h before being allowed to cool to room temperature. The reaction was then diluted with water (20 ml). A precipitate formed which was collected via vacuum filtration using a Buchner funnel. The solids were washed with additional water (2 x 25 mL), dried, and collected. This material was suspended in methanol (~ 5 mL) and treated with KOH (200 mg). After 2 h the MeOH was removed in vacuo and the crude material was suspended in water (~ 20 mL) and the resulting solids were collected via vacuum filtration using a Buchner funnel. The solids were washed with additional water, were collected, and dried in vacuo to afford tert-butyl 4-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenylcarbamate (362 mg, 0.907 mmol) as a light yellow solid. LCMS M/Z (M+H) 494.

Step 9:

A 50 mL round bottom flask was charged with a magnetic stir bar, tert-butyl 4-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenylcarbamate (350 mg, 1.031 mmol), MeOH (2.062 mL, 1.031 mmol), and HCl (1.031 mL, 4.12 mmol) (4N in dioxane). The reaction was then allowed to stir at rt for 4 h before being diluted with dioxane (25 mL). A precipitate formed which was collected via vacuum filtration using a Buchner funnel, washed with additional dioxane, and dried in vacuo to afford 4-(4-aminophenyl)-6-methyl-1H-pyrrolo[2,3-c]pyridin-7(6H)-one (188 mg, 0.786 mmol, 76 % yield) as a white solid. LCMS M/Z (M+H) 240.

Step 10:

A 25 mL vial was charged with a magnetic stir bar, 4-(4-aminophenyl)-6-methyl-1Hpyrrolo[2,3-c]pyridin-7(6H)-one (0.038 g, 0.159 mmol), anhydrous DMF (0.794 ml, 0.159 mmol), DIPEA (0.139 ml, 0.794 mmol), 17-oxo-21-((3aS,4S,6aR)-2-oxohexahydro-1Hthieno[3,4-d]imidazol-4-yl)-4,7,10,13-tetraoxa-16-azahenicosan-1-oic acid (0.078 g, 0.159 mmol), and HATU (0.075 g, 0.199 mmol). The crude reaction mixture was directly purified via reverse phase HPLC to afford N-(4-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl)-1-(5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamido)-3,6,9,12-tetraoxapentadecan-15-amide (31 mg, 0.041 mmol, 26.0 % yield). LCMS M/Z (M+2H)/2 357.

EXAMPLE 294

The inhibitory activity of representative compounds against bromodomains can be evaluated using known methods or using one of the following assay protocols.

IC_{50} measurements for inhibitors using BRD4 AlphaLisa Binding Assay

His/Flag epitope tagged BRD4 $BD1_{42-168}$ was cloned, expressed, and purified to. BRD4 binding and inhibition was assessed by monitoring the engagement of biotinylated H4-tetraacetyl peptide (New England Peptide, NEP2069-1/13) with the target using the AlphaLisa technology (Perkin-Elmer). Specifically, in a 384 well ProxiPlate BRD4(BD1) (30 nM final) was combined with peptide (200 nM final) in 40 mM HEPES (pH 7.0), 40 mM NaCl, 1 mM DTT, 0.01% (w/v) BSA, and 0.008% (w/v) Brij-35 either in the presence of DMSO (final 1.2% DMSO) or compound dilution series in DMSO. After 20 minutes incubation at room temperature Alpha streptavidin donor beads and AlphaLisa anti-Flag acceptor beads were added to a final concentration of 10 ug/mL each. After three hours equilibration plates were read on an Envision instrument and IC_{50}s calculated using a four parameter non-linear curve fit.

IC_{50} measurements for inhibitors using BRD9 AlphaLisa Binding Assay

His/Flag epitope tagged $BRD9_{134-239}$ was cloned, expressed, and purified to homogeneity. BRD9 binding and inhibition was assessed by monitoring the engagement of biotinylated H4-tetraacetyl peptide (New England Peptide , NEP2069-11/13) with the target using the AlphaLisa technology (Perkin-Elmer). Specifically, in a 384 well ProxiPlate BRD9 (50 nM final) was combined with peptide (3 nM final) in 50 mM HEPES (pH 7.5), 150 mM NaCl, 1 mM TCEP, 0.01% (w/v) BSA, and 0.008% (w/v) Brij-35 either in the presence of DMSO (final 0.8% DMSO) or compound dilution series in DMSO. After 20 minutes incubation at room temperature AlphaLisa Streptavidin Acceptor Beads (Perkin-AL125C) and AlphaLisa Nickel donor beads (Perkin AS 10 ID) were added to a final concentration of 15 ug/mL each. After ninety minutes of equilibration in the dark, the plates were read on an Envision instrument and IC_{50}s calculated using a four parameter non-linear curve fit.

IC_{50} measurements for inhibitors using TAF1-BD2 TR-FRET Binding Assay

His/Flag epitope tagged TAF1-$BD2_{1504-1635}$ was cloned, expressed, and purified to homogeneity. TAF1-BD2 binding and inhibition was assessed by monitoring the engagement of a biotinylated small molecule compound **1000** (Example 292) with the target using the TR-FRET assay technology (Perkin-Elmer). Specifically, in a 384 well ProxiPlate TAF1-BD2 (6 nM final) was combined with biotin-ligand (50 nM final) in 50 mM HEPES (pH 7.5), 50 mM NaCl, 1 mM TCEP, 0.01% (w/v) BSA, and 0.008% (w/v) Brij-35 either in the presence of DMSO (final 0.2% DMSO) or compound dilution series in DMSO. After 10 minutes incubation at room temperature, a mixture Eu-W1024 Anti-6xHis antibody (Perkin Elmer AD0110) and SureLight™ Allophycocyanin-Streptavidin (APC-SA , Perkin Elmer CR130-100) were added to a final concentrations of 0.2 nMolar antibody and 25 nMolar APC-SA, respectively. After twenty minutes of equilibration, the plates were read on an Envision instrument and IC_{50}s calculated using a four parameter non-linear curve fit. Novel compound **1000** and the TAF1-BD2 TR-FRET Binding Assay described above represent additional embodiments of the invention.

IC50 measurements for inhibitors using CECR2 TR-FRET Binding Assay

His/Flag epitope tagged $CECR2_{424-538}$ was cloned, expressed, and purified to homogeneity. CECR2 binding and inhibition was assessed by monitoring the engagement of a biotinylated small molecule compound **1001** (Example 293) with the target using the TR-FRET assay technology (Perkin-Elmer). Specifically, in a 384 well ProxiPlate CECR2 (1.5 nM final) was combined with biotin-ligand (25 nM final) in 50 mM HEPES (pH 7.5), 50 mM NaCl, 1 mM TCEP, 0.01% (w/v) BSA, and 0.008% (w/v) Brij-35 either in the presence of DMSO (final 0.2% DMSO) or compound dilution series in DMSO. After 15 minutes incubation at room temperature, a mixture Eu-W1024 Anti-6xHis antibody (Perkin Elmer AD0110) and SureLight™ Allophycocyanin-Streptavidin (APC-SA , Perkin Elmer CR130-100) were added to a final concentrations of 0.2 nMolar antibody and 12.5 nMolar APC-SA, respectively. After forty minutes of equilibration, the plates were read on an Envision instrument and IC_{50}s calculated using a four parameter non-linear curve fit. Novel compound **1001** and the CECR2 TR-FRET Binding Assay described above represent additional embodiments of the invention.

Data for representative compounds of formula (I) from the four assays described above is provided in the following table.

Example	Assay	IC50 (uM)
8	BRD4	4.9
28	BRD4	19
31	BRD4	17
32	BRD4	9.8
46	BRD4	6.4
50	BRD4	16
55	BRD4	9.5
57	BRD4	4.1
64	BRD4	8.0
92	BRD4	8.4
93	BRD4	2.9
94	BRD4	3.1
95	BRD4	11
96	BRD4	5.0
101	BRD4	17
105	BRD4	19
116	BRD4	4.3
117	BRD4	4.0
119	BRD4	1.2
123	BRD4	11
126	BRD4	3.2
127	BRD4	1.2
128	BRD4	16
132	BRD4	13
179	BRD4	2.1
198	BRD4	1.1
215	BRD4	3.8
222	BRD4	16
256	BRD4	3.8
258	BRD4	0.80
261	BRD4	2.7
262	BRD4	3.3
265	BRD4	5.3
1	BRD9	3.0
3	BRD9	3.5
5	BRD9	0.79
6	BRD9	1.5
7	BRD9	0.99
9	BRD9	0.92
11	BRD9	5.4
12	BRD9	0.84
18	BRD9	2.1
19	BRD9	0.075
22	BRD9	7.3
33	BRD9	5.4
34	BRD9	2.2
35	BRD9	11
38	BRD9	8.0
39	BRD9	19
45	BRD9	6.1
85	BRD9	0.57
86	BRD9	0.16
87	BRD9	1.0
88	BRD9	1.5
89	BRD9	4.1
90	BRD9	0.30
91	BRD9	0.20

97	BRD9	0.49
98	BRD9	0.55
102	BRD9	0.86
103	BRD9	0.49
104	BRD9	0.98
106	BRD9	0.24
107	BRD9	3.4
108	BRD9	0.20
109	BRD9	0.27
110	BRD9	0.85
111	BRD9	0.24
112	BRD9	0.46
114	BRD9	0.073
115	BRD9	0.64
118	BRD9	0.24
120	BRD9	0.44
121	BRD9	0.10
122	BRD9	2.2
124	BRD9	2.9
125	BRD9	0.13
129	BRD9	0.22
131	BRD9	1.6
134	BRD9	0.28
136	BRD9	0.40
138	BRD9	0.31
146	BRD9	1.6
159	BRD9	4.3
161	BRD9	2.9
190	BRD9	15
217	BRD9	4.7
248	BRD9	3.3
257	BRD9	0.18
259	BRD9	0.60
260	BRD9	0.18
263	BRD9	0.48
264	BRD9	0.44
2	CECR2	14
21	CECR2	0.89
23	CECR2	2.1
26	CECR2	3.2
29	CECR2	1.8
30	CECR2	3.8
37	CECR2	3.1
41	CECR2	0.77
59	CECR2	0.89
60	CECR2	10.3
61	CECR2	1.0
62	CECR2	1.5
65	CECR2	1.4
66	CECR2	2.4
67	CECR2	1.8
68	CECR2	3.0
69	CECR2	0.45
72	CECR2	2.2
73	CECR2	2.5
74	CECR2	5.9
75	CECR2	4.8
76	CECR2	0.35
77	CECR2	2.7
78	CECR2	9.9

79	CECR2	5.1
80	CECR2	0.51
113	CECR2	0.31
139	CECR2	0.24
140	CECR2	0.34
141	CECR2	0.39
142	CECR2	0.29
143	CECR2	0.40
144	CECR2	0.43
145	CECR2	0.41
147	CECR2	0.51
158	CECR2	0.79
160	CECR2	0.18
162	CECR2	0.12
163	CECR2	0.091
164	CECR2	0.21
165	CECR2	0.087
167	CECR2	0.12
168	CECR2	0.042
169	CECR2	0.023
170	CECR2	0.042
172	CECR2	1.0
173	CECR2	0.99
174	CECR2	0.59
175	CECR2	0.76
176	CECR2	0.93
177	CECR2	0.69
178	CECR2	0.74
181	CECR2	0.73
182	CECR2	0.41
183	CECR2	0.49
184	CECR2	0.47
185	CECR2	0.91
186	CECR2	0.44
187	CECR2	0.79
188	CECR2	2.0
189	CECR2	1.0
191	CECR2	0.59
192	CECR2	1.4
197	CECR2	0.73
201	CECR2	0.99
202	CECR2	1.3
203	CECR2	1.1
204	CECR2	1.1
205	CECR2	0.71
206	CECR2	0.37
207	CECR2	0.81
208	CECR2	1.2
211	CECR2	2.2
212	CECR2	1.7
213	CECR2	0.71
214	CECR2	0.66
216	CECR2	1.2
218	CECR2	0.77
220	CECR2	1.1
221	CECR2	0.67
223	CECR2	0.97
224	CECR2	0.78
225	CECR2	1.4
226	CECR2	0.70

227	CECR2	2.0
229	CECR2	0.64
230	CECR2	0.79
232	CECR2	1.2
233	CECR2	0.77
234	CECR2	1.0
239	CECR2	2.3
241	CECR2	1.1
242	CECR2	1.4
243	CECR2	2.0
244	CECR2	19
249	CECR2	4.8
251	CECR2	6.2
253	CECR2	0.98
254	CECR2	0.70
266	CECR2	0.030
267	CECR2	0.017
268	CECR2	0.023
269	CECR2	0.033
270	CECR2	0.018
271	CECR2	0.011
272	CECR2	0.035
273	CECR2	4.90
274	CECR2	0.074
275	CECR2	0.11
276	CECR2	0.038
277	CECR2	0.053
278	CECR2	0.057
279	CECR2	0.012
280	CECR2	0.049
281	CECR2	0.032
282	CECR2	0.067
283	CECR2	0.044
284	CECR2	0.053
285	CECR2	0.15
286	CECR2	0.041
287	CECR2	0.084
288	CECR2	0.041
289	CECR2	0.045
290	CECR2	0.050
291	CECR2	0.140
4	TAF-1	0.32
10	TAF-1	4.7
14	TAF-1	3.7
15	TAF-1	0.97
16	TAF-1	6.0
17	TAF-1	3.6
20	TAF-1	1.5
24	TAF-1	0.15
25	TAF-1	0.69
27	TAF-1	6.9
36	TAF-1	1.7
40	TAF-1	0.069
42	TAF-1	0.21
43	TAF-1	0.72
44	TAF-1	0.34
47	TAF-1	2.3
48	TAF-1	1.5
49	TAF-1	3.9

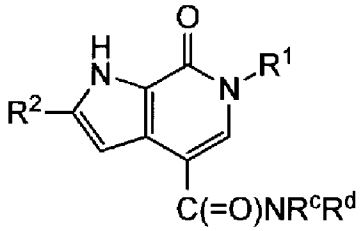
51	TAF-1	4.4
52	TAF-1	7.1
53	TAF-1	8.2
54	TAF-1	2.9
56	TAF-1	2.5
58	TAF-1	1.5
63	TAF-1	4.7
70	TAF-1	6.4
71	TAF-1	3.0
81	TAF-1	0.71
82	TAF-1	7.0
83	TAF-1	0.67
84	TAF-1	5.7
100	TAF-1	1.7
130	TAF-1	1.2
133	TAF-1	0.85
135	TAF-1	1.3
137	TAF-1	0.51
148	TAF-1	0.44
149	TAF-1	0.32
150	TAF-1	0.36
151	TAF-1	0.55
152	TAF-1	0.57
153	TAF-1	0.49
154	TAF-1	0.53
155	TAF-1	0.33
156	TAF-1	0.99
157	TAF-1	1.6
166	TAF-1	2.1
171	TAF-1	0.26
180	TAF-1	0.16
193	TAF-1	1.6
199	TAF-1	18
200	TAF-1	8.0
209	TAF-1	0.58
210	TAF-1	5.3
219	TAF-1	3.6
228	TAF-1	3.3
231	TAF-1	9.9
235	TAF-1	9.9
236	TAF-1	14
238	TAF-1	2.1
240	TAF-1	3.4
250	TAF-1	14
252	TAF-1	5.0
255	TAF-1	4.8

While a number of embodiments have been described, these examples may be altered to provide other embodiments that utilize the compounds and methods described herein. Therefore, the scope of this invention is to be defined by the appended claims rather than by the specific embodiments that have been represented by way of example.

CLAIMS

We claim:

1. A compound of formula (I):



(I)

or a salt thereof, wherein:

R^1 is H, C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, or carbocyclyl, wherein each C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, and carbocyclyl of R^1 is optionally substituted with one or more groups R^a;

R^2 is H, C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, or C_{3-8}cycloalkyl, wherein each C_{1-12}alkyl, C_{2-12}alkenyl, C_{2-12}alkynyl, and C_{3-8}cycloalkyl of R^2 is optionally substituted with one or more groups R^b; and

each R^a is independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^v)_2$, $-S(O)-N(R^v)_2$, $-S(O)_2-N(R^v)_2$, $-O-R^v$, $-S-R^v$, $-O-C(O)-R^v$, $-O-C(O)-O-R^v$, $-C(O)-R^v$, $-C(O)-O-R^v$, $-S(O)-R^v$, $-S(O)_2-R^v$, $-O-C(O)-N(R^v)_2$, $-N(R^v)-C(O)-OR^v$, $-N(R^v)-C(O)-N(R^v)_2$, $-N(R^v)-C(O)-R^v$, $-N(R^v)-S(O)-R^v$, $-N(R^v)-S(O)_2-R^v$, $-N(R^v)-S(O)-N(R^v)_2$, and $-N(R^v)-S(O)_2-N(R^v)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl, is optionally substituted with one or more groups independently selected from oxo, halo, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^v)_2$, $-S(O)-N(R^v)_2$, $-S(O)_2-N(R^v)_2$, $-O-R^v$, $-S-R^v$, $-O-C(O)-R^v$, $-C(O)-R^v$, $-C(O)-O-R^v$, $-S(O)-R^v$, $-S(O)_2-R^v$, $-C(O)-N(R^v)_2$, $-N(R^v)-C(O)-R^v$, $-N(R^v)-S(O)-R^v$, $-N(R^v)-S(O)_2-R^v$ and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^b is independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^w)_2$, -CN, $-C(O)-N(R^w)_2$, $-S(O)-N(R^w)_2$, $-S(O)_2-N(R^w)_2$, $-O-R^w$, $-S-R^w$, $-O-C(O)-R^w$, $-O-C(O)-O-R^w$, $-C(O)-R^w$, $-C(O)-O-R^w$, $-S(O)-R^w$, $-S(O)_2-R^w$, $-O-C(O)-N(R^w)_2$, $-N(R^w)-C(O)-OR^w$, $-N(R^w)-C(O)-N(R^w)_2$, $-N(R^w)-C(O)-R^w$, $-N(R^w)-S(O)-R^w$, $-N(R^w)-S(O)_2-R^w$, $-N(R^w)-S(O)-N(R^w)_2$, and $-N(R^w)-S(O)_2-N(R^w)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, $-NO_2$, $-N(R^w)_2$, -CN, $-C(O)-N(R^w)_2$, $-S(O)-N(R^w)_2$, $-S(O)_2-N(R^w)_2$, $-O-R^w$, $-S-R^w$, $-O-C(O)-R^w$,

-C(O)-R^w, -C(O)-O-R^w, -S(O)-R^w, -$S(O)_2$-R^w, -C(O)-$N(R^w)_2$, -$N(R^w)$-C(O)-R^w, -$N(R^w)$-S(O)-R^w, -$N(R^w)$-$S(O)_2$-R^w and C_{1-6}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^c and R^d is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^v)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl of the substituent groups, is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, -NO_2, -$N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, N(R^h)-$S(O)_2$-R^h, and C_{1-6}alkyl, which heterocyclyl, carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, -O-R^h, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo, and C_{1-6}alkyl;

or R^c and R^d are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^v)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from C_{1-6}alkyl , carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, which C_{1-6}alkyl , carbocyclyl, and heterocyclyl are optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl;

each R^h is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and

heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, carbocyclyl, heterocyclyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^h are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, halo and C_{1-3}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo;

each R^v is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^v are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, halo and C_{1-3}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; and

each R^w is independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl,wherein each C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from oxo, halo, amino, hydroxyl, and C_1-C_6 alkyl that is optionally substituted with one or more groups independently selected from oxo and halo; or two R^w are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, halo and C_{1-3}alkyl that is optionally substituted with one or more groups independently selected from oxo and halo.

2. The compound of claim 1 wherein R^1 is C_{1-12}alkyl or C_{2-12}alkenyl, wherein each C_{1-12}alkyl and, C_{2-12}alkenyl is optionally substituted with one or more groups R^a.

3. The compound of claim 1 wherein R^1 is C_{1-6}alkyl or C_{2-6}alkenyl, wherein each C_{1-6}alkyl and, C_{2-6}alkenyl is optionally substituted with one or more groups R^a.

4. The compound of claim 1 wherein R^1 is C_{1-6}alkyl or C_{2-6}alkenyl, wherein each C_{1-6}alkyl and C_{2-6}alkenyl is optionally substituted with one or more groups independently selected from carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -$N(R^v)_2$, -CN, -C(O)-$N(R^v)_2$, -O-R^v, -O-C(O)-R^v, -C(O)-R^v, and -C(O)-O-R^v.

5. The compound of claim 1 wherein R^1 is C_{1-6}alkyl or C_{2-6}alkenyl, wherein each C_{1-6}alkyl and C_{2-6}alkenyl is optionally substituted with one or more groups independently selected from carbocyclyl, -F, -Cl, -O-R^v, -O-C(O)-R^v, -C(O)-R^v, and -C(O)-O-R^v.

6. The compound of claim 1 wherein R^1 is C_{1-6}alkyl or C_{2-6}alkenyl, wherein each C_{1-6}alkyl and C_{2-6}alkenyl is optionally substituted with one or more groups independently selected from C_{3-6}cycloalkyl.

7. The compound of claim 1 wherein R^1 is methyl, butyl, 2-propenyl, 2-buten-1-yl, 3-buten-1-yl or 2-cyclopropylethyl.

8. The compound of any one of claims 1-7 wherein R^2 is H or C_{1-12}alkyl wherein each C_{1-12}alkyl is optionally substituted with one or more groups R^b.

9. The compound of any one of claims 1-7 wherein R^2 is H or C_{1-6}alkyl wherein each C_{1-6}alkyl is optionally substituted with one or more groups R^b.

10. The compound of any one of claims 1-7 wherein R^2 is H or C_{1-6}alkyl wherein each C_{1-12}alkyl is optionally substituted with one or more carbocyclyl, -F, -Cl, -O-R^w, -O-C(O)-R^w, -C(O)-R^w, -C(O)-O-R^w.

11. The compound of any one of claims 1-7 wherein R^2 is H or methyl.

12. The compound of any one of claims 1-7 wherein R^2 is H.

13. The compound of any one of claims 1-12 wherein R^c is hydrogen, C_{1-6}alkyl, or carbocyclyl, wherein each C_{1-6}alkyl and carbocyclyl is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^v)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, carbocyclyl, and heterocyclyl of the substituent groups, is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, -NO_2, -$N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-

$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, $N(R^h)$-$S(O)_2$-R^h, and C_{1-6}alkyl, which carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, -O-R^h, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

14. The compound of any one of claims 1-12 wherein R^c is hydrogen, C_{1-6}alkyl, or C_{3-8}cycloalkyl, wherein each C_{1-6}alkyl and C_{3-8}cycloalkyl is optionally substituted with one or more substituent groups independently selected from -O-R^h.

15. The compound of any one of claims 1-12 wherein R^c is hydrogen, methyl, ethyl, cyclopropyl, cyclobutyl, or 2-methoxyethyl.

16. The compound of any one of claims 1-12 wherein R^c is hydrogen.

17. The compound of any one of claims 1-12 wherein R^c is methyl, ethyl, cyclopropyl, cyclobutyl, or 2-methoxyethyl.

18. The compound of any one of claims 1-17 wherein R^d is C_{1-6}alkyl, carbocyclyl or heterocyclyl,wherein each C_{1-6}alkyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^v)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, -NO_2, -$N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, $N(R^h)$-$S(O)_2$-R^h, and C_{1-6}alkyl, which heterocyclyl, carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, -O-R^h, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

19. The compound of any one of claims 1-17 wherein R^d is C_{1-6}alkyl that is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $N(R^h)-S(O)_2-R^h$, and C_{1-6}alkyl, which heterocyclyl, carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, $-O-R^h$, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

20. The compound of any one of claims 1-17 wherein R^d is carbocyclyl that is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $N(R^h)-S(O)_2-R^h$, and C_{1-6}alkyl, which heterocyclyl, carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, $-O-R^h$, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

21. The compound of any one of claims 1-17 wherein R^d is heterocyclyl that is optionally substituted with one or more substituent groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, $-NO_2$, $-N(R^v)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, -

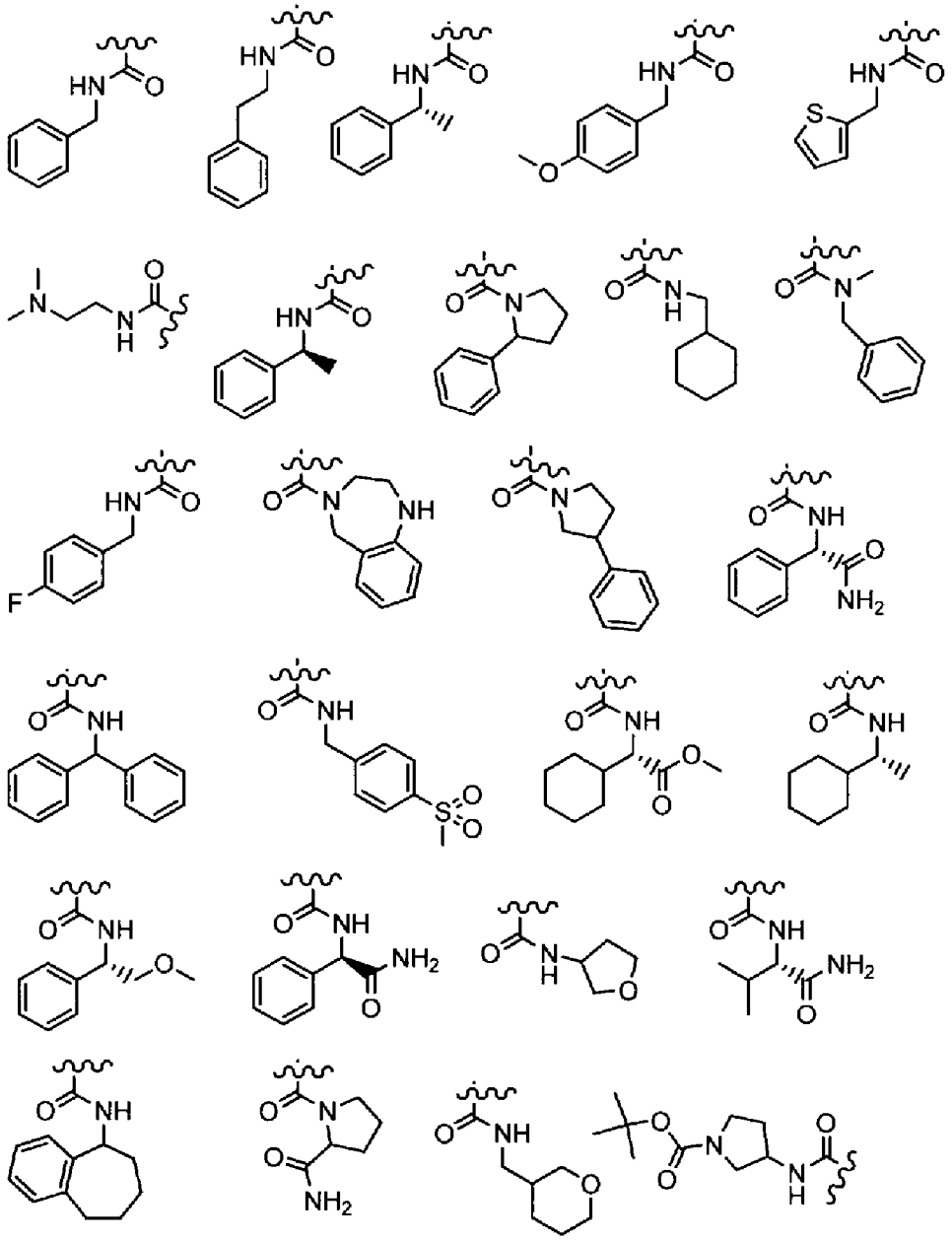
$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl of the substituent groups is optionally substituted with one or more groups independently selected from oxo, carbocyclyl, heterocyclyl, halo, -NO_2, -$N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, $N(R^h)$-$S(O)_2$-R^h, and C_{1-6}alkyl, which heterocyclyl, carbocyclyl and C_{1-6}alkyl are optionally substituted with one or more groups independently selected from oxo, halo, C_{1-6}alkyl, cyano, -O-R^h, heterocyclyl, and carbocyclyl that is optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

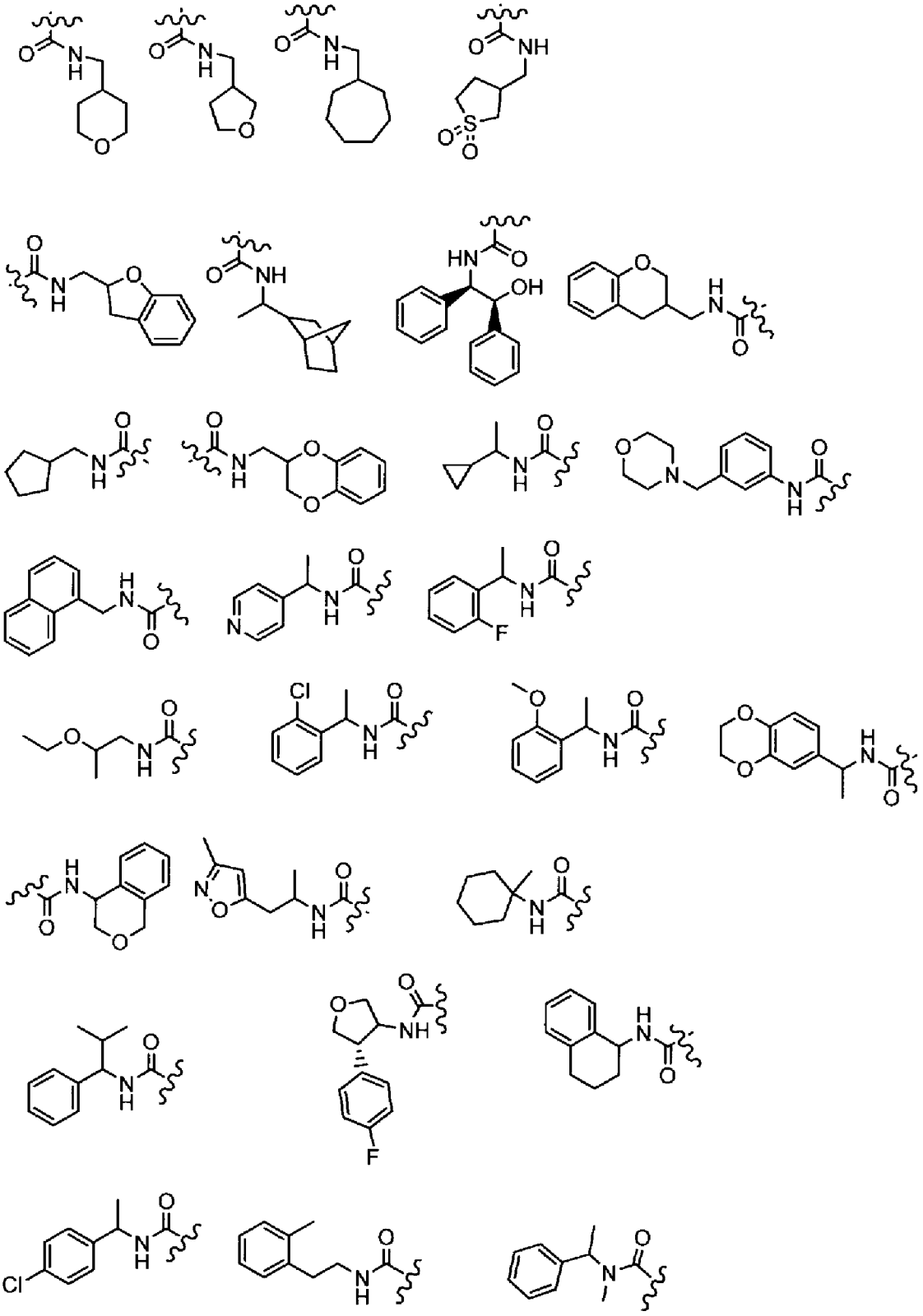
22. The compound of any one of claims 1-12 wherein R^c and R^d are taken together with the nitrogen to which they are attached to form a heterocyclyl that is optionally substituted with one or more groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^v)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from C_{1-6}alkyl , carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^h)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, which C_{1-6}alkyl , carbocyclyl, and heterocyclyl are optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

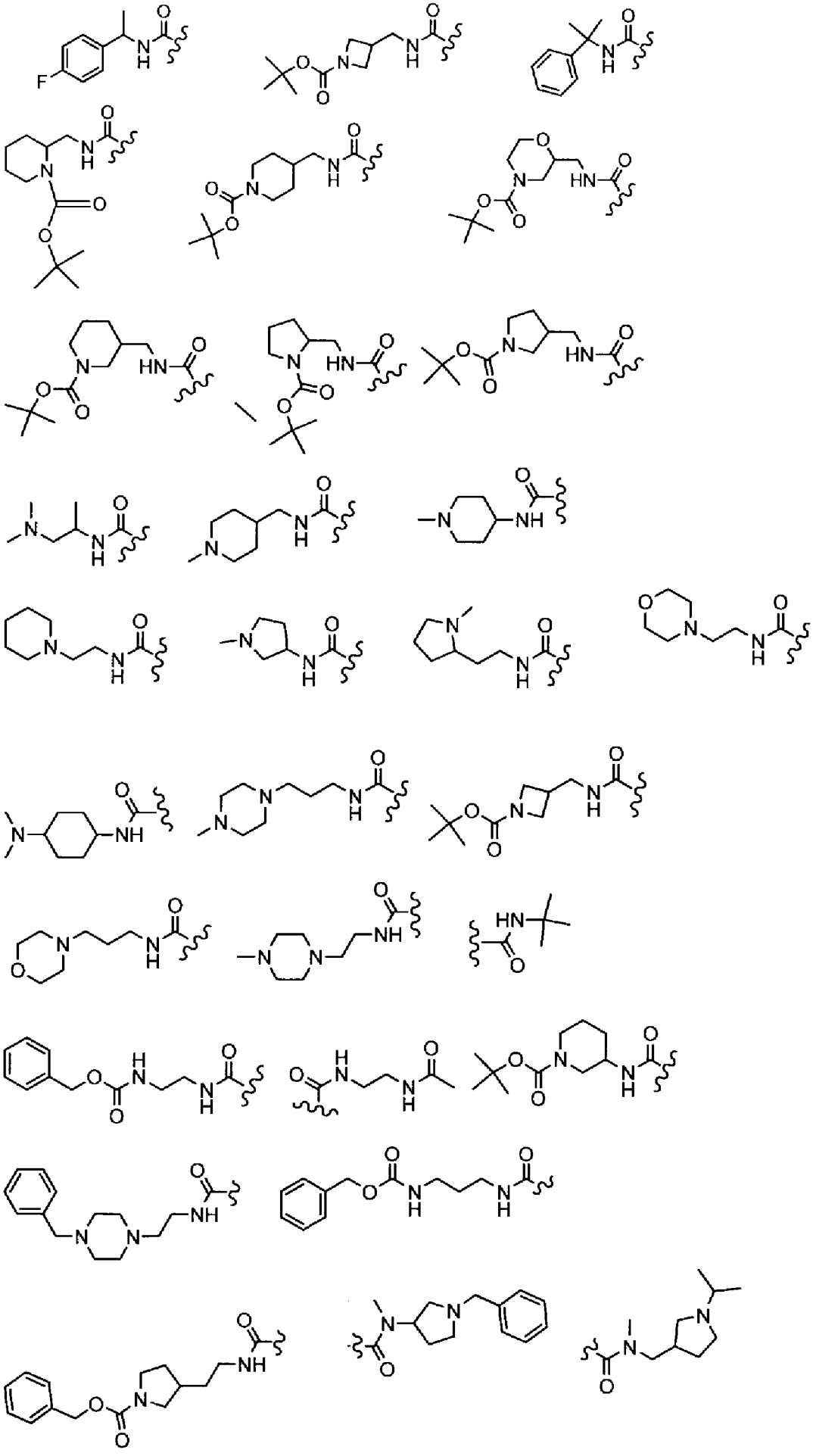
23. The compound of any one of claims 1-12 wherein R^c and R^d are taken together with the nitrogen to which they are attached to form a 5-6 membered monocyclic heterocyclyl or a 8-12 membered bicyclic heterocyclyl, wherein the monocyclic or bicyclic heterocyclyl is optionally substituted with one or more groups independently selected from oxo, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, heterocyclyl, -F, -Cl, -Br, -I, -NO_2, -$N(R^v)_2$, -CN, -C(O)-$N(R^h)_2$, -S(O)-$N(R^h)_2$, -$S(O)_2$-$N(R^h)_2$, -O-R^h, -S-R^h, -O-C(O)-R^h, -O-C(O)-O-R^h, -C(O)-R^h, -C(O)-O-R^h, -S(O)-R^h, -$S(O)_2$-R^h, -O-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-OR^h, -$N(R^h)$-C(O)-$N(R^h)_2$, -$N(R^h)$-C(O)-R^h, -$N(R^h)$-S(O)-R^h, -$N(R^h)$-$S(O)_2$-R^h, -$N(R^h)$-S(O)-$N(R^h)_2$, and -$N(R^h)$-$S(O)_2$-$N(R^h)_2$, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, carbocyclyl, and heterocyclyl is optionally substituted with one or more groups independently selected from C_{1-6}alkyl , carbocyclyl, heterocyclyl, -F, -Cl, -

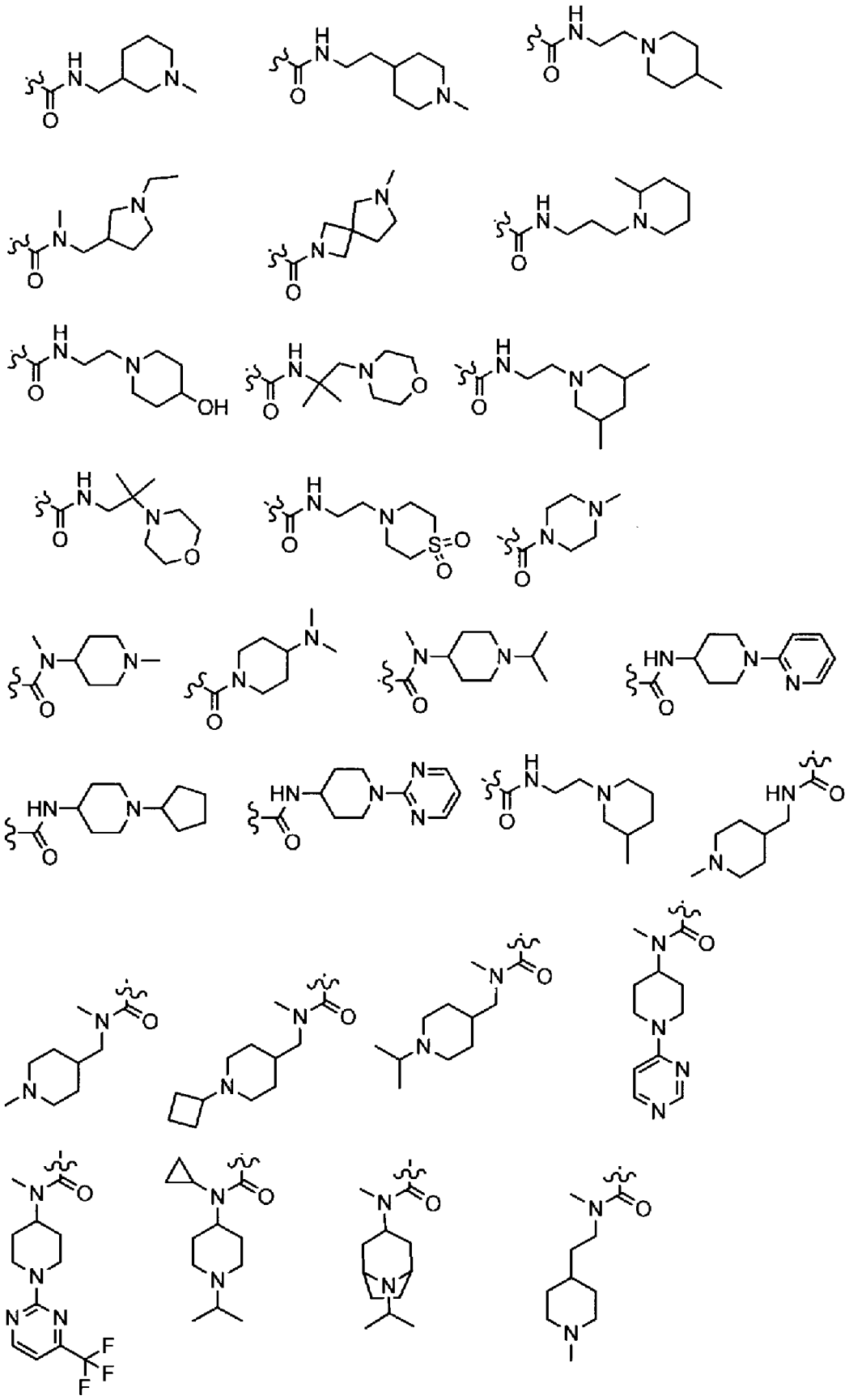
Br, -I, $-NO_2$, $-N(R^h)_2$, -CN, $-C(O)-N(R^h)_2$, $-S(O)-N(R^h)_2$, $-S(O)_2-N(R^h)_2$, $-O-R^h$, $-S-R^h$, $-O-C(O)-R^h$, $-O-C(O)-O-R^h$, $-C(O)-R^h$, $-C(O)-O-R^h$, $-S(O)-R^h$, $-S(O)_2-R^h$, $-O-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-OR^h$, $-N(R^h)-C(O)-N(R^h)_2$, $-N(R^h)-C(O)-R^h$, $-N(R^h)-S(O)-R^h$, $-N(R^h)-S(O)_2-R^h$, $-N(R^h)-S(O)-N(R^h)_2$, and $-N(R^h)-S(O)_2-N(R^h)_2$, which C_{1-6}alkyl , carbocyclyl, and heterocyclyl are optionally substituted with one or more groups independently selected from halo and C_{1-6}alkyl.

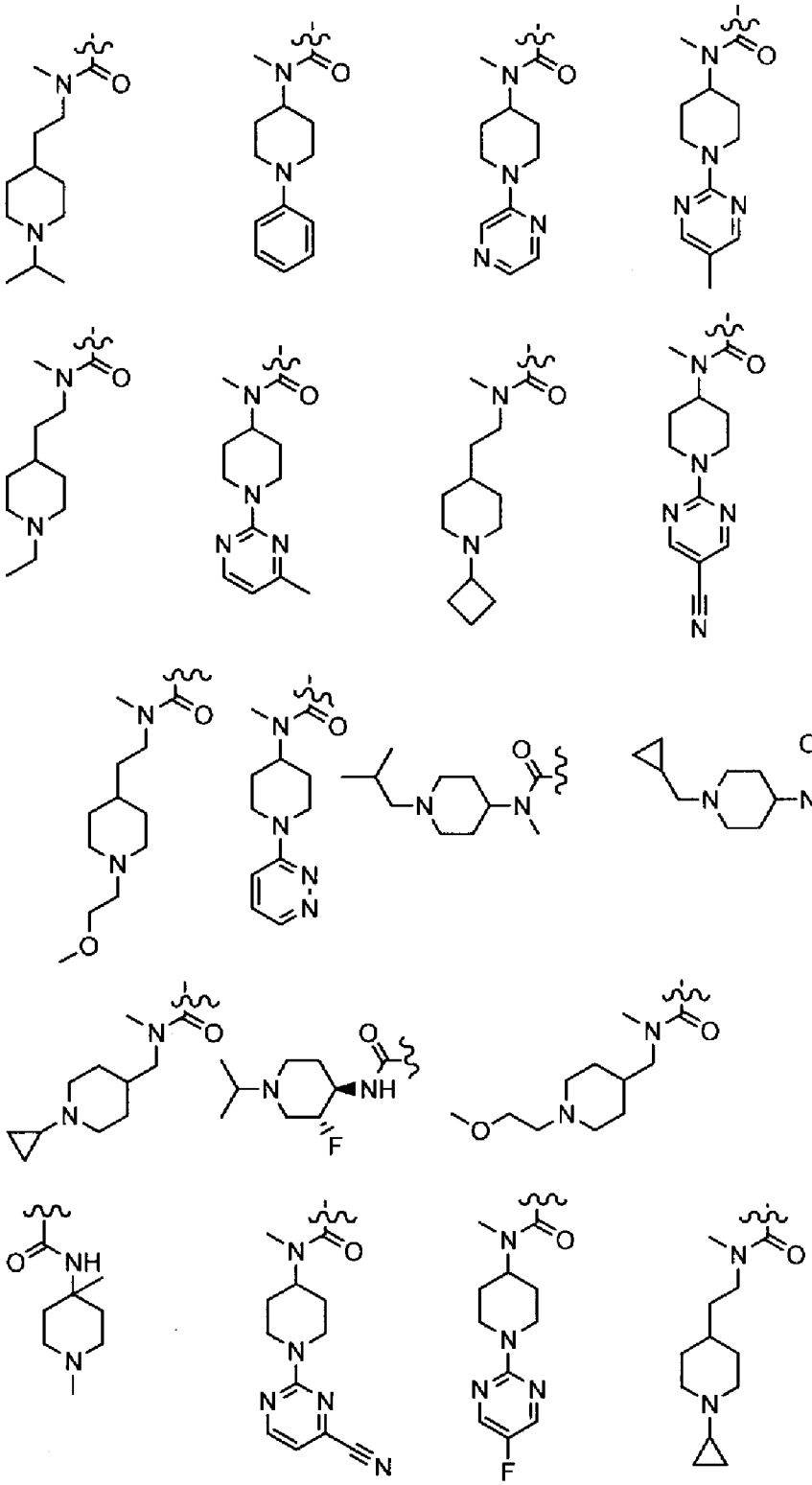
24. The compound of any one of claims 1-12 wherein $-C(=O)NR^cR^d$ is selected from:

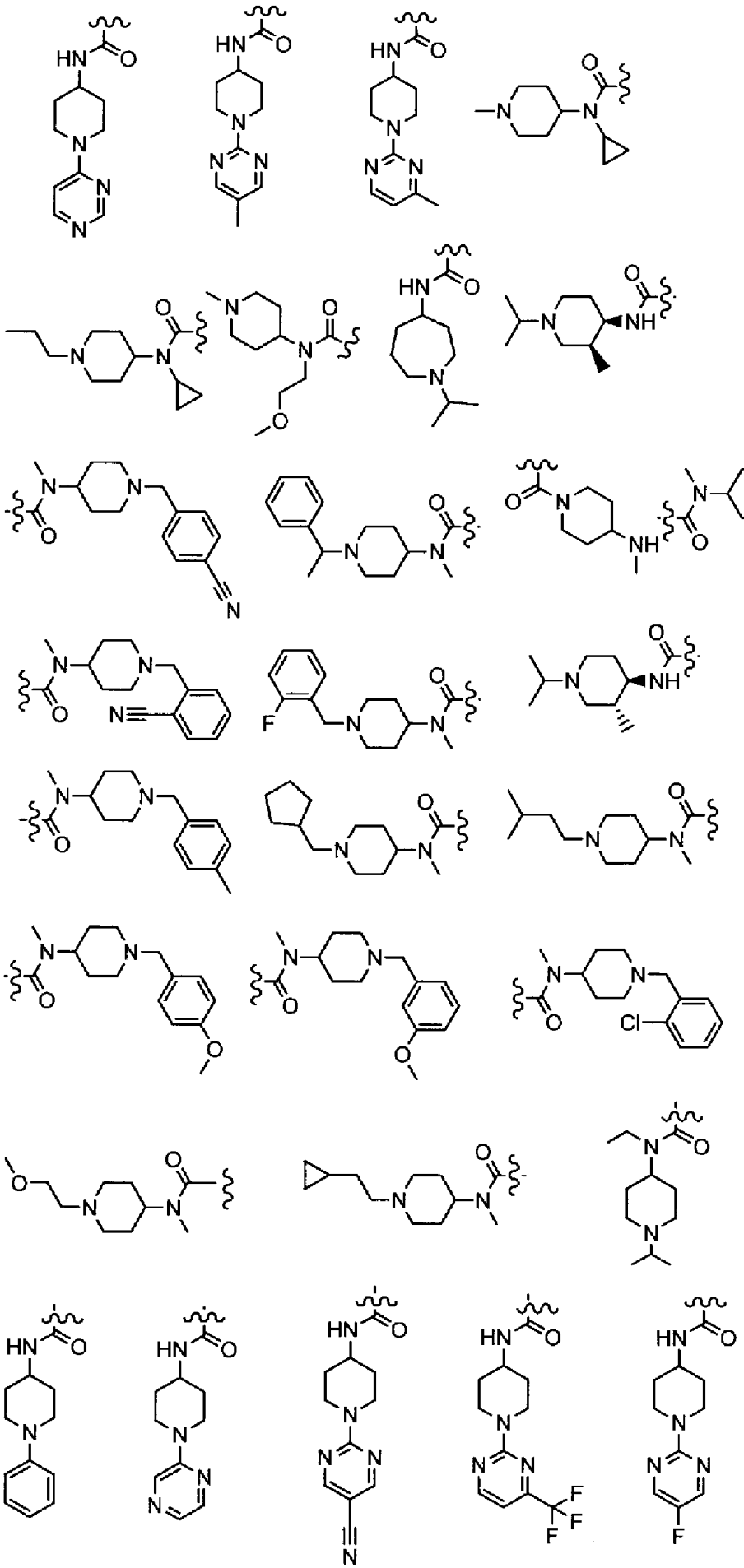


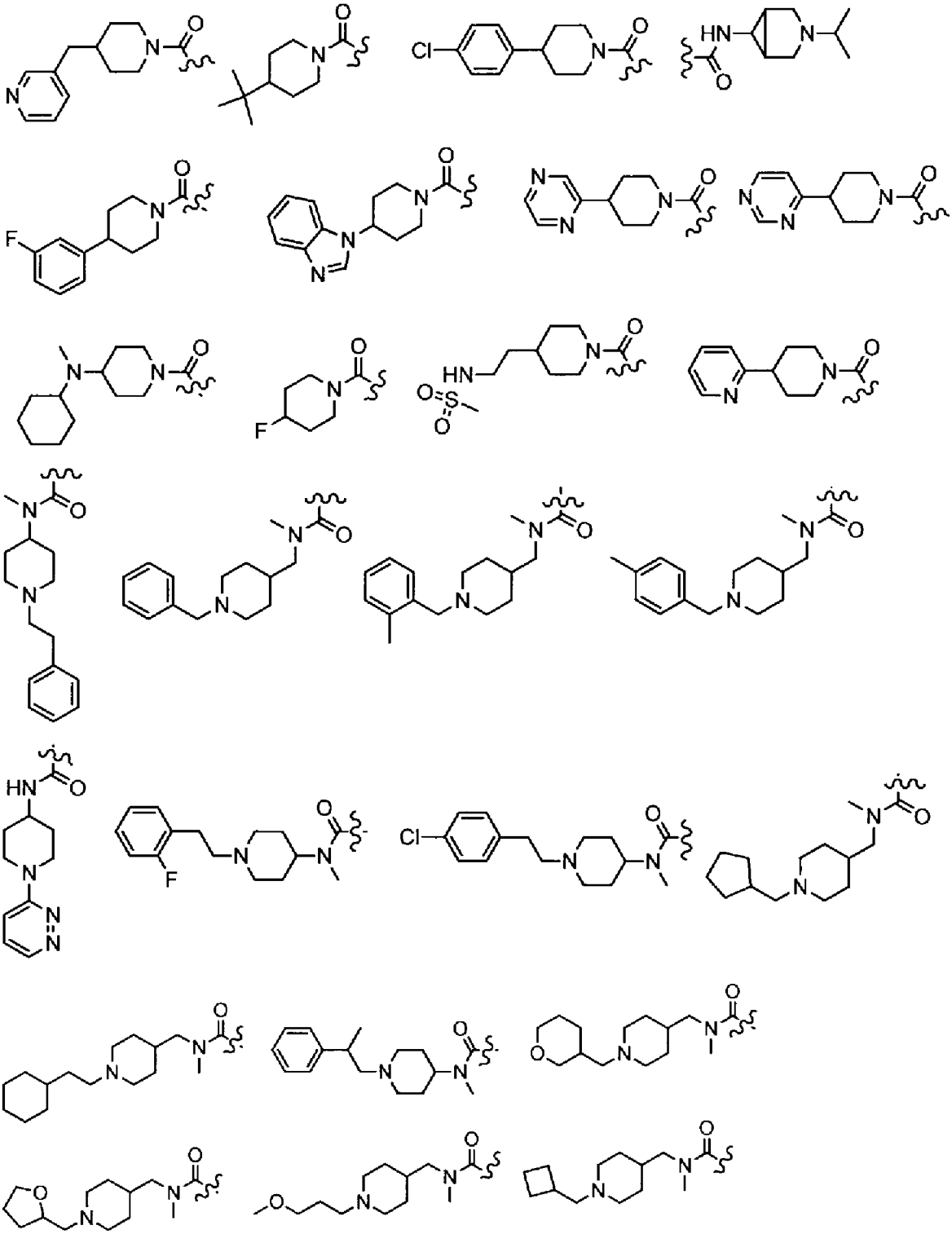


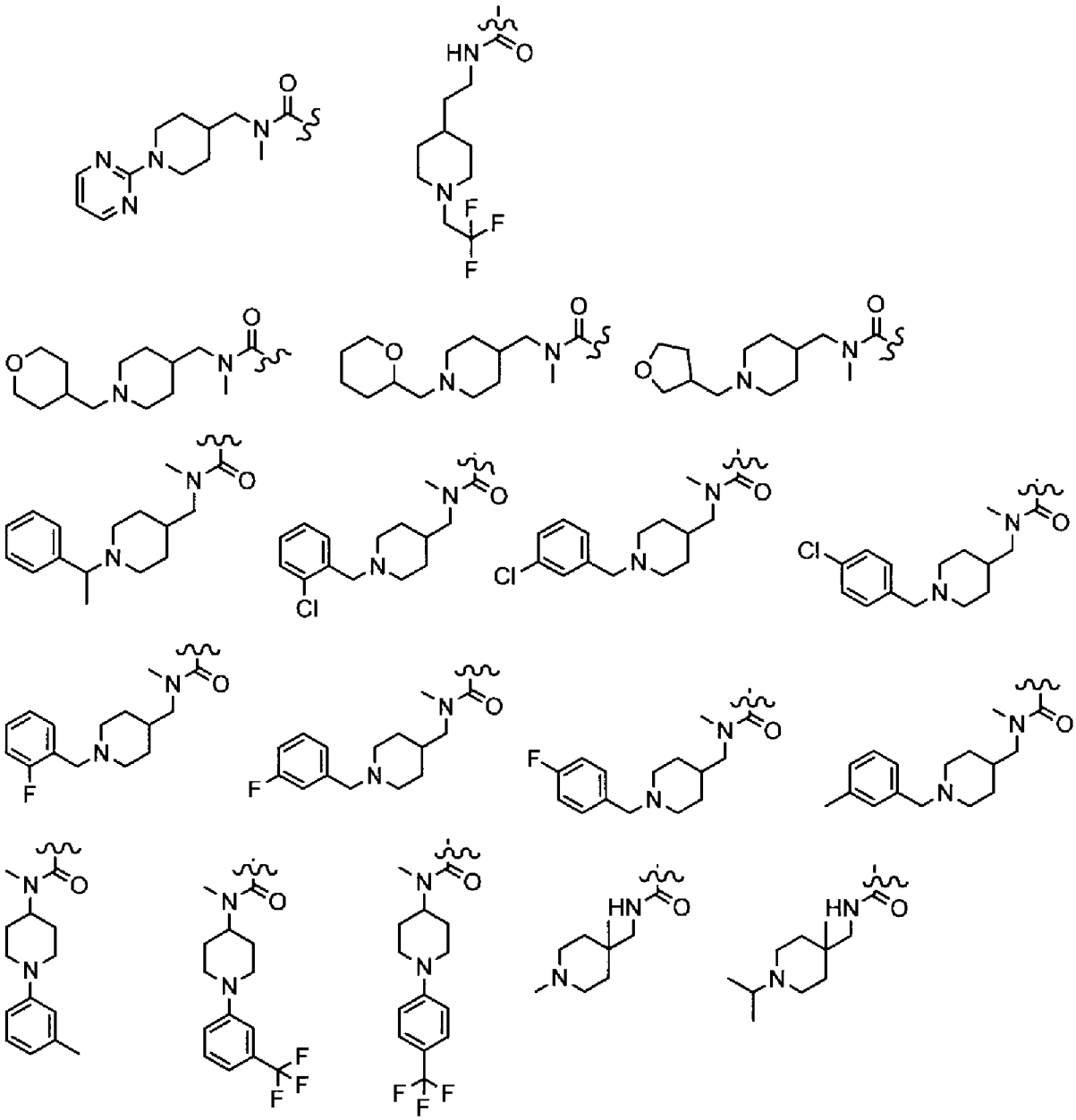












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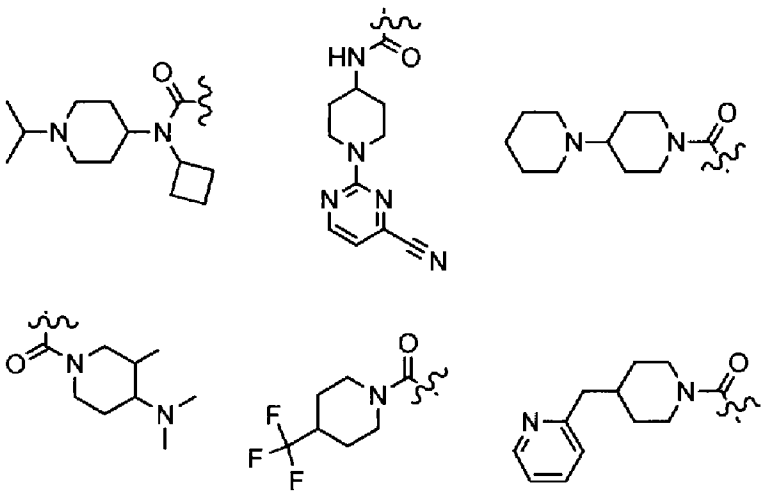

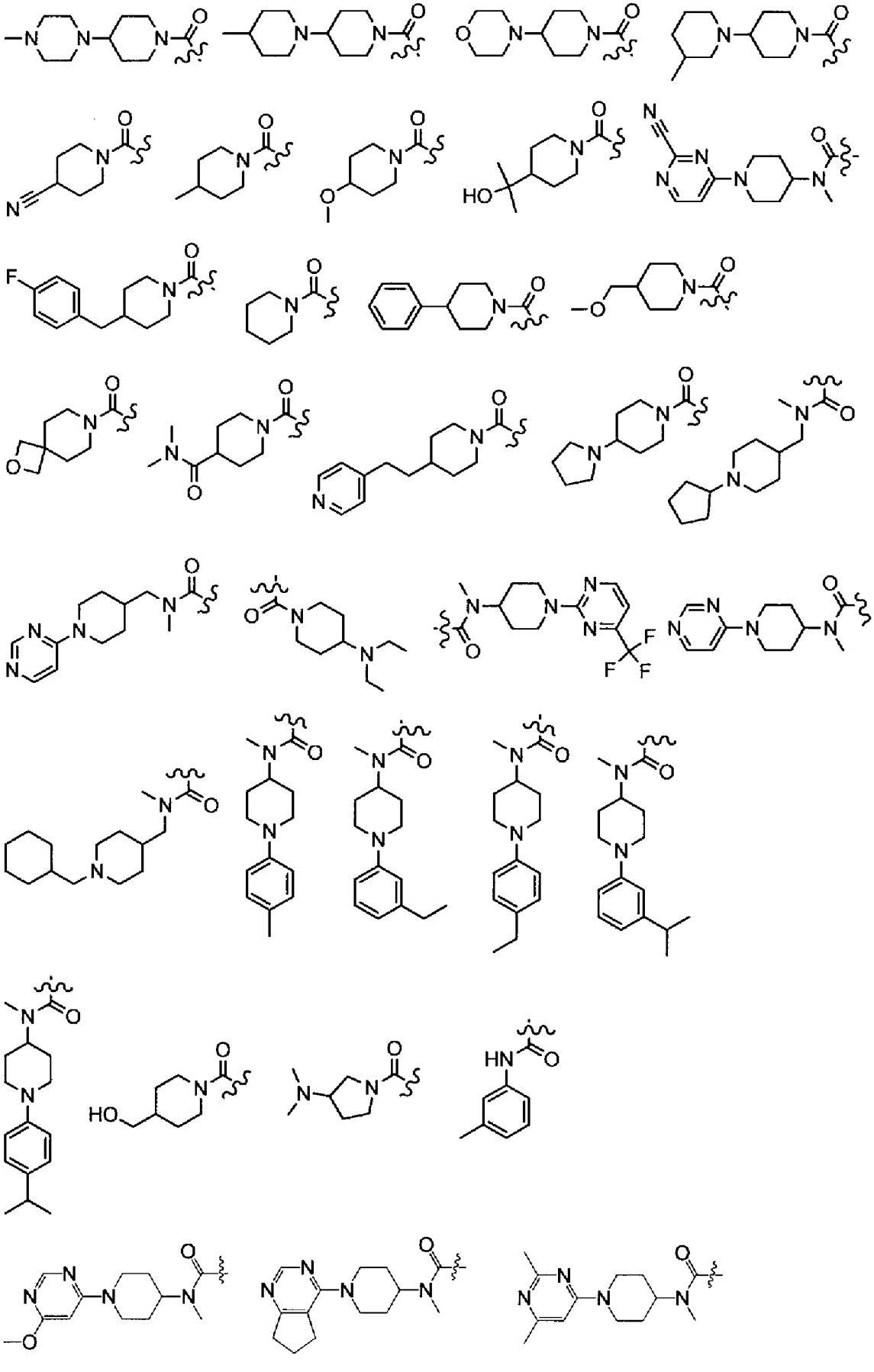

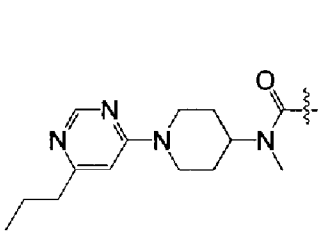
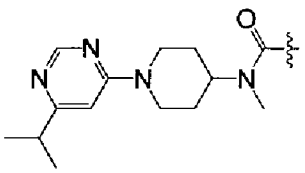
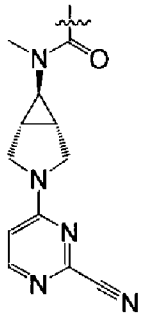
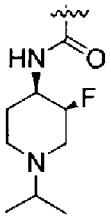
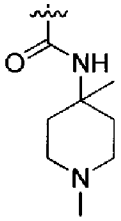
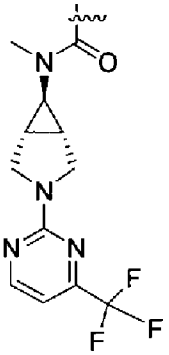
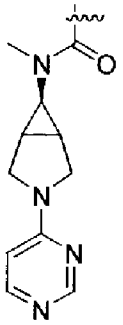
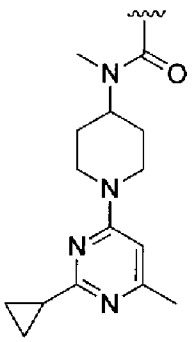
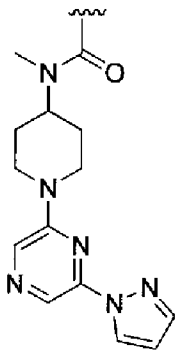
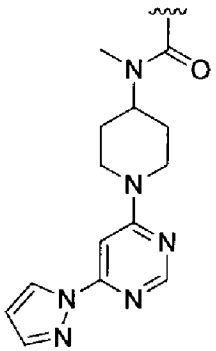
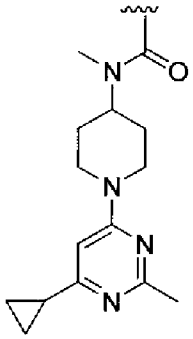
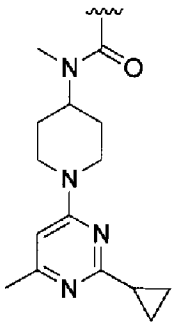
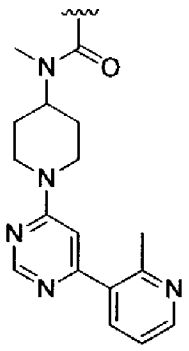
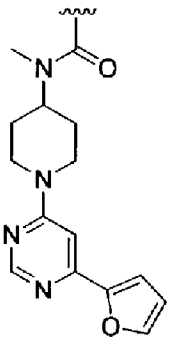
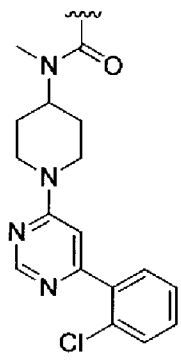

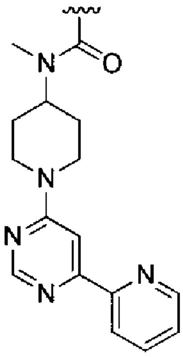
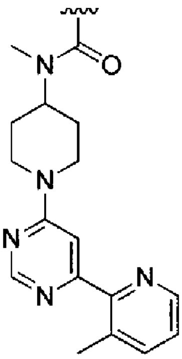
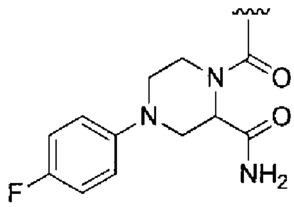
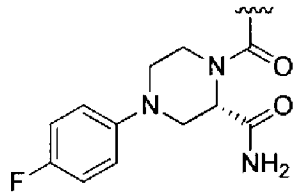
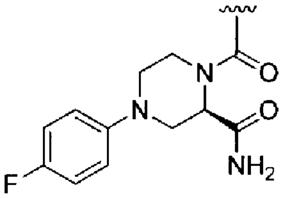
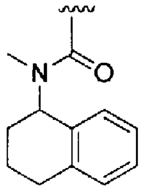
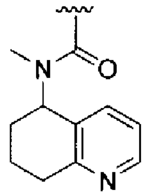
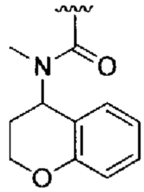
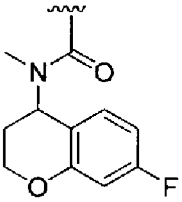
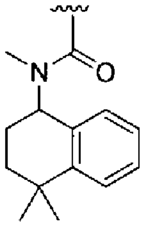
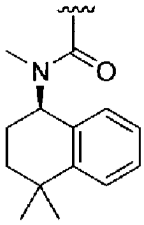
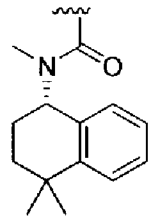
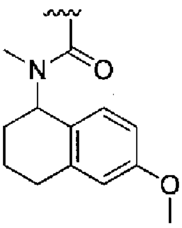
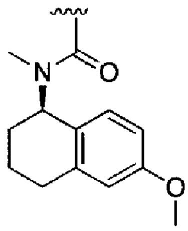
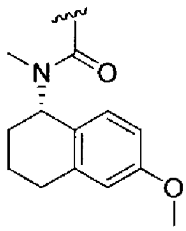
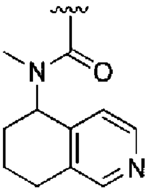
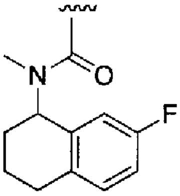
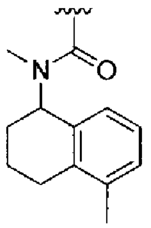
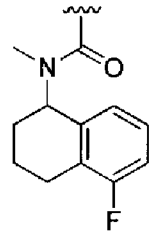
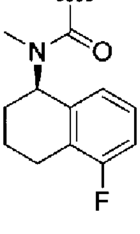
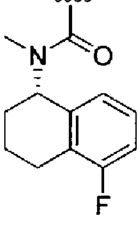
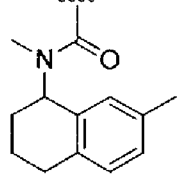
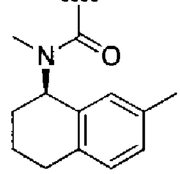
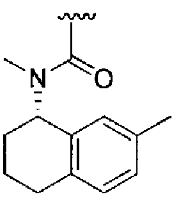
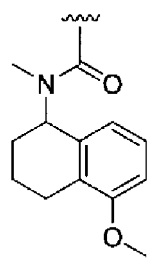
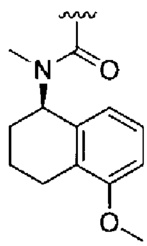
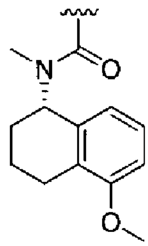

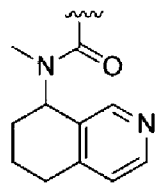
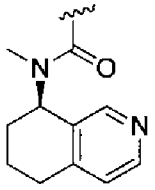
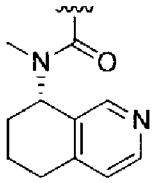
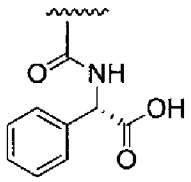
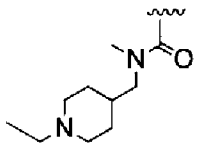
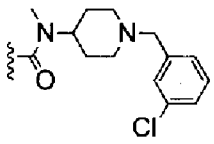
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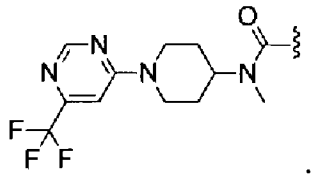

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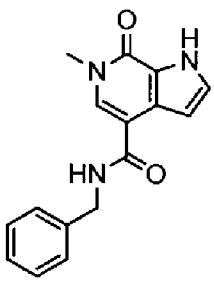
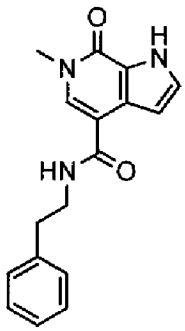
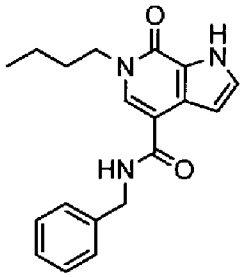
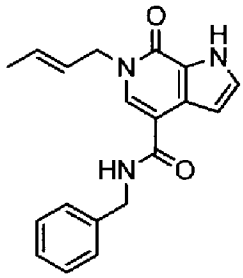
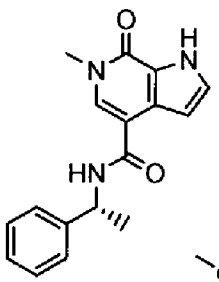
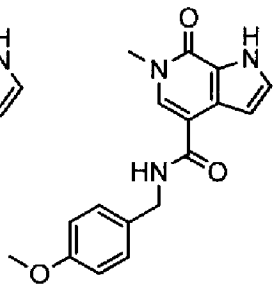
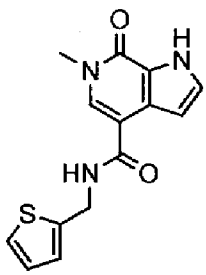
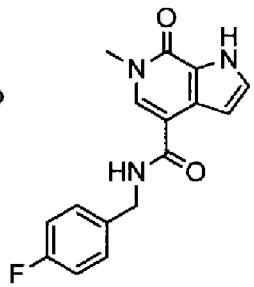
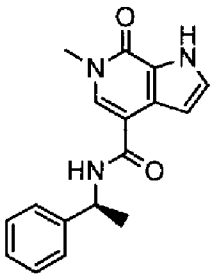
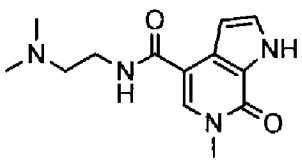
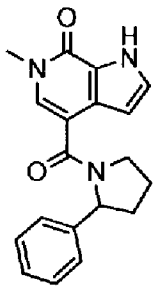
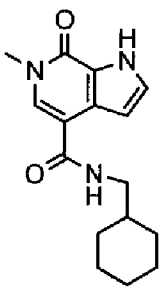
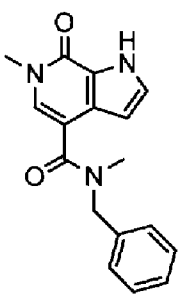
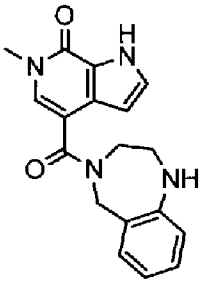
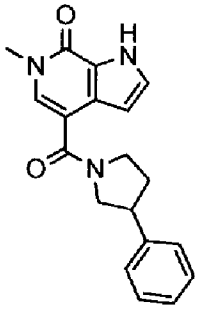
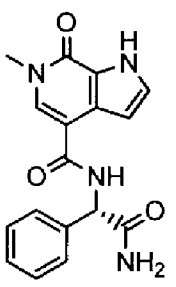

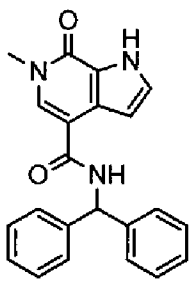
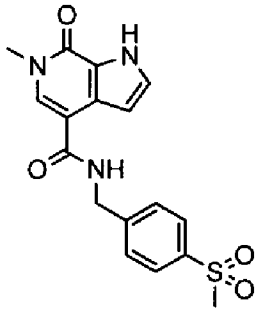
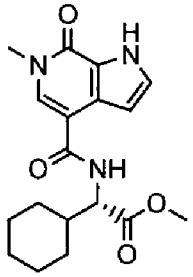
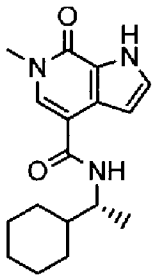
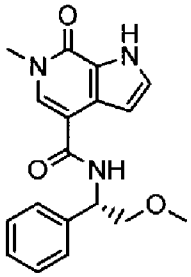
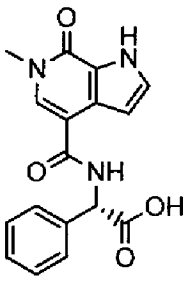
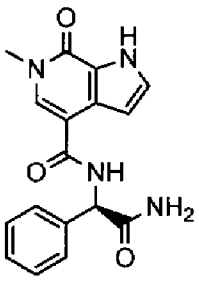
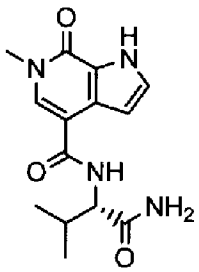
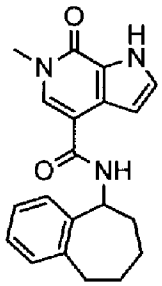
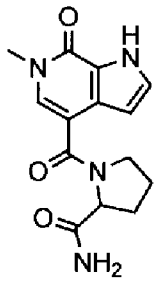
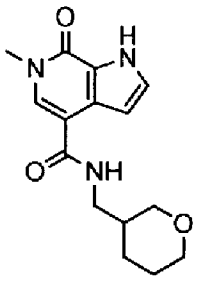
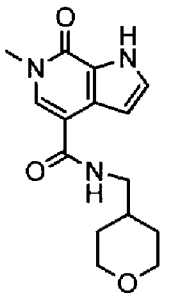
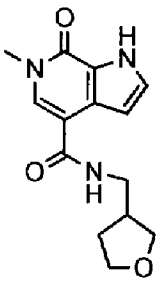
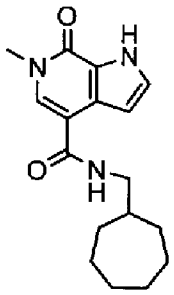
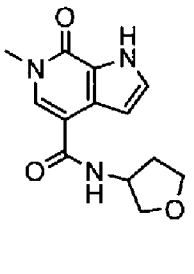
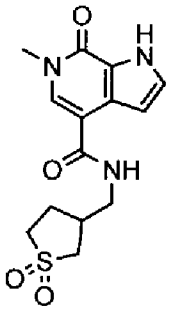
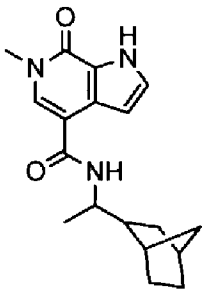
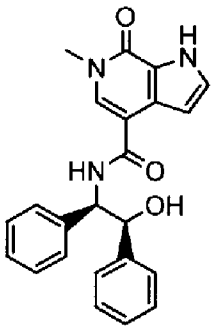
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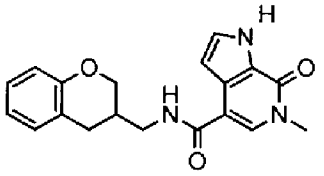
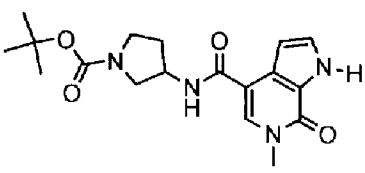
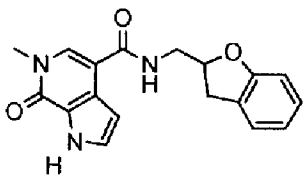

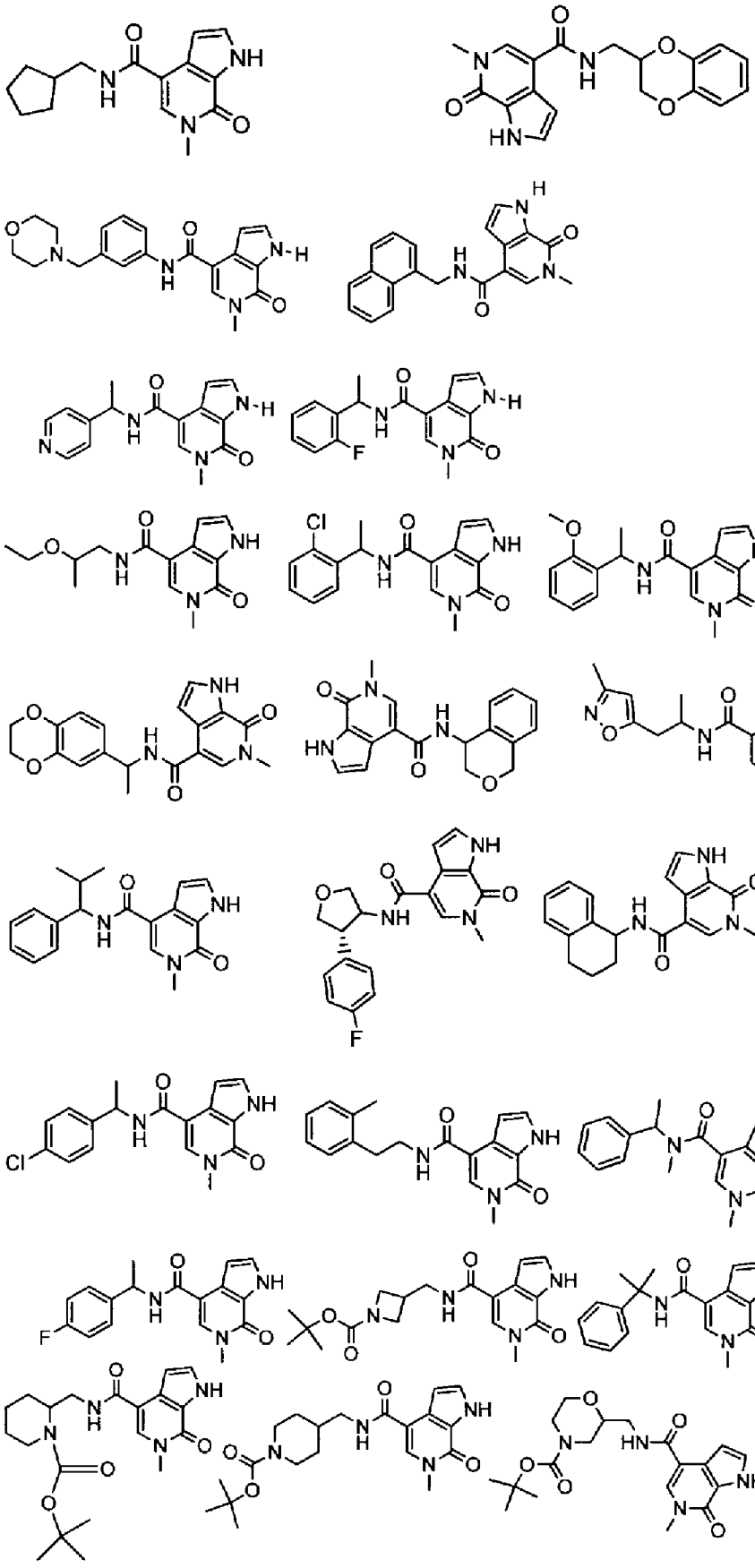

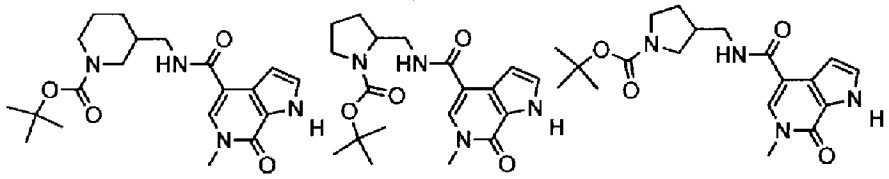

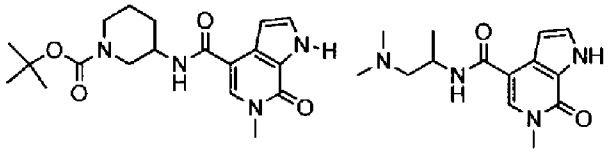

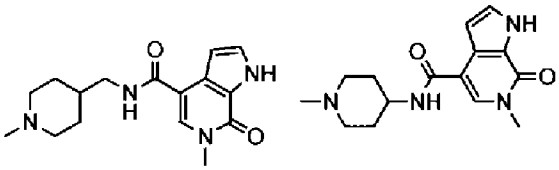

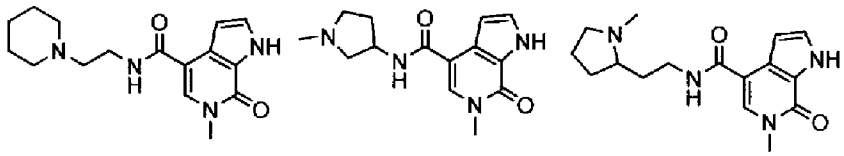

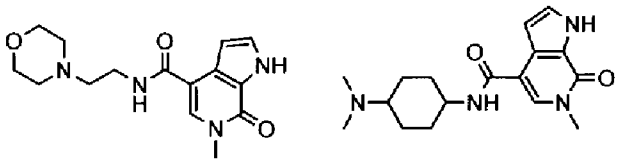

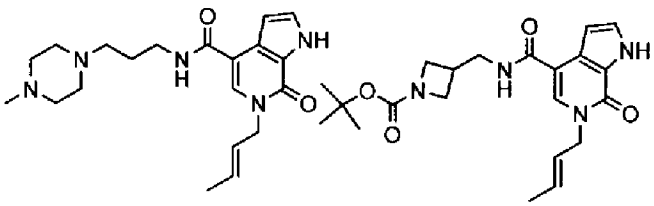

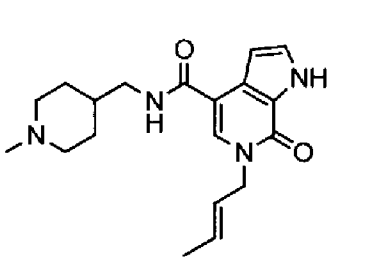

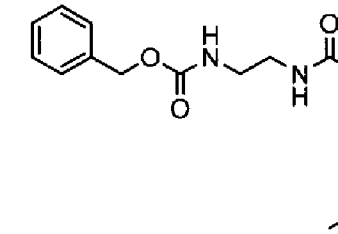

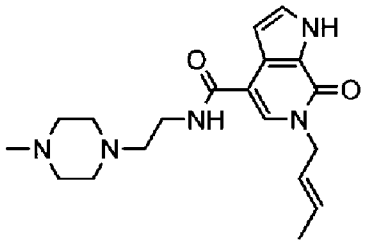

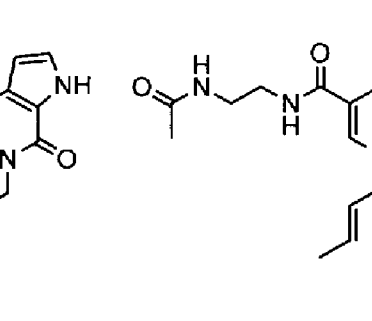

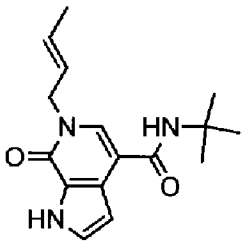

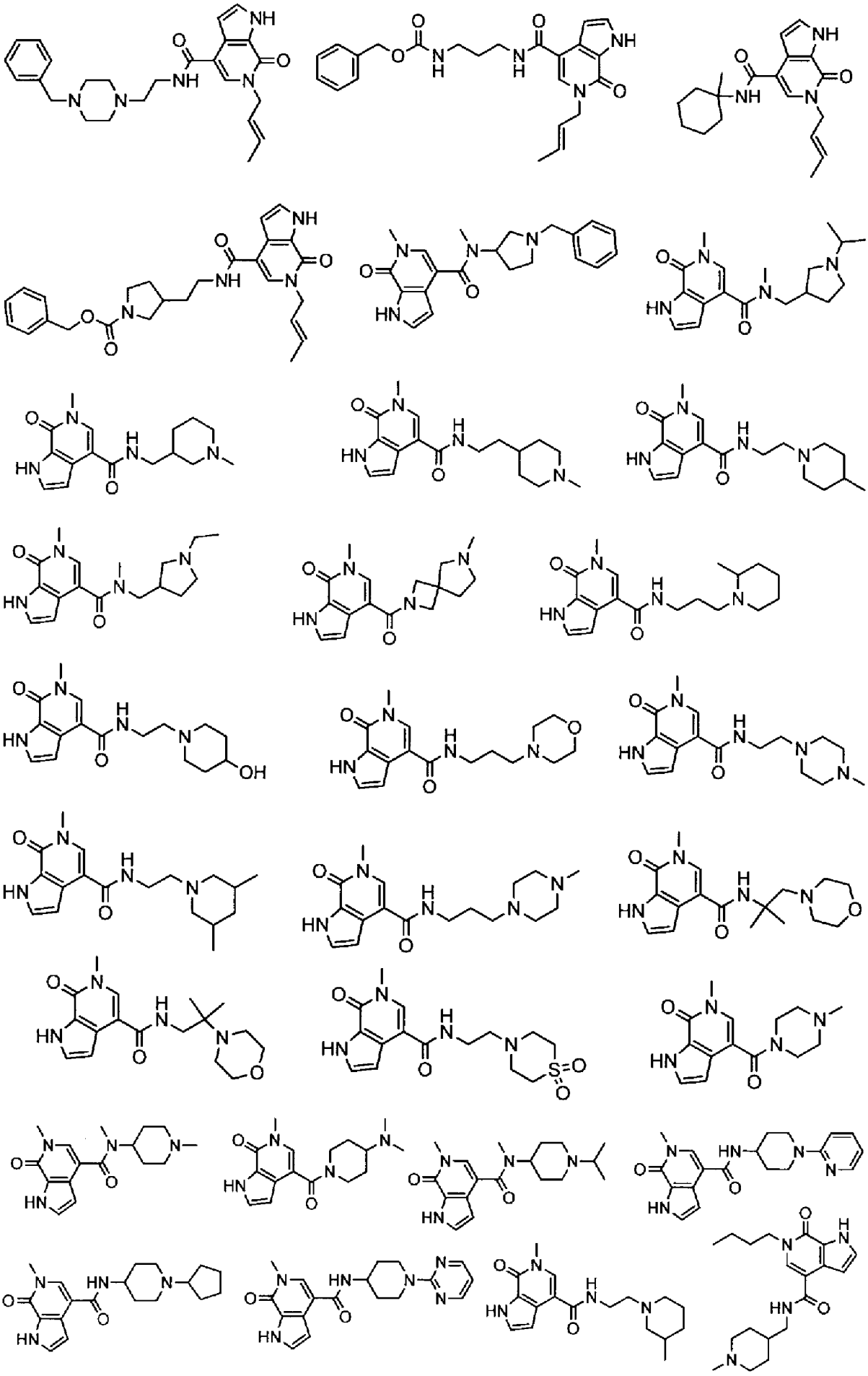

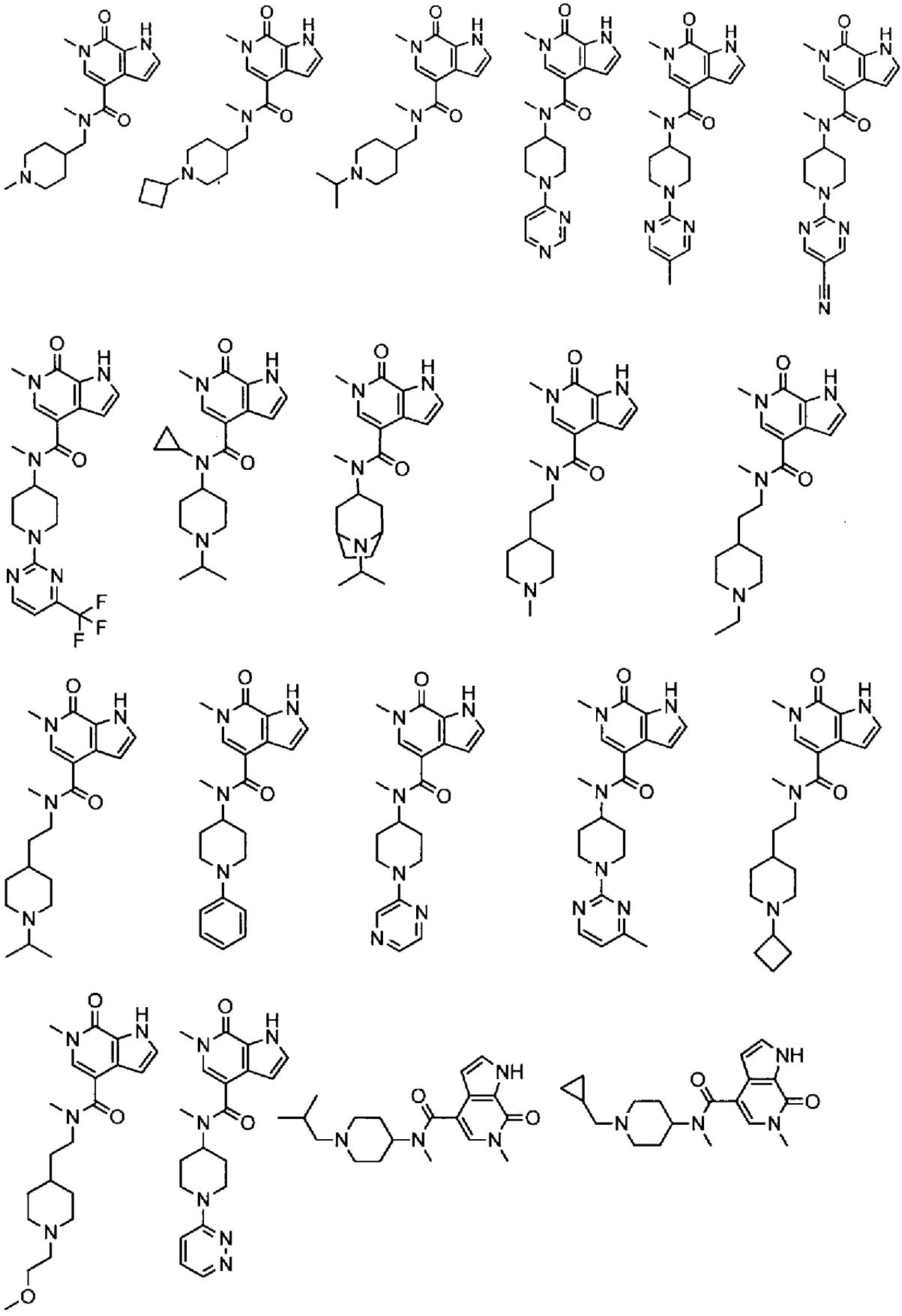

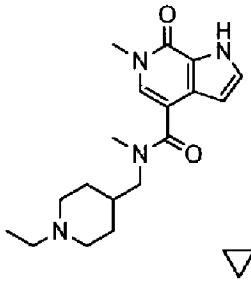
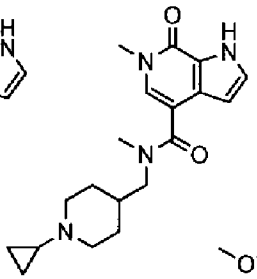
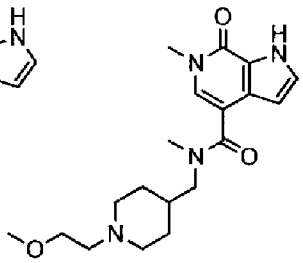
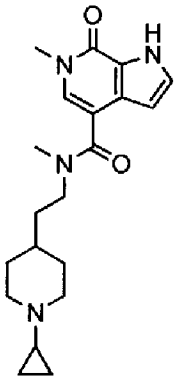
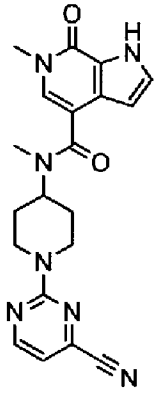
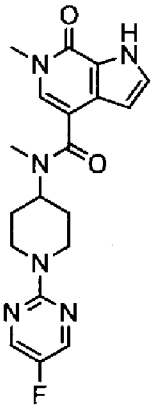
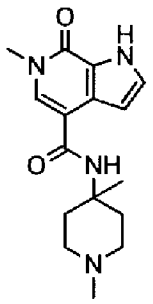
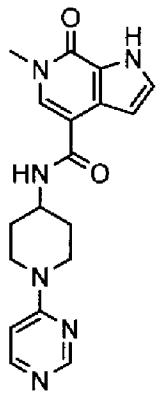
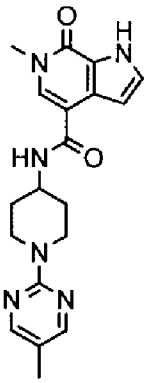
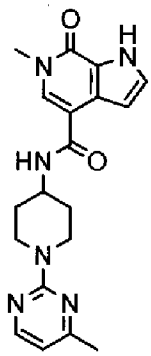
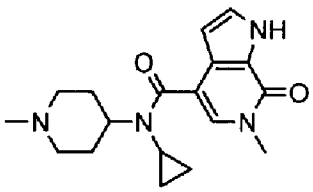
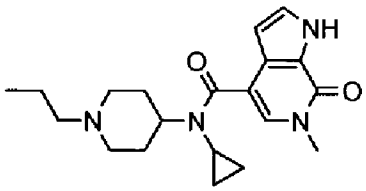
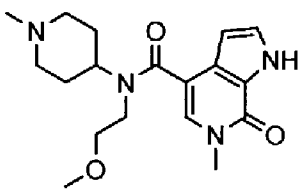
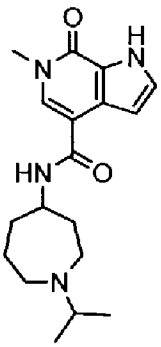
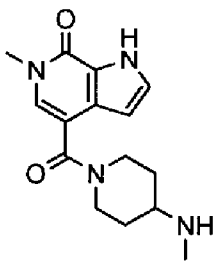
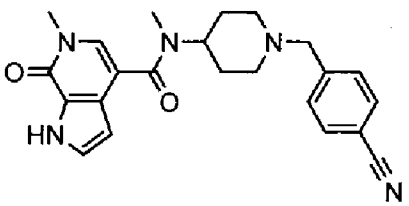
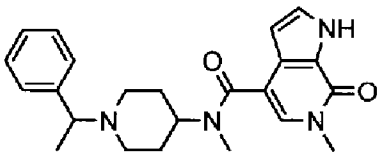
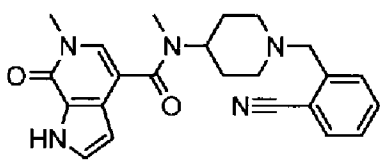
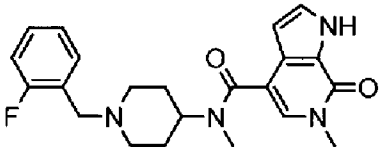
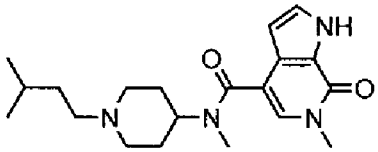

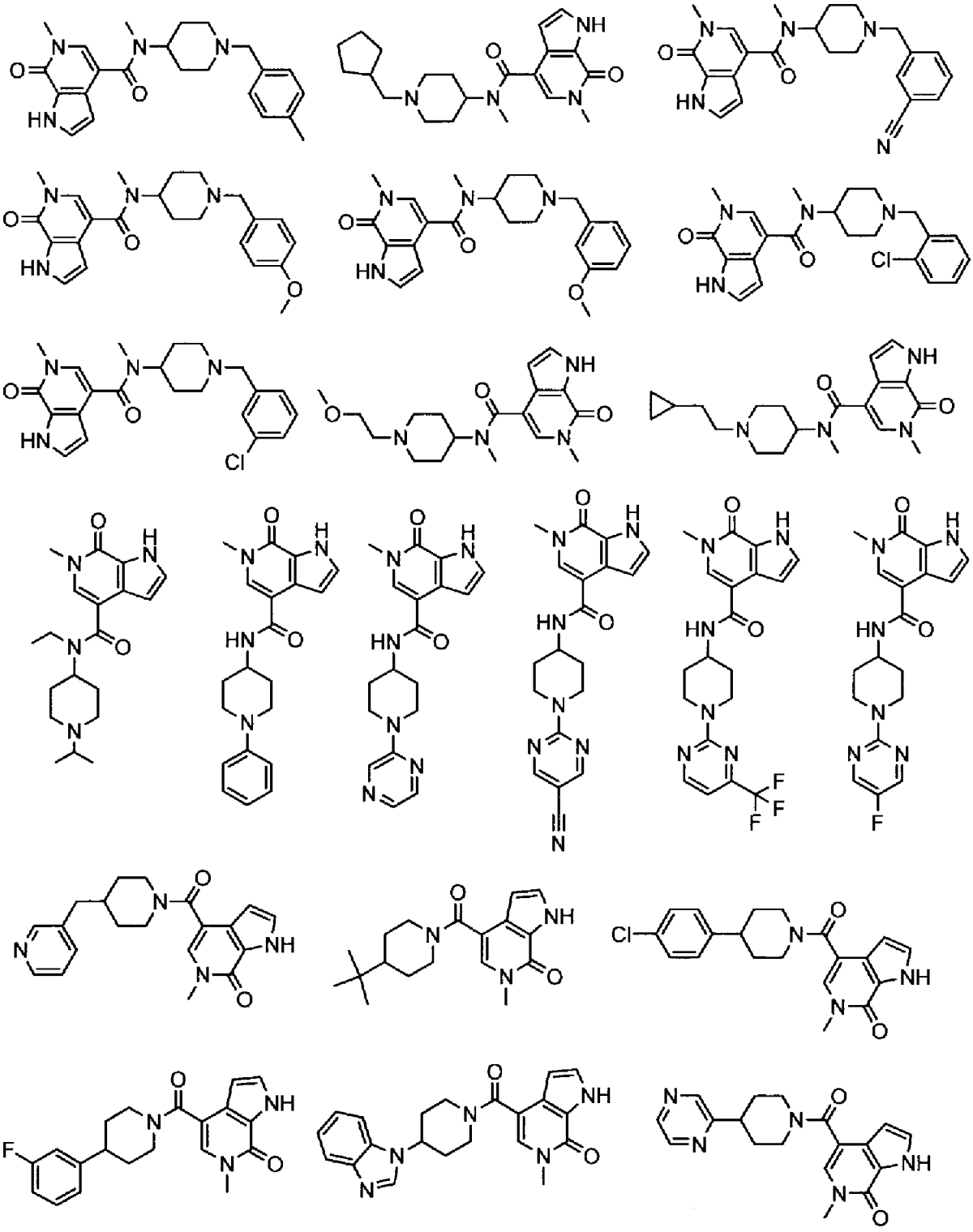

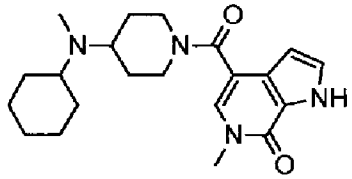
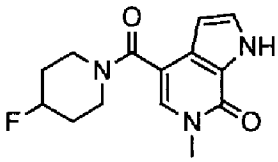
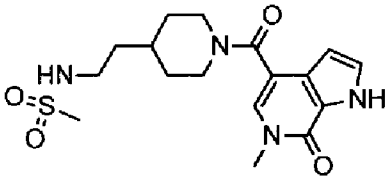
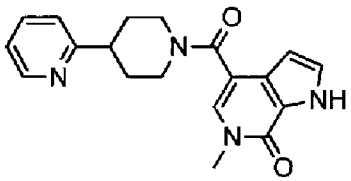
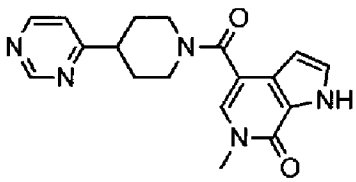
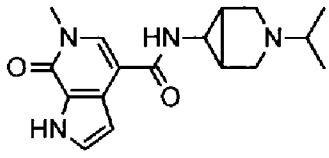
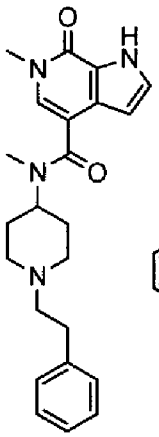
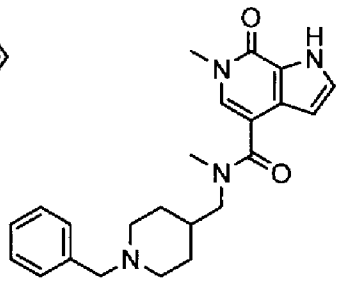
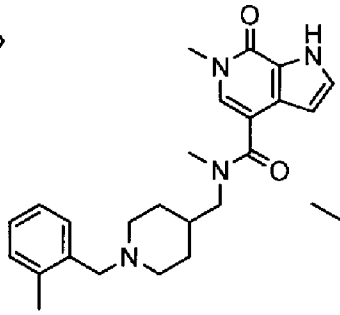
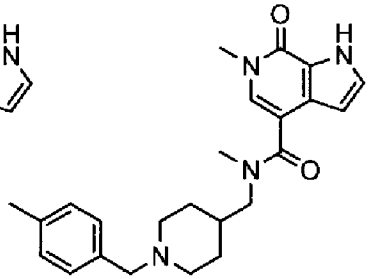
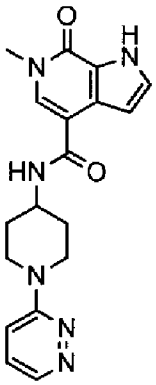
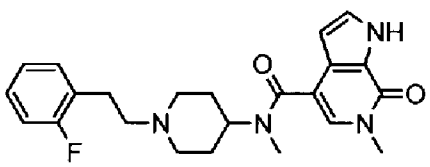
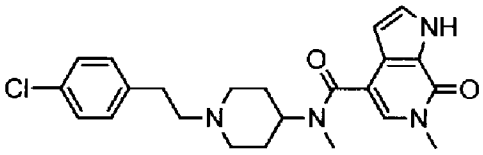
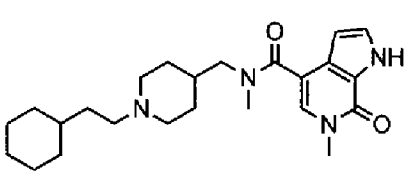
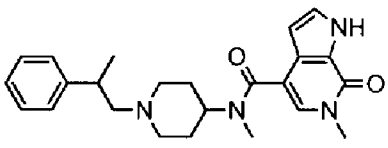
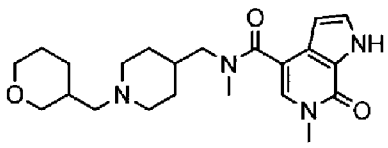
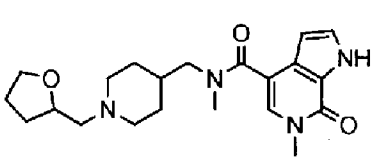
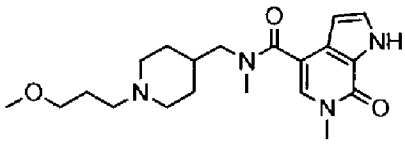
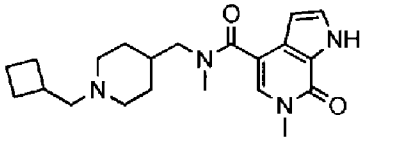

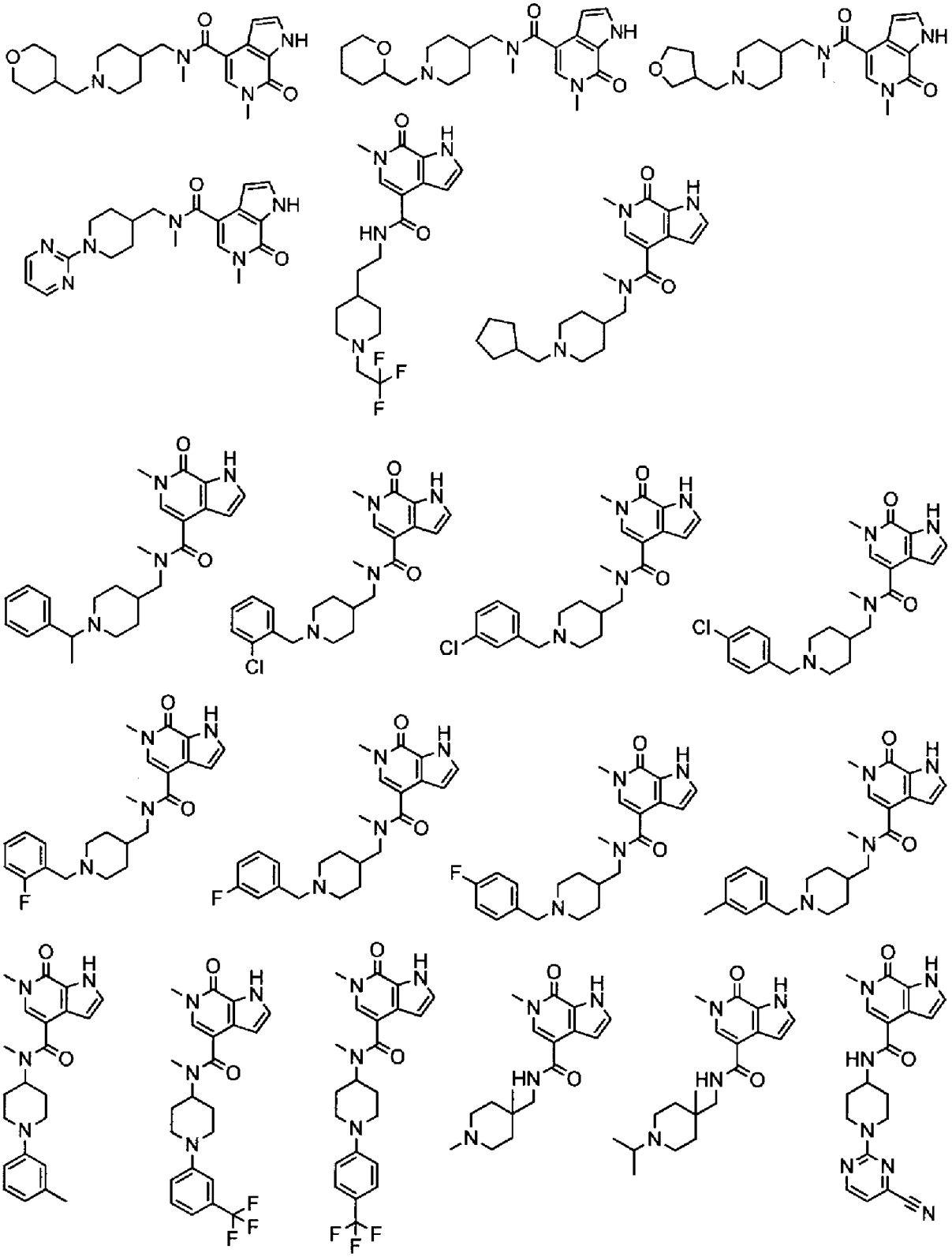

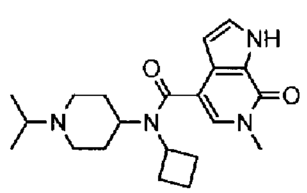
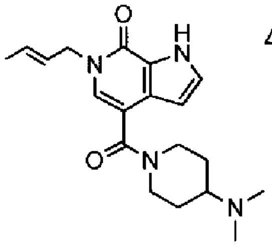
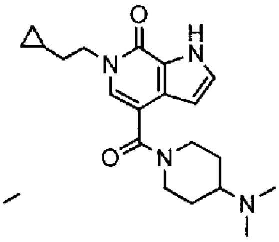
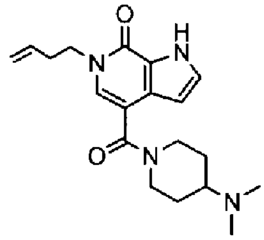
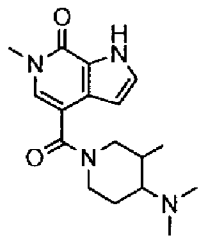
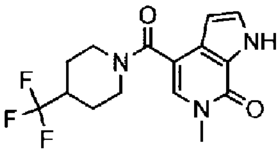
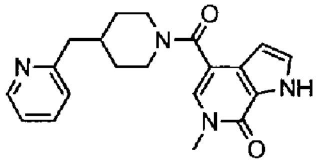
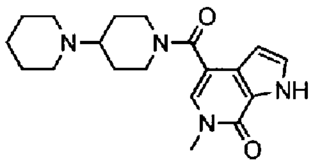
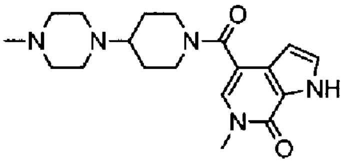
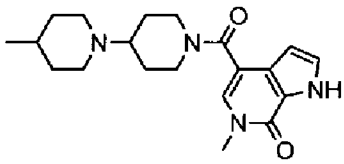
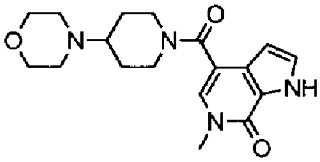
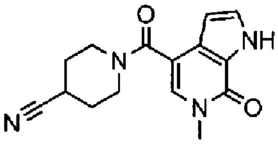
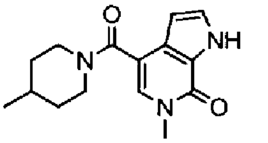
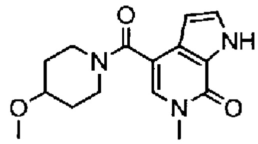
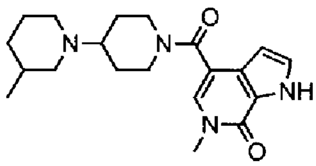
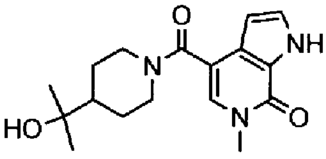
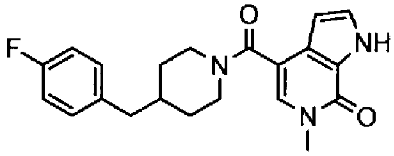
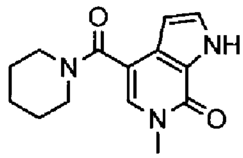
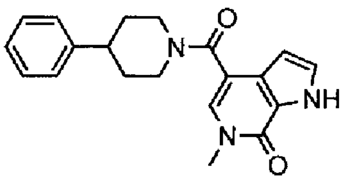
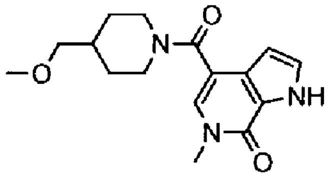
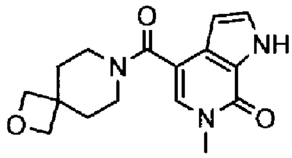

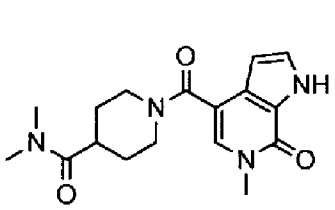
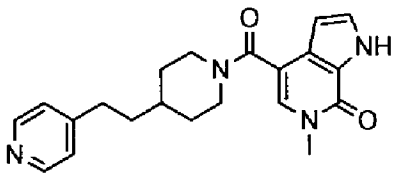
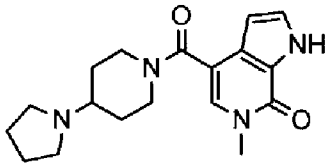
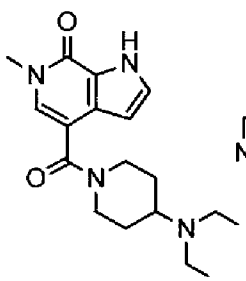
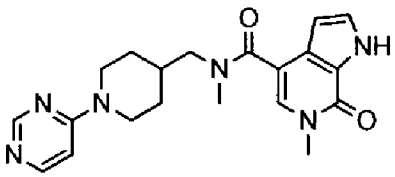
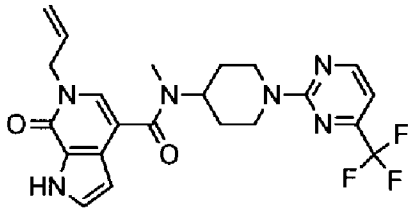
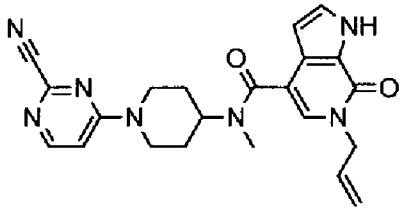
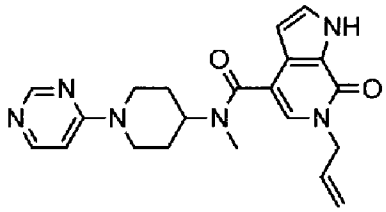
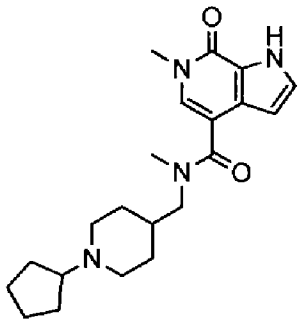
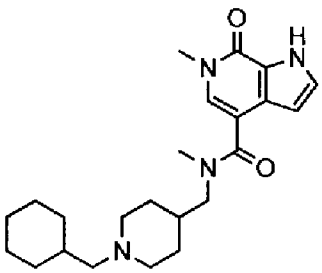
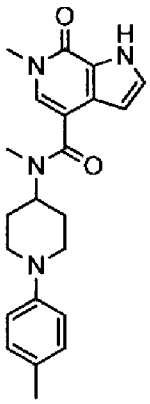
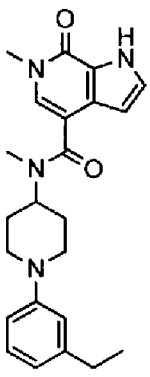
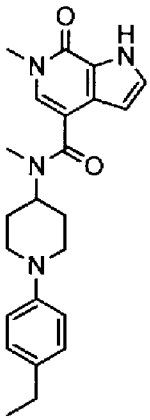
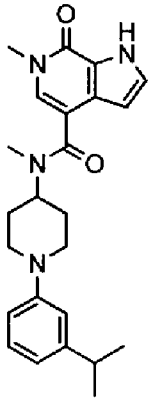
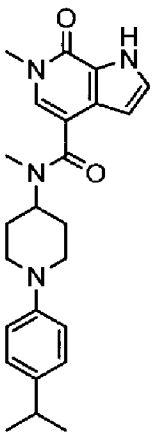
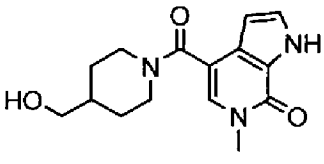
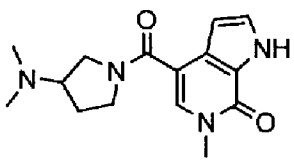
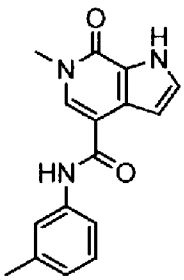

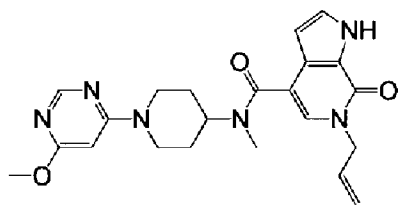
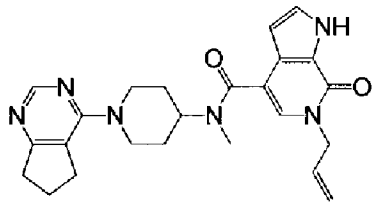
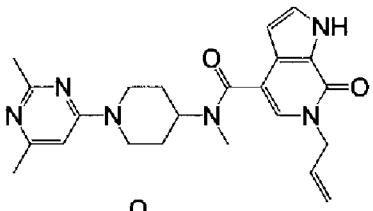
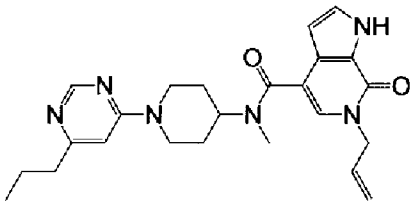
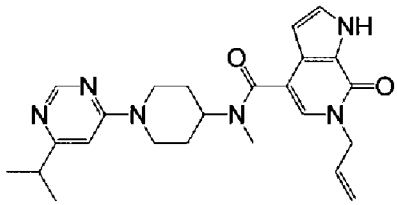
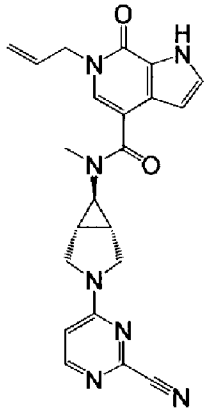
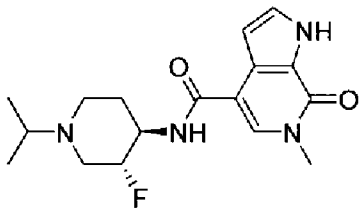
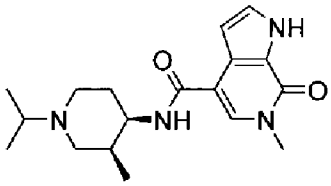
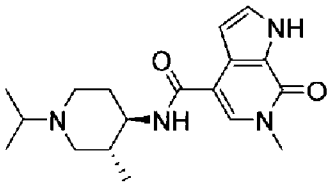
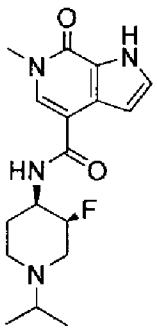
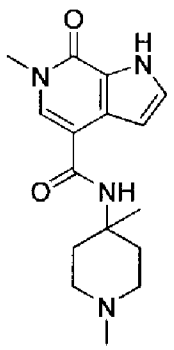
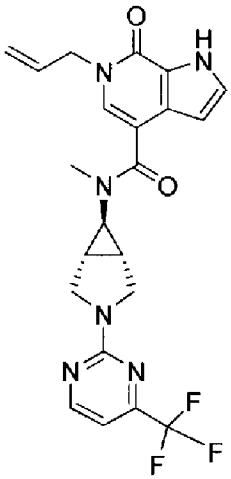
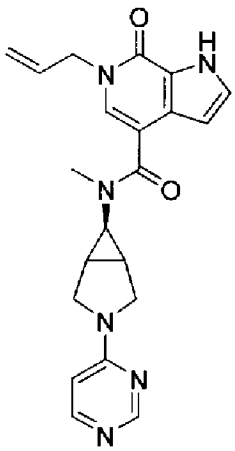
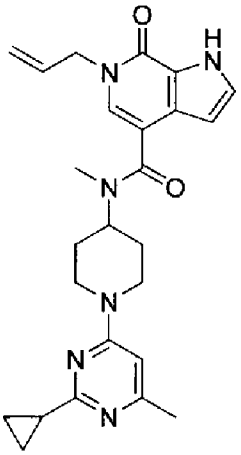
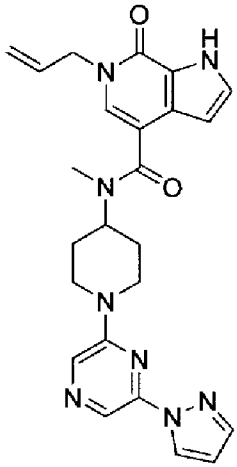
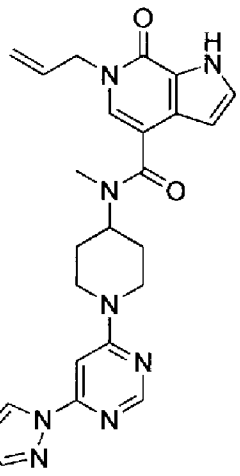

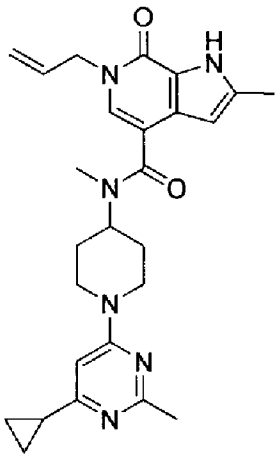
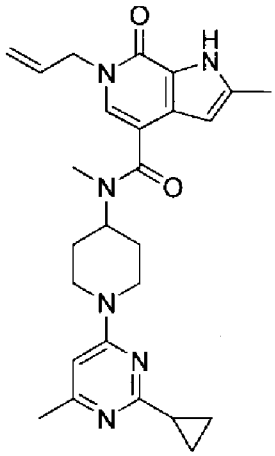
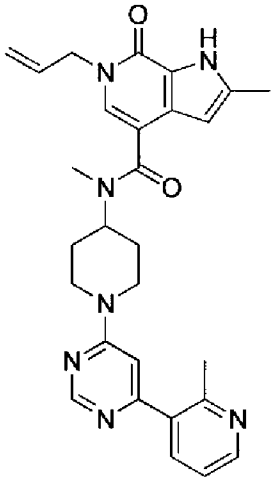
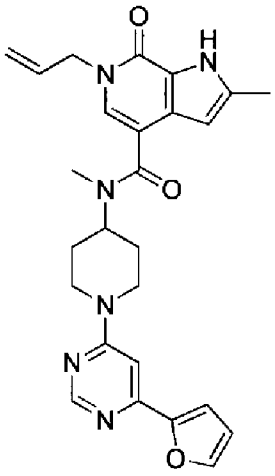
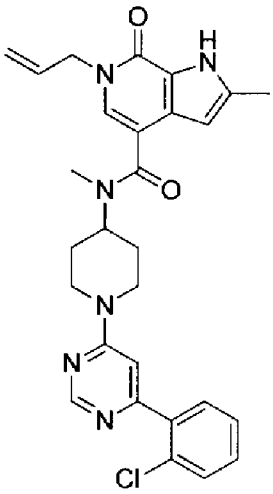
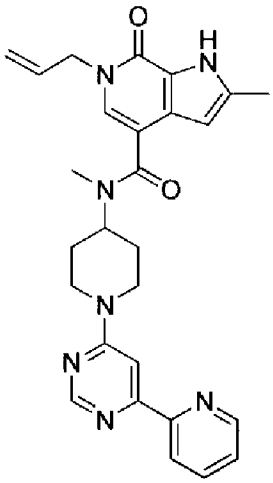
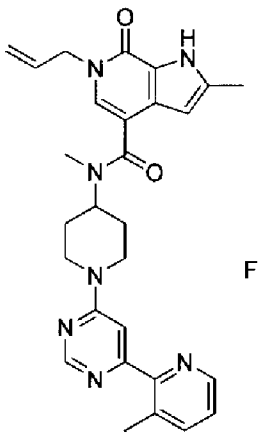
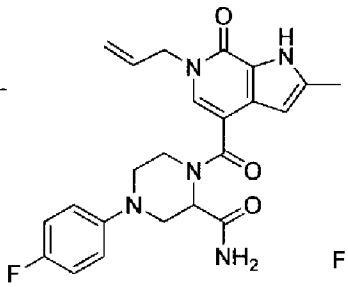
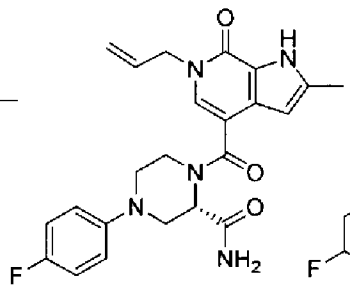
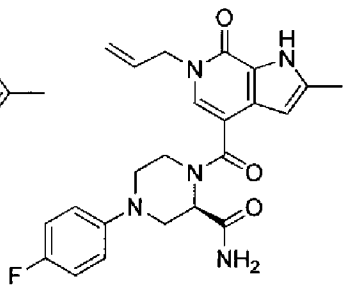
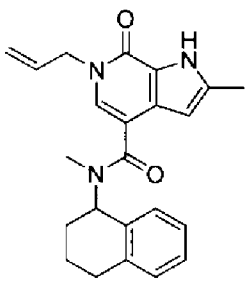
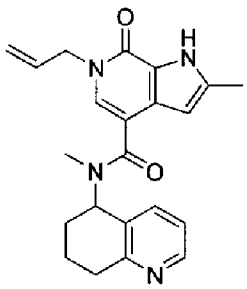
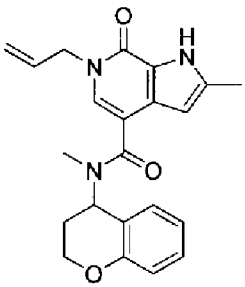
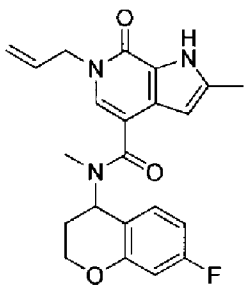

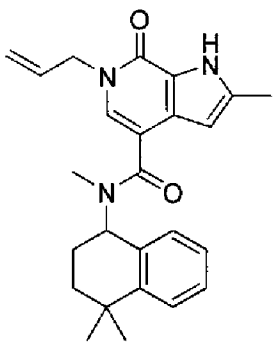
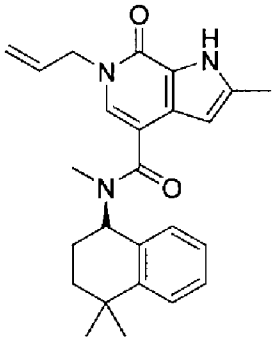
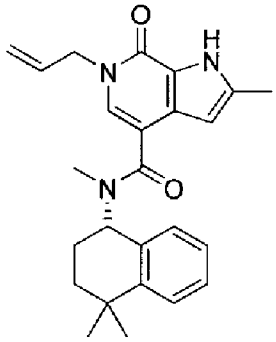
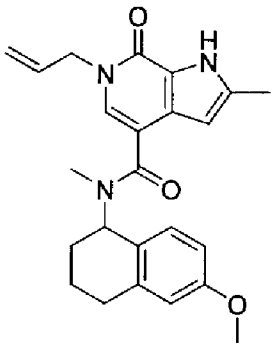
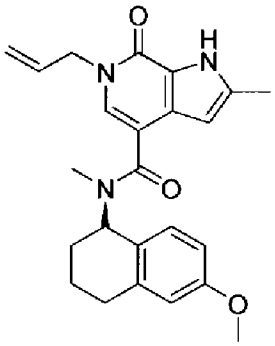
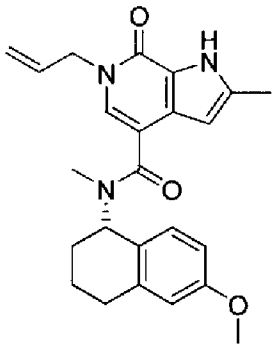
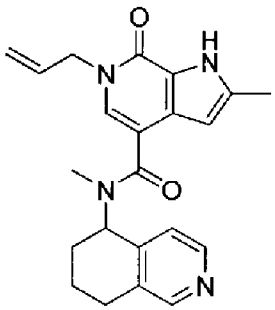
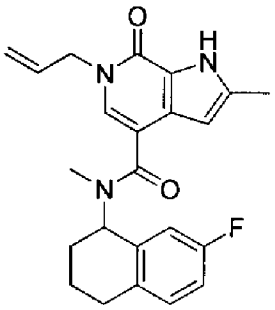
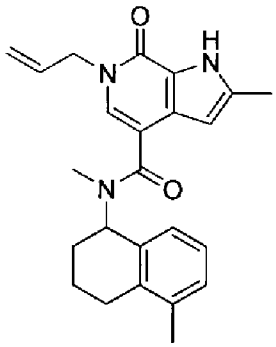
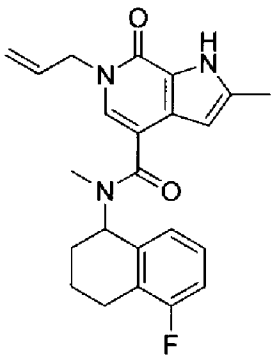
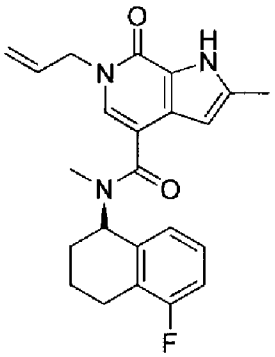
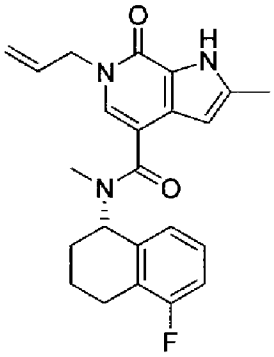

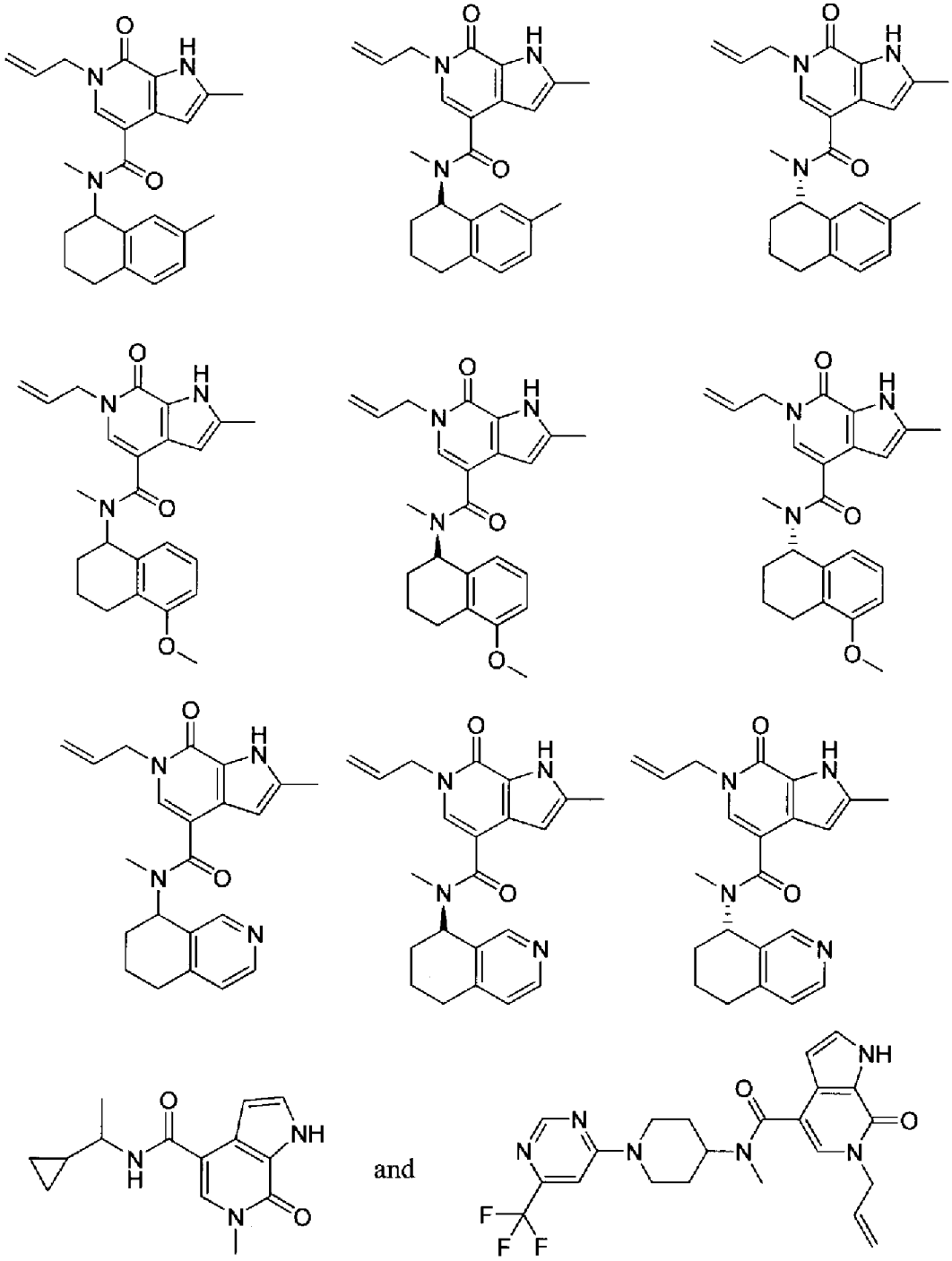

and salts thereof.

26. A composition comprising a compound of formula (I) as described in any one of claims 1-25 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

27. The composition according to claim 26, in combination with an additional therapeutic agent.

28. The composition according to claim 27, wherein the additional therapeutic agent is a chemotherapeutic agent.

29. A method for treating a bromodomain-mediated disorder in an animal comprising administering a compound of formula (I), or a pharmaceutically acceptable salt thereof as described in any one of claims 1-25, to the animal.

30. The method of claim 29 wherein the disorder is cancer, an inflammatory disorder, or an autoimmune disease.

31. The method of claim 30 wherein the cancer is selected from acoustic neuroma, acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemia, acute T-cell leukemia, basal cell carcinoma, bile duct carcinoma, bladder cancer, brain cancer, breast cancer, bronchogenic carcinoma, cervical cancer, chondrosarcoma, chordoma, choriocarcinoma, chronic leukemia, chronic lymphocytic leukemia, chronic myelocytic leukemia, chronic myelogenous leukemia, colon cancer, colorectal cancer, craniopharyngioma, cystadenocarcinoma, diffuse large B-cell lymphoma, dysproliferative changes, embryonal carcinoma, endometrial cancer, endotheliosarcoma, ependymoma, epithelial carcinoma, erythroleukemia, esophageal cancer, estrogen-receptor positive breast cancer, essential thrombocythemia, Ewing's tumor, fibrosarcoma, follicular lymphoma, germ cell testicular cancer, glioma, glioblastoma, gliosarcoma, heavy chain disease, head and neck cancer, hemangioblastoma, hepatoma, hepatocellular cancer, hormone insensitive prostate cancer, leiomyosarcoma, leukemia, liposarcoma, lung cancer, lymphagioendotheliosarcoma, lymphangiosarcoma, lymphoblastic leukemia, lymphoma, lymphoid malignancies of T-cell or B-cell origin, medullary carcinoma, medulloblastoma, melanoma, meningioma, mesothelioma, multiple myeloma, myelogenous leukemia, myeloma, myxosarcoma, neuroblastoma, NUT midline carcinoma (NMC), non-small cell lung cancer, oligodendroglioma, oral cancer, osteogenic sarcoma, ovarian cancer, pancreatic cancer, papillary adenocarcinomas, papillary carcinoma, pinealoma, polycythemia vera, prostate cancer, rectal cancer, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, sebaceous gland carcinoma, seminoma, skin cancer, small cell lung carcinoma, solid tumors (carcinomas and sarcomas), small cell lung cancer, stomach cancer, squamous cell carcinoma, synovioma, sweat gland carcinoma, thyroid cancer, Waldenstrom's macroglobulinemia, testicular tumors, uterine cancer, and Wilms' tumor.

32. The method of claim 30 wherein the cancer is selected from lung cancer, breast cancer, pancreatic cancer, colorectal cancer, and melanoma.

33. The method of claim 30 wherein the inflammatory disorder or the autoimmune disease is selected from Addison's disease, acute gout, ankylosing spondylitis, asthma, atherosclerosis, Behcet's disease, bullous skin diseases, chronic obstructive pulmonary disease, Crohn's disease, dermatitis, eczema, giant cell arteritis, fibrosis, glomerulonephritis, hepatic vascular occlusion, hepatitis, hypophysitis, immunodeficiency syndrome, inflammatory bowel disease, Kawasaki disease, lupus nephritis, multiple sclerosis, myocarditis, myositis, nephritis, organ transplant rejection, osteoarthritis, pancreatitis, pericarditis, Polyarteritis nodosa, pneumonitis, primary biliary cirrhosis, psoriasis, psoriatic arthritis, rheumatoid arthritis, scleritis, sclerosing cholangitis, sepsis, systemic lupus erythematosus, Takayasu's Arteritis, toxic shock, thyroiditis, type I diabetes, ulcerative colitis, uveitis, vitiligo, vasculitis, and Wegener's granulomatosis.

34. The method of claim 29 wherein the bromodomain is selected from ASH1L, ATAD2, ATAD2B, BAZ1A, BAZ1B, BAZ2A, BAZ2B, BPTF, BRD1, BRD2, BRD3, BRD4, BRD7, BRD8, BRD9, BRDT, BRPF1, BRPF3, BRWD1, BRWD3, CECR2, CREBBP (aka, CBP), EP300, GCN5L2, KIAA2026, MLL, MLL4, PBRM, PCAF, PHIP, SMARCA2, SMARCA4, SP100, SP110, SP140, SP140L, TAF1, TAF1L, TRIM24, TRIM28, TRIM33, TRIM66, ZMYND8, and ZMYND11.

35. A compound of formula (I) or a pharmaceutically acceptable salt thereof as described in any one of claims 1-25 for use in medical therapy.

36. A compound of formula (I) or a pharmaceutically acceptable salt thereof as described in any one of claims 1-25 for the prophylactic or therapeutic treatment of a bromodomain-mediated disorder.

37. The use of a compound of formula (I) or a pharmaceutically acceptable salt thereof as described in any one of claims 1-25 to prepare a medicament for treating a bromodomain-mediated disorder in an animal.

38. A method of increasing efficacy of a cancer treatment comprising a cytotoxic agent in an animal comprising administering to the animal an effective amount of a compound of formula (I), a pharmaceutically acceptable salt thereof, or a composition thereof as described in any one of claims 1-26.

39. The method of claim 38 further comprising administering the cytotoxic agent to the animal.

40. A method of delaying or preventing development of cancer resistance to a cytotoxic agent in an animal, comprising administering to the animal a compound of formula (I), a pharmaceutically acceptable salt thereof, or a composition thereof as described in any one of claims 1-26.

41. A method of extending the duration of response to a cancer therapy in an animal, comprising administering to an animal undergoing the cancer therapy a compound of formula (I), a pharmaceutically acceptable salt thereof, or a composition thereof as described in any one of claims 1-26, wherein the duration of response to the cancer therapy when the compound of formula (I) or the pharmaceutically acceptable salt thereof is administered is extended over the duration of response to the cancer therapy in the absence of the administration of the compound of formula (I) or the pharmaceutically acceptable salt thereof.

42. A method of treating cancer in an individual comprising administering to the individual (a) a compound of formula (I), a pharmaceutically acceptable salt thereof, or a composition thereof as described in any one of claims 1-26, and (b) a cytotoxic agent.

43. The method of claim 42 wherein the cytotoxic agent is selected from anti-microtubule agents, platinum coordination complexes, alkylating agents, antibiotic agents, topoisomerase II inhibitors, antimetabolites, topoisomerase I inhibitors, hormones and hormonal analogues, signal transduction pathway inhibitors, non-receptor tyrosine kinase angiogenesis inhibitors, immunotherapeutic agents, proapoptotic agents, inhibitors of LDH-A, inhibitors of fatty acid biosynthesis, cell cycle signaling inhibitors, HDAC inhibitors, proteasome inhibitors, and inhibitors of cancer metabolism.

44. The method of claim 42 wherein the cytotoxic agent is a taxane.

45. The method of claim 44, wherein the taxane is paclitaxel or docetaxel.

46. The method of claim 42 wherein the cytotoxic agent is a platinum agent.

47. The method of claim 42 wherein the cytotoxic agent is an antagonist of EGFR.

48. The method of claim 47, wherein the antagonist of EGFR is N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine or a pharmaceutically acceptable salt thereof.

49. The method of claim 42, wherein the cytotoxic agent is a RAF inhibitor.

50. The method of claim 49, wherein the RAF inhibitor is a BRAF or CRAF inhibitor.

51. The method of claim 49, wherein the RAF inhibitor is vemurafenib.

52. The method of claim 42 wherein the cytotoxic agent is a PI3K inhibitor.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2015/059997

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D471/04 C07D519/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2014/162971 A1 (WANG LE [US] ET AL) 12 June 2014 (2014-06-12) paragraphs [1416], [1425]; claim 1 -----	1-24, 26-52
A	US 2014/256710 A1 (LIU DACHUN [US] ET AL) 11 September 2014 (2014-09-11) the whole document -----	1-52
A	DANIEL GALLENKAMP ET AL: "Bromodomains and Their Pharmacological Inhibitors", CHEMMEDCHEM, vol. 9, no. 3, 4 March 2014 (2014-03-04), pages 438-464, XP055124420, ISSN: 1860-7179, DOI: 10.1002/cmdc.201300434 the whole document ----- -/--	1-52

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 January 2016	08/02/2016

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Grassi, Damian

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Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JEAN-MARC GARNIER ET AL: "BET bromodomain inhibitors: a patent review", EXPERT OPINION ON THERAPEUTIC PATENTS, vol. 24, no. 2, February 2014 (2014-02), pages 185-199, XP055121821, ISSN: 1354-3776, DOI: 10.1517/13543776.2014.859244 the whole document -----	1-52

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2015/059997

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